QUANTITY LIMIT CRITERIA

DRUG CLASS **5-HT$_1$ AGONISTS, COMBINATIONS (ALL DOSAGE FORMS)**

BRAND NAME
(generic)

(almotriptan)

AMERGE
(naratriptan)

FROVA
(frovatriptan)

IMITREX
(sumatriptan)

MAXALT/MAXALT-MLT
(rizatriptan)

ONZETRA XSAIL
(sumatriptan)

RELPAX
(eletriptan)

RIZAFILM
(rizatriptan)

TOSYMRA
(sumatriptan)

TREXIMET
(sumatriptan/naproxen)

ZEMBRACE SYMTOUCH
(sumatriptan)

ZOMIG / ZOMIG-ZMT
(zolmitriptan)

Status: CVS Caremark® Criteria
Type: Quantity Limit

POLICY

FDA-APPROVED INDICATIONS

Almotriptan

Adults: Almotriptan tablets are indicated for the acute treatment of migraine attacks in patients with a history of migraine with or without aura.

Adolescents Age 12 to 17 Years: Almotriptan tablets are indicated for the acute treatment of migraine headache pain in patients with a history of migraine attacks with or without aura usually lasting 4 hours or more (when untreated).

Limitations of Use:

Almotriptan tablets should only be used where a clear diagnosis of migraine has been established. If a patient has no response for the first migraine attack treated with almotriptan tablets, the diagnosis of migraine should be reconsidered before almotriptan tablets are administered to treat any subsequent attacks. In adolescents age 12 to 17 years, efficacy of almotriptan tablets on migraine-associated symptoms (nausea, photophobia, and phonophobia) was not established. Almotriptan tablets are not intended for the prophylactic therapy of migraine or for use in the management of hemiplegic or basilar migraine. Safety and effectiveness of almotriptan tablets have not been established for cluster headache which is present in an older, predominantly male population.

Amerge

Amerge is indicated for the acute treatment of migraine with or without aura in adults.

Limitations of Use:

Use only if a clear diagnosis of migraine has been established. If a patient has no response to the first migraine attack treated with Amerge, reconsider the diagnosis of migraine before Amerge is administered to treat any subsequent attacks. Amerge is not indicated for the prevention of migraine attacks. Safety and effectiveness of Amerge have not been established for cluster headache.

Frova

Frova is indicated for the acute treatment of migraine with or without aura in adults.

Limitations of Use:

Use only if a clear diagnosis of migraine has been established. If a patient has no response for the first migraine attack treated with Frova, reconsider the diagnosis of migraine before Frova is administered to treat any subsequent attacks. Frova is not indicated for the prevention of migraine attacks. Safety and effectiveness of Frova have not been established for cluster headache.

Imitrex Injection

Imitrex injection is indicated in adults for (1) the acute treatment of migraine, with or without aura, and (2) the acute treatment of cluster headache.

Limitations of Use:

Use only if a clear diagnosis of migraine or cluster headache has been established. If a patient has no response to the first migraine or cluster headache attack treated with Imitrex injection, reconsider the diagnosis before Imitrex injection is administered to treat any subsequent attacks. Imitrex injection is not indicated for the prevention of migraine or cluster headache attacks.

Imitrex Nasal Spray and Imitrex Tablets

Imitrex nasal spray and Imitrex tablets are indicated for the acute treatment of migraine with or without aura in adults.

Limitations of Use:

Use only if a clear diagnosis of migraine headache has been established. If a patient has no response to the first migraine attack treated with Imitrex, reconsider the diagnosis of migraine before Imitrex is administered to treat any subsequent attacks. Imitrex is not indicated for the prevention of migraine attacks. Safety and effectiveness of Imitrex nasal spray and Imitrex tablets have not been established for cluster headache.

Maxalt and Maxalt-MLT

Maxalt and Maxalt-MLT are indicated for the acute treatment of migraine with or without aura in adults and in pediatric patients 6 to 17 years old.

Limitations of Use:

Maxalt should only be used where a clear diagnosis of migraine has been established. If a patient has no response for the first migraine attack treated with Maxalt, the diagnosis of migraine should be reconsidered before Maxalt is administered to treat any subsequent attacks. Maxalt is not indicated for use in the management of hemiplegic or basilar migraine.

Maxalt is not indicated for the prevention of migraine attacks. Safety and effectiveness of Maxalt have not been established for cluster headache.

Onzetra Xsail
Onzetra Xsail is indicated for the acute treatment of migraine with or without aura in adults.
Limitations of Use:
Use only if a clear diagnosis of migraine has been established. If a patient has no response to the first migraine attack treated with Onzetra Xsail, reconsider the diagnosis of migraine before treatment of subsequent attacks with Onzetra Xsail. Onzetra Xsail is not indicated for the prevention of migraine attacks. Safety and effectiveness of Onzetra Xsail have not been established for the treatment of cluster headache.

Relpax
Relpax is indicated for the acute treatment of migraine attacks with or without aura in adults.
Limitations of Use:
Use only if a clear diagnosis of migraine has been established. If a patient has no response to the first migraine attack treated with Relpax, reconsider the diagnosis of migraine before Relpax is administered to treat any subsequent attacks. Relpax is not indicated for the prevention of migraine attacks. Safety and effectiveness of Relpax have not been established for the treatment of cluster headache.

RizaFilm
RizaFilm is indicated for the acute treatment of migraine with or without aura in adults and in pediatric patients 12 to 17 years of age weighing 40 kg or more.
Limitations of Use:
RizaFilm should only be used where a clear diagnosis of migraine has been established. If a patient has no response for the first migraine attack treated with RizaFilm, the diagnosis of migraine should be reconsidered before RizaFilm is administered to treat any subsequent attacks. RizaFilm is not indicated for the preventive treatment of migraine. Safety and effectiveness of RizaFilm have not been established for cluster headache.

Tosymra
Tosymra is indicated for the acute treatment of migraine with or without aura in adults.
Limitations of Use:
Use only if a clear diagnosis of migraine has been established. If a patient has no response to the first migraine attack treated with Tosymra, reconsider the diagnosis before Tosymra is administered to treat any subsequent attacks. Tosymra is not indicated for the preventive treatment of migraine. Tosymra is not indicated for the treatment of cluster headache.

Treximet
Treximet is indicated for the acute treatment of migraine with or without aura in adults and pediatric patients 12 years of age and older.
Limitations of Use:
Use only if a clear diagnosis of migraine headache has been established. If a patient has no response to the first migraine attack treated with Treximet, reconsider the diagnosis of migraine before Treximet is administered to treat any subsequent attacks. Treximet is not indicated for the prevention of migraine attacks. Safety and effectiveness of Treximet have not been established for cluster headache.

Zembrace SymTouch
Zembrace SymTouch is indicated for the acute treatment of migraine with or without aura in adults.
Limitations of Use:
Use only if a clear diagnosis of migraine has been established. If a patient has no response to the first migraine attack treated with Zembrace SymTouch, reconsider the diagnosis before Zembrace SymTouch is administered to treat any subsequent attacks. Zembrace SymTouch injection is not indicated for the prevention of migraine attacks.

Zomig Nasal Spray
Zomig nasal spray is indicated for the acute treatment of migraine with or without aura in adults and pediatric patients 12 years of age and older.
Limitations of Use:

Only use Zomig if a clear diagnosis of migraine has been established. If a patient has no response to Zomig treatment for the first migraine attack, reconsider the diagnosis of migraine before Zomig is administered to treat any subsequent attacks. Zomig is not indicated for the prevention of migraine attacks. Safety and effectiveness of Zomig have not been established for cluster headache. Not recommended in patients with moderate or severe hepatic impairment.

Zomig Tablets and Zomig-ZMT
Zomig is indicated for the acute treatment of migraine with or without aura in adults.
Limitations of Use:
Only use Zomig if a clear diagnosis of migraine has been established. If a patient has no response to Zomig treatment for the first migraine attack, reconsider the diagnosis of migraine before Zomig is administered to treat any subsequent attacks. Zomig is not indicated for the prevention of migraine attacks. Safety and effectiveness of Zomig have not been established for cluster headache.

INITIAL LIMIT QUANTITY
The intent is for the patient to receive only one drug from this drug class at a time.
PLEASE NOTE: Since manufacturer package sizes may vary, it is the discretion of the dispensing pharmacy to fill quantities per package size up to these quantity limits. In such cases the filling limit and day supply may be less than what is indicated.

Medication	Strength	Dose per headache	Maximum dose per 24 hours	Package Size	1 Month Limit * 3 Months Limit *
almotriptan	6.25 mg	1-2 tablets	2 tablets**	6 tablets	12 tablets / 25 days 36 tablets / 75 days
	12.5 mg	1-2 tablets	2 tablets 25 mg	6 tablets 12 tablets	
Amerge (naratriptan)	1 mg	1-2 tablets	2 tablets**	9 tablets	12 tablets / 25 days 36 tablets / 75 days
	2.5 mg	1-2 tablets	2 tablets 5 mg		
Frova (frovatriptan)	2.5 mg	1-2 tablets	3 tablets 7.5 mg	9 tablets	18 tablets / 25 days 54 tablets / 75 days
Imitrex Injection (sumatriptan) vials	6 mg	1-2 injections	2 injections 12 mg	5 single dose vials 0.5mL each	12 vials (6mL) / 25 days 40 vials (20mL) / 75 days
Imitrex Injection (sumatriptan) syringes STATdose / Refill	4 mg	1-2 injections	3 injections 12 mg	2 prefilled syringes 0.5mL each	18 syringes (9mL) / 25 days 54 syringes (27mL) / 75 days
	6 mg	1-2 injections	2 injections 12 mg		12 syringes (6mL) / 25 days 36 syringes (18mL) / 75 days
Imitrex Nasal Spray (sumatriptan)	5 mg	1-4 sprays	4 sprays**	6 nasal spray units	24 units / 25 days 72 units / 75 days
	20 mg	1-2 sprays	2 sprays 40 mg		12 units / 25 days 36 units / 75 days
Imitrex Tablets (sumatriptan)	25mg, 50mg	1-2 tablets	2 tablets**	9 tablets (brand and generic) 27, 36, 90, 100 tablets (generic)	12 tablets / 25 days 36 tablets / 75 days
	100 mg	1-2 tablets	2 tablets 200 mg		
Maxalt Maxalt-MLT (rizatriptan)	5 mg	1-2 tablets	3 tablets**	12, 18 tablets (generic), 3, 9, 12, 18 orally disintegrating tablets (generic)	18 tablets / 25 days 54 tablets / 75 days
	10 mg	1-2 tablets	3 tablets 30 mg	18 tablets (brand and generic) 12 tablets (generic), 3 orally disintegrating tablets (brand and generic), 9, 12, 18 orally disintegrating tablets (generic)	
Onzetra Xsail (sumatriptan)	11mg	2 nosepieces	4 nosepieces 44mg	16 nosepieces – 2 nosepieces per pouch 8 pouches per kit	16 nosepieces / 25 days (1 kit, 8 pouches) 64 nosepieces / 75 days (4 kits, 32 pouches)
Relpax	20 mg	1-2 tablets	2 tablets**	6 tablets	12 tablets / 25 days

(eletriptan)	40 mg	1-2 tablets	2 tablets 80 mg	6 tablets 12 tablets	36 tablets / 75 days
RizaFilm (rizatriptan)	10mg	1-3 oral films	3 oral films 30mg	6, 12, or 18 individually packaged films	18 films / 25 days 54 films / 75 days
Tosymra (sumatriptan nasal)	10 mg	1-3 sprays	3 sprays 30 mg	6 nasal spray units	18 units / 25 days 54 units / 75 days
Treximet (sumatriptan/naproxen)	85mg/500mg	1-2 tablets	1-2 tablets 170mg/1000mg	9 tablets dispense in original container	9 tablets / 25 days 36 tablets / 75 days
Zembrace SymTouch (sumatriptan)	3 mg	1-4 injections	4 injections 12mg	4 autoinjectors 0.5mL each	24 injectors (12mL) / 25 days 72 injectors (36mL) / 75 days
Zomig Nasal Spray (zolmitriptan)	2.5 mg	1-2 sprays	2 sprays**	6 nasal spray units	12 units / 25 days 36 units / 75 days
	5 mg	1-2 sprays	2 sprays 10 mg		
Zomig Tablets Zomig-ZMT (zolmitriptan)	2.5 mg	1/2-2 tablets	2 tablets**	6 tablets	12 tablets / 25 days 36 tablets / 75 days
	5 mg	1-2 tablets	2 tablets 10 mg	3 tablets	
** The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.* ***Utilize higher strength available.*					

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2. Amerge [package insert]. Research Triangle Park, NC: GlaxoSmithKline; October 2020.
3. Frova [package insert]. Malvern, PA: Endo Pharmaceuticals Inc.; August 2018.
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7. Maxalt and Maxalt-MLT [package insert]. Jersey City, NJ: Organon LLC; June 2021.
8. Onzetra Xsail [package insert]. Morristown, NJ: Currax Pharmaceuticals LLC; December 2019.
9. Relpax [package insert]. New York, NY: Pfizer, Inc.; March 2020.
10. RizaFilm [package insert]. Saint-Laurent, Quebec: IntelGenx Corp.; April 2023.
11. Tosymra [package insert]. Maple Grove, MN: Upsher-Smith Laboratories, LLC; February 2021.
12. Treximet [package insert]. Morristown, NJ: Currax Therapeutics, LLC; October 2021.
13. Zembrace SymTouch [package insert]. Maple Grove, MN: Upsher-Smith Laboratories LLC; February 2021.
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PRIOR AUTHORIZATION CRITERIA

DRUG CLASS **5-HT$_1$ AGONISTS, COMBINATIONS (ALL DOSAGE FORMS)**

BRAND NAME
(generic)

(almotriptan)

AMERGE
(naratriptan)

FROVA
(frovatriptan)

IMITREX
(sumatriptan)

MAXALT/MAXALT-MLT
(rizatriptan)

ONZETRA XSAIL
(sumatriptan)

RELPAX
(eletriptan)

RIZAFILM
(rizatriptan)

TOSYMRA
(sumatriptan)

TREXIMET
(sumatriptan/naproxen)

ZEMBRACE SYMTOUCH
(sumatriptan)

ZOMIG / ZOMIG-ZMT
(zolmitriptan)

Status: CVS Caremark® Criteria
Type: Post Limit Prior Authorization

POLICY

FDA-APPROVED INDICATIONS
Almotriptan

Adults: Almotriptan tablets are indicated for the acute treatment of migraine attacks in patients with a history of migraine with or without aura.
Adolescents Age 12 to 17 Years: Almotriptan tablets are indicated for the acute treatment of migraine headache pain in patients with a history of migraine attacks with or without aura usually lasting 4 hours or more (when untreated).
Limitations of Use:
Almotriptan tablets should only be used where a clear diagnosis of migraine has been established. If a patient has no response for the first migraine attack treated with almotriptan tablets, the diagnosis of migraine should be reconsidered before almotriptan tablets are administered to treat any subsequent attacks. In adolescents age 12 to 17 years, efficacy of almotriptan tablets on migraine-associated symptoms (nausea, photophobia, and phonophobia) was not established. Almotriptan tablets are not intended for the prophylactic therapy of migraine or for use in the management of hemiplegic or basilar migraine. Safety and effectiveness of almotriptan tablets have not been established for cluster headache which is present in an older, predominantly male population.

Amerge
Amerge is indicated for the acute treatment of migraine with or without aura in adults.
Limitations of Use:
Use only if a clear diagnosis of migraine has been established. If a patient has no response to the first migraine attack treated with Amerge, reconsider the diagnosis of migraine before Amerge is administered to treat any subsequent attacks. Amerge is not indicated for the prevention of migraine attacks. Safety and effectiveness of Amerge have not been established for cluster headache.

Frova
Frova is indicated for the acute treatment of migraine with or without aura in adults.
Limitations of Use:
Use only if a clear diagnosis of migraine has been established. If a patient has no response for the first migraine attack treated with Frova, reconsider the diagnosis of migraine before Frova is administered to treat any subsequent attacks. Frova is not indicated for the prevention of migraine attacks. Safety and effectiveness of Frova have not been established for cluster headache.

Imitrex Injection
Imitrex injection is indicated in adults for (1) the acute treatment of migraine, with or without aura, and (2) the acute treatment of cluster headache.
Limitations of Use:
Use only if a clear diagnosis of migraine or cluster headache has been established. If a patient has no response to the first migraine or cluster headache attack treated with Imitrex injection, reconsider the diagnosis before Imitrex injection is administered to treat any subsequent attacks. Imitrex injection is not indicated for the prevention of migraine or cluster headache attacks.

Imitrex Nasal Spray and Imitrex Tablets
Imitrex Nasal Spray and Imitrex Tablets are indicated for the acute treatment of migraine with or without aura in adults.
Limitations of Use:
Use only if a clear diagnosis of migraine headache has been established. If a patient has no response to the first migraine attack treated with Imitrex, reconsider the diagnosis of migraine before Imitrex is administered to treat any subsequent attacks. Imitrex is not indicated for the prevention of migraine attacks. Safety and effectiveness of Imitrex nasal spray and Imitrex tablets have not been established for cluster headache.

Maxalt and Maxalt-MLT
Maxalt and Maxalt-MLT are indicated for the acute treatment of migraine with or without aura in adults and in pediatric patients 6 to 17 years old.
Limitations of Use:
Maxalt should only be used where a clear diagnosis of migraine has been established. If a patient has no response for the first migraine attack treated with Maxalt, the diagnosis of migraine should be reconsidered before Maxalt is administered to treat any subsequent attacks. Maxalt is not indicated for use in the management of hemiplegic or basilar migraine. Maxalt is not indicated for the prevention of migraine attacks. Safety and effectiveness of Maxalt have not been established for cluster headache.

Onzetra Xsail
Onzetra Xsail is indicated for the acute treatment of migraine with or without aura in adults.

Limitations of Use:
Use only if a clear diagnosis of migraine has been established. If a patient has no response to the first migraine attack treated with Onzetra Xsail, reconsider the diagnosis of migraine before treatment of subsequent attacks with Onzetra Xsail. Onzetra Xsail is not indicated for the prevention of migraine attacks. Safety and effectiveness of Onzetra Xsail have not been established for the treatment of cluster headache.

Relpax
Relpax is indicated for the acute treatment of migraine attacks with or without aura in adults.
Limitations of Use:
Use only if a clear diagnosis of migraine has been established. If a patient has no response to the first migraine attack treated with Relpax, reconsider the diagnosis of migraine before Relpax is administered to treat any subsequent attacks. Relpax is not indicated for the prevention of migraine attacks. Safety and effectiveness of Relpax have not been established for the treatment of cluster headache.

RizaFilm
RizaFilm is indicated for the acute treatment of migraine with or without aura in adults and in pediatric patients 12 to 17 years of age weighing 40 kg or more.
Limitations of Use:
RizaFilm should only be used where a clear diagnosis of migraine has been established. If a patient has no response for the first migraine attack treated with RizaFilm, the diagnosis of migraine should be reconsidered before RizaFilm is administered to treat any subsequent attacks. RizaFilm is not indicated for the preventive treatment of migraine. Safety and effectiveness of RizaFilm have not been established for cluster headache.

Tosymra
Tosymra is indicated for the acute treatment of migraine with or without aura in adults.
Limitations of Use:
Use only if a clear diagnosis of migraine has been established. If a patient has no response to the first migraine attack treated with Tosymra, reconsider the diagnosis before Tosymra is administered to treat any subsequent attacks. Tosymra is not indicated for the preventive treatment of migraine. Tosymra is not indicated for the treatment of cluster headache.

Treximet
Treximet is indicated for the acute treatment of migraine with or without aura in adults and pediatric patients 12 years of age and older.
Limitations of Use:
Use only if a clear diagnosis of migraine headache has been established. If a patient has no response to the first migraine attack treated with Treximet, reconsider the diagnosis of migraine before Treximet is administered to treat any subsequent attacks. Treximet is not indicated for the prevention of migraine attacks. Safety and effectiveness of Treximet have not been established for cluster headache.

Zembrace SymTouch
Zembrace SymTouch is indicated for the acute treatment of migraine with or without aura in adults.
Limitations of Use:
Use only if a clear diagnosis of migraine has been established. If a patient has no response to the first migraine attack treated with Zembrace SymTouch, reconsider the diagnosis before Zembrace SymTouch is administered to treat any subsequent attacks. Zembrace SymTouch injection is not indicated for the prevention of migraine attacks.

Zomig Nasal Spray
Zomig nasal spray is indicated for the acute treatment of migraine with or without aura in adults and pediatric patients 12 years of age and older.
Limitations of Use:
Only use Zomig if a clear diagnosis of migraine has been established. If a patient has no response to Zomig treatment for the first migraine attack, reconsider the diagnosis of migraine before Zomig is administered to treat any subsequent attacks. Zomig is not indicated for the prevention of migraine attacks. Safety and effectiveness of Zomig have not been established for cluster headache. Not recommended in patients with moderate or severe hepatic impairment.

Zomig Tablets and Zomig-ZMT
Zomig is indicated for the acute treatment of migraine with or without aura in adults.
Limitations of Use:

Only use Zomig if a clear diagnosis of migraine has been established. If a patient has no response to Zomig treatment for the first migraine attack, reconsider the diagnosis of migraine before Zomig is administered to treat any subsequent attacks. Zomig is not indicated for the prevention of migraine attacks. Safety and effectiveness of Zomig have not been established for cluster headache.

Compendial Uses[17]
Imitrex Nasal Spray
Acute treatment of cluster headache
Onzetra Xsail
Acute treatment of cluster headache
Tosymra
Acute treatment of cluster headache
Zomig Nasal Spray
Acute treatment of cluster headache

COVERAGE CRITERIA
The requested drug will be covered with prior authorization when the following criteria are met:

- The patient does not have confirmed or suspected cardiovascular or cerebrovascular disease, or uncontrolled hypertension

AND

- The patient has a diagnosis of migraine headache

AND

- Medication overuse headache has been considered and ruled out

AND

- The patient is currently using migraine prophylactic therapy
  [Note: Examples of prophylactic therapy are divalproex sodium, topiramate, valproate sodium, metoprolol, propranolol, timolol, atenolol, nadolol, amitriptyline, venlafaxine.]

OR

- The patient is unable to take migraine prophylactic therapies due to inadequate treatment response, intolerance or contraindication
  [Note: Examples of prophylactic therapy are divalproex sodium, topiramate, valproate sodium, metoprolol, propranolol, timolol, atenolol, nadolol, amitriptyline, venlafaxine.]

OR

- The request is for sumatriptan injection, sumatriptan nasal spray, or zolmitriptan nasal spray (e.g., Imitrex Injection, Imitrex Nasal Spray, Onzetra Xsail, Tosymra, Zomig Nasal Spray) for the treatment of cluster headache

AND

- The requested drug is not being used concurrently with another triptan 5-HT1 agonist

OR

- The requested drug is being used concurrently with another triptan 5-HT1 agonist AND the patient requires more than one triptan 5-HT1 agonist due to clinical need for differing routes of administration

Quantity Limits apply.

POST LIMIT QUANTITY

PLEASE NOTE: Since manufacturer package sizes may vary, it is the discretion of the dispensing pharmacy to fill quantities per package size up to these quantity limits. In such cases the filling limit and day supply may be less than what is indicated.

Medication	Strength	Maximum dose per 24 hours	1 Month Limit *	3 Months Limit *
almotriptan	6.25 mg	2 tablets**	18 tablets / 25 days	54 tablets / 75 days
	12.5 mg	2 tablets 25 mg		
Amerge (naratriptan)	1 mg	2 tablets**	18 tablets / 25 days	54 tablets / 75 days
	2.5 mg	2 tablets 5 mg		
Frova	2.5 mg	3 tablets	27 tablets / 25 days	81 tablets / 75 days

(frovatriptan)		7.5 mg		
Imitrex Injection (sumatriptan) single dose vials	6 mg	2 injections 12 mg	18 vials (9mL) / 25 days	55 vials (27.5mL) / 75 days
Imitrex Injection (sumatriptan) syringes STATdose / Refill	4 mg	3 injections 12 mg	27 syringes (13.5mL) / 25 days	81 syringes (40.5mL) / 75 days
	6 mg	2 injections 12 mg	18 syringes (9mL) / 25 days	54 syringes (27mL) / 75 days
Imitrex Nasal Spray (sumatriptan)	5 mg	4 sprays**	36 units / 25 days	108 units / 75 days
	20 mg	2 sprays 40 mg	18 units / 25 days	54 units / 75 days
Imitrex Tablets (sumatriptan)	25mg, 50mg	2 tablets**	18 tablets / 25 days	54 tablets / 75 days
	100 mg	2 tablets 200 mg		
Maxalt Maxalt-MLT (rizatriptan)	5 mg	3 tablets**	27 tablets / 25 days	81 tablets / 75 days
	10 mg	3 tablets 30 mg		
Onzetra Xsail (sumatriptan)	11mg	4 nosepieces 44mg	32 nosepieces / 25 days (2 kits, 16 pouches)	96 nosepieces / 75 days (6 kits, 48 pouches)
Relpax (eletriptan)	20 mg	2 tablets**	18 tablets / 25 days	54 tablets / 75 days
	40 mg	2 tablets 80 mg		
RizaFilm (rizatriptan)	10mg	3 oral films 30mg	27 films / 25 days	81 films / 75 days
Tosymra (sumatriptan)	10 mg	3 sprays 30 mg	24 units / 25 days	72 units / 75 days
Treximet (sumatriptan/naproxen)	85mg/500mg	1-2 tablets 170mg/1000mg	18 tablets / 25 days	54 tablets / 75 days
Zembrace SymTouch (sumatriptan)	3 mg	4 injections 12mg	36 autoinjectors (18mL) / 25 days	108 autoinjectors (54mL) / 75 days
Zomig Nasal Spray (zolmitriptan)	2.5 mg	2 sprays**	18 units / 25 days	54 units / 75 days
	5 mg	2 sprays 10 mg		
Zomig Tablets Zomig-ZMT (zolmitriptan)	2.5 mg	2 tablets**	18 tablets / 25 days	54 tablets / 75 days
	5 mg	2 tablets 10 mg		
** The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.* ***Utilize higher strength available.*				

Duration of Approval (DOA):

- MMT 903-J: DOA: 12 months
- 1-J: DOA: 36 months

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Reference number(s)
1934-A

SPECIALTY GUIDELINE MANAGEMENT

ZYTIGA (abiraterone)
abiraterone

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. Indicated in combination with prednisone for the treatment of patients with metastatic castration-resistant prostate cancer (CRPC).
   2. Indicated in combination with prednisone for the treatment of patients with metastatic high-risk castration-sensitive prostate cancer (CSPC).

B. Compendial Uses
   1. Node-positive (N_1), non-metastatic (M_0) prostate cancer
   2. Very-high-risk prostate cancer

All other indications are considered experimental/investigational and not medically necessary.

II. EXCLUSIONS

Coverage will not be provided if the requested medication is used in combination with a second-generation oral anti-androgen (e.g., apalutamide [Erleada]) or an oral androgen metabolism inhibitor (e.g., fine-particle abiraterone acetate [Yonsa]).

III. CRITERIA FOR INITIAL APPROVAL

Node positive, metastatic and very-high-risk prostate cancer
Authorization of 12 months may be granted for the treatment of node positive, metastatic or very-high-risk prostate cancer when the member has had a bilateral orchiectomy or will be using the requested medication in combination with a GnRH analog.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

V. REFERENCES

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PRIOR AUTHORIZATION CRITERIA

BRAND NAME*
(generic)
(acamprosate calcium)

Status: CVS Caremark Criteria ***Ref # 502-A***
Type: Initial Prior Authorization ***Ref # 905-A***

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Acamprosate calcium is indicated for the maintenance of abstinence from alcohol in patients with alcohol dependence who are abstinent at treatment initiation. Treatment with acamprosate calcium should be part of a comprehensive management program that includes psychosocial support.

The efficacy of acamprosate calcium in promoting abstinence has not been demonstrated in subjects who have not undergone detoxification and not achieved alcohol abstinence prior to beginning acamprosate calcium treatment. The efficacy of acamprosate calcium in promoting abstinence from alcohol in polysubstance abusers has not been adequately assessed.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has a diagnosis of alcohol use disorder as defined by the Diagnostic and Statistical Manual of Mental Disorders (DSM-5)

AND

- The requested drug will be used as part of a comprehensive management program that includes psychosocial support

AND

- The patient is, or the patient will be, abstinent from alcohol at treatment initiation

AND

- The patient has experienced an inadequate treatment response to oral naltrexone
  OR
- The patient has experienced an intolerance to oral naltrexone
  OR
- The patient has a contraindication that would prohibit a trial of oral naltrexone

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Acamprosate calcium is indicated for the maintenance of abstinence from alcohol in patients with alcohol dependence who are abstinent at treatment initiation. Treatment with acamprosate calcium should be part of a comprehensive management program that includes psychosocial support.[1-3] The criteria used to diagnose alcohol use disorder are defined in the Fifth Edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5).[8]

Acamprosate calcium has not been shown to provide therapeutic benefit in individuals who have not undergone detoxification and have not achieved abstinence from alcohol ingestion prior to initiation of the drug.[1-4] Therefore, the patient should be abstinent from alcohol at the time acamprosate calcium therapy is initiated.[1-3]

Naltrexone is an opioid-receptor antagonist that is also indicated for use in the treatment of alcohol dependence in conjunction with psychosocial interventions.[2-5] Acamprosate and oral naltrexone have the best evidence for improving

alcohol consumption outcomes for patients with alcohol-use disorders. Head-to-head trials have not consistently established the superiority of one medication over the other. Because of this, other factors may guide medication choices, such as frequency of administration, potential adverse events, coexisting symptoms, and availability of treatments.[6-9] The recommended dose of acamprosate is two tablets taken three times daily whereas the recommended dose of naltrexone is one tablet taken once daily.[1-3, 5] Therefore, coverage will be provided when the patient has had an inadequate treatment response, intolerance, or contraindication to oral naltrexone.

According to the Agency for Healthcare Research and Quality (AHRQ) research protocol, FDA approved medications for the treatment of alcohol use disorder are usually prescribed for 3 to 12 months. Additionally, as stated by the National Institutes of Health/National Institute on Alcohol Abuse and Alcoholism, the risk for relapse to alcohol use disorder is very high in the first 6 to 12 months after initiating abstinence and gradually diminishes over several years. Although optimal treatment duration has not been established, it is reasonable to continue treatment for a year or longer if the patient responds to medication during this time when the risk of relapse is highest.[4, 6]

REFERENCES

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Written by:	UM Development (SE)
Date Written:	12/2009
Revised:	(KD/SE) 09/2010 (CAS adapted; (CT) 08/2011, 06/2012, 10/2012 (extended duration); (RP) 05/2013, 05/2014; (LN) 04/2015 (added denial reasons); (CT) 05/2015, 05/2016; (JG) 05/2017 (removed contraindication); (DS) 11/2017 (no clinical changes), 11/2018 (specified oral naltrexone; combined comm and MDC-2), 11/2019 (updated alcohol dependence to alcohol use disorder, removed MDC designation), (SF) 11/2020 (updated document title, separated diagnosis and treatment question), 02/2021 (updated Q1); (DRS) 10/2021 (no clinical changes)
Reviewed:	Medical Affairs: (WLF) 12/2009; (KP) 10/2010, 08/2011, 06/2012, 10/2012; (LMS) 05/2013, 05/2014; (KJC) 05/2015; (ME) 05/2016; (JG) 05/2017; (AM) 11/2018; (CHART) 11/27/2019, 02/27/2020 (FYI for CPO rec), 12/03/2020, 12/02/2021 External Review: 03/2010, 12/2010, 10/2011, 10/2012; 08/2013, 08/2014, 08/2015, 08/2016, 08/2017, 02/2018, 02/2019, 02/2020, 02/2021, 02/2022

CRITERIA FOR APPROVAL

1	Does the patient have a diagnosis of alcohol use disorder as defined by the Diagnostic and Statistical Manual of Mental Disorders (DSM-5)? [If no, then no further questions.]	Yes	No

2	Will the requested drug be used as part of a comprehensive management program that includes psychosocial support? [If no, then no further questions.]	Yes	No
3	Is the patient, or will the patient be, abstinent from alcohol at treatment initiation? [If no, then no further questions.]	Yes	No
4	Has the patient experienced an inadequate treatment response to oral naltrexone? [If yes, then no further questions.]	Yes	No
5	Has the patient experienced an intolerance to oral naltrexone? [If yes, then no further questions.]	Yes	No
6	Does the patient have a contraindication that would prohibit a trial of oral naltrexone?	Yes	No

Mapping Instructions (502-A)			
	Yes	**No**	**DENIAL REASONS – DO NOT USE FOR MEDICARE PART D**
1.	Go to 2	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you meet specific criteria for having a certain condition. Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]
2.	Go to 3	Deny	You do not meet the requirements of your plan. Your plan covers this drug when your health care provider prescribes it as part of a total treatment program. Your request has been denied based on the information we have. [Short Description: Not part of a treatment program]
3.	Go to 4	Deny	You do not meet the requirements of your plan. Your plan covers this drug if you meet certain conditions at the start of treatment. Your request has been denied based on the information we have. [Short Description: Not abstinent from alcohol]
4.	Approve, 36 months	Go to 5	
5.	Approve, 36 months	Go to 6	
6.	Approve, 36 months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have tried oral naltrexone and it did not work for you, or you cannot use it. Your request has been denied based on the information we have. [Short Description: No trial of oral naltrexone]

Mapping Instructions (905-A)			
	Yes	**No**	**DENIAL REASONS – DO NOT USE FOR MEDICARE PART D**
1.	Go to 2	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you meet specific criteria for having a certain condition. Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]

2.	Go to 3	Deny	You do not meet the requirements of your plan. Your plan covers this drug when your health care provider prescribes it as part of a total treatment program Your request has been denied based on the information we have. [Short Description: Not part of a treatment program]
3.	Go to 4	Deny	You do not meet the requirements of your plan. Your plan covers this drug if you meet certain conditions at the start of treatment. Your request has been denied based on the information we have. [Short Description: Not abstinent from alcohol]
4.	Approve, 12 months	Go to 5	
5.	Approve, 12 months	Go to 6	
6.	Approve, 12 months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you tried oral naltrexone and it did not work for you, or you cannot use it. Your request has been denied based on the information we have. [Short Description: No trial of oral naltrexone]

QUANTITY LIMIT PRIOR AUTHORIZATION CRITERIA

DRUG CLASS	**CLINDAMYCIN-BENZOYL PEROXIDE AND ERYTHROMYCIN-BENZOYL PEROXIDE**
BRAND NAME (generic)	**BENZAMYCIN (erythromycin/benzoyl peroxide gel)** **ACANYA (clindamycin phosphate-benzoyl peroxide gel)** **BENZACLIN (clindamycin phosphate-benzoyl peroxide gel)** **DUAC (clindamycin phosphate-benzoyl peroxide gel)** **ONEXTON (clindamycin phosphate-benzoyl peroxide gel)**

Status: CVS Caremark Criteria
Type: Quantity Limit; Post Limit Prior Authorization

POLICY

FDA-APPROVED INDICATIONS

Benzamycin
Benzamycin Topical Gel is indicated for the topical treatment of acne vulgaris.

Acanya
Acanya Gel is indicated for the topical treatment of acne vulgaris in patients 12 years or older.

BenzaClin
BenzaClin Topical Gel is indicated for the topical treatment of acne vulgaris.

Duac, Clindamycin Phosphate-Benzoyl Peroxide Gel 1.2% / 5%
Clindamycin Phosphate and Benzoyl Peroxide Gel, 1.2% / 5% is indicated for the topical treatment of inflammatory acne vulgaris in patients 12 years and older.

Onexton
Onexton (clindamycin phosphate and benzoyl peroxide) Gel, 1.2% / 3.75% is indicated for the topical treatment of acne vulgaris in patients 12 years of age and older.

INITIAL QUANTITY LIMIT**

LIMIT CRITERIA
Limits should accumulate across same chemical entity up to highest quantity listed depending on the order the claims are processed. Accumulation does not apply if limit is coded for daily dose.

PLEASE NOTE: Since manufacturer package sizes may vary, it is the discretion of the dispensing pharmacy to fill quantities per package size up to these quantity limits. In such cases the filling limit and day supply may be less than what is indicated.

Drug	1 Month Limit*	3 Month Limit*
Benzamycin (erythromycin-benzoyl peroxide gel)	47 grams / 25 days	141 grams / 75 days
Acanya (clindamycin phosphate-benzoyl peroxide gel)	50 grams / 25 days	150 grams / 75 days
BenzaClin (clindamycin phosphate-benzoyl peroxide gel)	50 grams / 25 days	150 grams / 75 days
Duac, clindamycin phosphate-benzoyl peroxide gel, 1.2%-5%	45 grams / 25 days	135 grams / 75 days
Onexton (clindamycin phosphate-benzoyl peroxide gel)	50 grams / 25 days	150 grams / 75 days

**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*

**If the patient is requesting more than the initial quantity limit, the claim will reject with a message indicating that a prior authorization is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

COVERAGE CRITERIA
The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for the treatment of acne vulgaris

Quantity Limits apply.

POST LIMIT QUANTITY
PLEASE NOTE: Since manufacturer package sizes may vary, it is the discretion of the dispensing pharmacy to fill quantities per package size up to these quantity limits. In such cases the filling limit and day supply may be less than what is indicated.

Medication	1 Month Limit*	3 Month Limit*
Benzamycin (erythromycin-benzoyl peroxide gel)	94 grams / 25 days	282 grams / 75 days
Acanya (clindamycin phosphate-benzoyl peroxide gel)	100 grams / 25 days	300 grams / 75 days
BenzaClin (clindamycin phosphate-benzoyl peroxide gel)	100 grams / 25 days	300 grams / 75 days
Duac, clindamycin phosphate-benzoyl peroxide gel, 1.2%-5%	90 grams / 25 days	270 grams / 75 days
Onexton (clindamycin phosphate-benzoyl peroxide gel)	100 grams / 25 days	300 grams / 75 days

** The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*

REFERENCES

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4. Clindamycin Phosphate-Benzoyl Peroxide Gel, 1.2% / 5% [package insert]. Princeton, NJ: Sandoz Inc.; October 2019.
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6. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: UpToDate, Inc.; 2022; Accessed July 1, 2022.
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Reference number
1959-A

SPECIALTY GUIDELINE MANAGEMENT

ACTEMRA (tocilizumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
1. Adult patients with moderately to severely active rheumatoid arthritis (RA) who have had an inadequate response to one or more disease-modifying antirheumatic drugs (DMARDs).
2. Patients 2 years of age and older with active polyarticular juvenile idiopathic arthritis.
3. Patients 2 years of age and older with active systemic juvenile idiopathic arthritis (sJIA).
4. Adult patients with giant cell arteritis (GCA).
5. Adult patients with systemic sclerosis-associated interstitial lung disease (SSc-ILD) for slowing the rate of decline in pulmonary function.
6. Adults and pediatric patients 2 years of age and older with chimeric antigen receptor (CAR) T cell-induced severe or life-threatening cytokine release syndrome (CRS).
7. Hospitalized adult patients with coronavirus disease 2019 (COVID-19) who are receiving systemic corticosteroids and require supplemental oxygen, non-invasive or invasive mechanical ventilation, or extracorporeal membrane oxygenation (ECMO).

B. Compendial Uses
1. Unicentric Castleman disease
2. Multicentric Castleman disease
3. Oligoarticular juvenile idiopathic arthritis
4. Immunotherapy-related inflammatory arthritis
5. Acute graft versus host disease
6. Cytokine release syndrome (other than severe or life-threatening CAR T cell-induced CRS)

Note: The criteria outlined in this policy is only applicable to coverage in the outpatient setting. Hospitalized members receiving Actemra for the treatment of COVID-19 will be managed according to the member's inpatient benefit.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

A. Rheumatoid arthritis (RA)
1. Initial requests:

i. Chart notes, medical record documentation, or claims history supporting previous medications tried (if applicable), including response to therapy. If therapy is not advisable, documentation of clinical reason to avoid therapy.
ii. Laboratory results, chart notes, or medical record documentation of biomarker testing (i.e., rheumatoid factor [RF], anti-cyclic citrullinated peptide [anti-CCP], and C-reactive protein [CRP] and/or erythrocyte sedimentation rate [ESR]) (if applicable).

2. Continuation requests: Chart notes or medical record documentation supporting positive clinical response.

B. Articular juvenile idiopathic arthritis
1. Initial requests: Chart notes, medical record documentation, or claims history supporting previous medications tried (if applicable), including response to therapy.
2. Continuation requests: Chart notes or medical record documentation supporting positive clinical response.

C. Systemic juvenile idiopathic arthritis (sJIA)
1. Initial requests: Chart notes, medical record documentation, or claims history supporting previous medications tried (if applicable), including response to therapy.
2. Continuation requests: Chart notes or medical record documentation supporting positive clinical response.

D. Cytokine release syndrome, immunotherapy-related inflammatory arthritis, and acute graft versus host disease: For initial requests: Chart notes, medical record documentation, or claims history supporting previous medications tried (if applicable), including response to therapy. If therapy is not advisable, documentation of clinical reason to avoid therapy.

E. Giant cell arteritis (GCA): For continuation requests: Chart notes or medical record documentation supporting positive clinical response.

F. Systemic sclerosis-associated interstitial lung disease (SSc-ILD): For initial requests: Result of a chest high-resolution computed tomography (HRCT) study.

III. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with one of the following:
A. Rheumatoid arthritis, articular juvenile idiopathic arthritis, systemic juvenile idiopathic arthritis, and giant cell arteritis: rheumatologist
B. Systemic sclerosis-associated interstitial lung disease: rheumatologist or pulmonologist
C. Immunotherapy-related inflammatory arthritis: oncologist, hematologist, or rheumatologist
D. Cytokine release syndrome, unicentric Castleman disease, multicentric Castleman disease, and acute graft versus host disease: oncologist or hematologist

IV. CRITERIA FOR INITIAL APPROVAL

A. Rheumatoid arthritis (RA)

1. Authorization of 12 months may be granted for adult members who have previously received a biologic or targeted synthetic drug (e.g., Rinvoq, Xeljanz) indicated for moderately to severely active rheumatoid arthritis.

2. Authorization of 12 months may be granted for adult members for treatment of moderately to severely active RA when all of the following criteria are met:
   i. Member meets either of the following criteria:
      a. Member has been tested for either of the following biomarkers and the test was positive:
         1. Rheumatoid factor (RF)
         2. Anti-cyclic citrullinated peptide (anti-CCP)
      b. Member has been tested for ALL of the following biomarkers:
         1. RF
         2. Anti-CCP
         3. C-reactive protein (CRP) and/or erythrocyte sedimentation rate (ESR)
   ii. Member meets either of the following criteria:
      a. Member has experienced an inadequate response to at least a 3-month trial of methotrexate despite adequate dosing (i.e., titrated to at least 15 mg/week).
      b. Member has an intolerance or contraindication to methotrexate (see Appendix A).

B. Articular juvenile idiopathic arthritis

1. Authorization of 12 months may be granted for members 2 years of age or older who have previously received a biologic or targeted synthetic drug (e.g., Xeljanz) indicated for active articular juvenile idiopathic arthritis.

2. Authorization of 12 months may be granted for members 2 years of age or older for treatment of active articular juvenile idiopathic arthritis when any of the following criteria is met:
   i. Member has had an inadequate response to methotrexate or another conventional synthetic drug (e.g., leflunomide, sulfasalazine, hydroxychloroquine) administered at an adequate dose and duration.
   ii. Member has had an inadequate response to a trial of scheduled non-steroidal anti-inflammatory drugs (NSAIDs) and/or intra-articular glucocorticoids (e.g., triamcinolone hexacetonide) and one of the following risk factors for poor outcome:
      a. Involvement of ankle, wrist, hip, sacroiliac joint, and/or temporomandibular joint (TMJ)
      b. Presence of erosive disease or enthesitis
      c. Delay in diagnosis
      d. Elevated levels of inflammation markers
      e. Symmetric disease
   iii. Member has risk factors for disease severity and potentially a more refractory disease course (see Appendix B) and the member also meets one of the following:
      a. High-risk joints are involved (e.g., cervical spine, wrist, or hip).
      b. High disease activity.
      c. Is judged to be at high risk for disabling joint disease.

C. Systemic juvenile idiopathic arthritis (sJIA)

1. Authorization of 12 months may be granted for members 2 years of age or older who have previously received a biologic indicated for active sJIA.

2. Authorization of 12 months may be granted for members 2 years of age or older for treatment of active sJIA when both of the following criteria are met:
   i. Member has active systemic features (e.g., fever, evanescent rash, lymphadenopathy, hepatomegaly, splenomegaly, serositis).
   ii. Member has had an inadequate response to non-steroidal anti-inflammatory drugs (NSAIDs) or systemic glucocorticoids.

D. Giant cell arteritis (GCA)

Authorization of 12 months may be granted for adult members for treatment of giant cell arteritis when the member's diagnosis was confirmed by the following:
1. Temporal artery biopsy or cross-sectional imaging; or
2. Acute-phase reactant elevation (i.e., high erythrocyte sedimentation rate [ESR] and/or high serum C-reactive protein [CRP]).

E. Systemic sclerosis-associated interstitial lung disease (SSc-ILD)
Authorization of 12 months may be granted for adult members for treatment of sclerosis-associated interstitial lung disease when the diagnosis was confirmed by a high-resolution computed tomography (HRCT) study of the chest.

F. Cytokine release syndrome
1. Authorization of 1 month may be granted for members 2 years of age or older for treatment of chimeric antigen receptor (CAR) T cell-induced cytokine release syndrome (CRS).
2. Authorization of 1 month may be granted for treatment of cytokine release syndrome in members with refractory CRS related to blinatumomab therapy.

G. Unicentric Castleman disease
Authorization of 12 months may be granted for treatment of unicentric Castleman disease when all of the following are met:
1. The member is HIV-negative.
2. The member is human herpesvirus-8-negative.
3. The requested medication will be used as a single agent.
4. The disease has progressed following treatment of relapsed/refractory disease.

H. Multicentric Castleman disease
Authorization of 12 months may be granted for treatment of multicentric Castleman disease when both of the following are met:
1. The requested medication will be used as a single agent.
2. The disease has progressed following treatment of relapsed/refractory or progressive disease.

I. Immunotherapy-related inflammatory arthritis
Authorization of 12 months may be granted for treatment of severe/refractory immunotherapy-related inflammatory arthritis when either of the following criteria is met:
1. Member has experienced an inadequate response to corticosteroids.
2. Member has an intolerance or contraindication to corticosteroids.

J. Acute graft versus host disease
Authorization of 12 months may be granted for treatment of acute graft versus host disease when either of the following criteria is met:
1. Member has experienced an inadequate response to systemic corticosteroids.
2. Member has an intolerance or contraindication to corticosteroids.

V. CONTINUATION OF THERAPY

A. Rheumatoid arthritis (RA)
Authorization of 12 months may be granted for all adult members (including new members) who are using the requested medication for moderately to severely active RA and who achieve or maintain a positive clinical response as evidenced by disease activity improvement of at least 20% from baseline in tender joint count, swollen joint count, pain, or disability.

B. Articular juvenile idiopathic arthritis
Authorization of 12 months may be granted for all members 2 years of age or older (including new members) who are using the requested medication for active articular juvenile idiopathic arthritis and who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition when there is improvement in any of the following from baseline:
1. Number of joints with active arthritis (e.g., swelling, pain, limitation of motion)
2. Number of joints with limitation of movement
3. Functional ability

C. Systemic juvenile idiopathic arthritis (sJIA)
Authorization of 12 months may be granted for all members 2 years of age or older (including new members) who are using the requested medication for sJIA and who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition when there is improvement in any of the following from baseline:
1. Number of joints with active arthritis (e.g., swelling, pain, limitation of motion)
2. Number of joints with limitation of movement
3. Functional ability
4. Systemic features (e.g., fever, evanescent rash, lymphadenopathy, hepatomegaly, splenomegaly, serositis)

D. Giant cell arteritis (GCA)
Authorization of 12 months may be granted for all adult members (including new members) who are using the requested medication for GCA and who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition when there is improvement in any of the following from baseline:
1. Headaches
2. Scalp tenderness
3. Tenderness and/or thickening of superficial temporal arteries
4. Constitutional symptoms (e.g., weight loss, fever, fatigue, night sweats)
5. Jaw and/or tongue claudication
6. Acute visual symptoms (e.g., amaurosis fugax, acute visual loss, diplopia)
7. Symptoms of polymyalgia rheumatica (e.g., shoulder and/or hip girdle pain)
8. Limb claudication

E. Systemic sclerosis-associated interstitial lung disease (SSc-ILD)
Authorization of 12 months may be granted for all adult members (including new members) who are using the requested medication for SSc-ILD when the member is currently receiving treatment with Actemra.

F. Cytokine release syndrome, immunotherapy-related inflammatory arthritis, and acute graft versus host disease
All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

G. All other diagnoses
Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section IV when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

VI. OTHER

For all indications: Member has had a documented negative tuberculosis (TB) test (which can include a tuberculosis skin test [PPD], an interferon-release assay [IGRA], or a chest x-ray)* within 6 months of initiating therapy for persons who are naïve to biologic drugs or targeted synthetic drugs associated with an increased risk of TB.

* If the screening testing for TB is positive, there must be further testing to confirm there is no active disease. Do not administer the requested medication to members with active TB infection. If there is latent disease, TB treatment must be started before initiation of the requested medication.

For all indications: Member cannot use the requested medication concomitantly with any other biologic drug or targeted synthetic drug.

VII. DOSAGE AND ADMINISTRATION

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

VIII. APPENDICES

Appendix A: Examples of clinical reasons to avoid pharmacologic treatment with methotrexate

1. Clinical diagnosis of alcohol use disorder, alcoholic liver disease, or other chronic liver disease
2. Drug interaction
3. Risk of treatment-related toxicity
4. Pregnancy or currently planning pregnancy
5. Breastfeeding
6. Significant comorbidity prohibits use of systemic agents (e.g., liver or kidney disease, blood dyscrasias, uncontrolled hypertension)
7. Hypersensitivity
8. History of intolerance or adverse event

Appendix B: Risk factors for articular juvenile idiopathic arthritis

1. Positive rheumatoid factor
2. Positive anti-cyclic citrullinated peptide antibodies
3. Pre-existing joint damage

IX. REFERENCES

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Reference number(s)
2375-A

SPECIALTY GUIDELINE MANAGEMENT

ACTIMMUNE (interferon gamma-1b)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. Actimmune is indicated for reducing the frequency and severity of serious infections associated with chronic granulomatous disease (CGD).
   2. Actimmune is indicated for delaying time to disease progression in patients with severe, malignant osteopetrosis (SMO).

B. Compendial Uses
   Mycosis fungoides/Sezary syndrome

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Chronic Granulomatous Disease
Authorization of 12 months may be granted to reduce the frequency and severity of infections associated with chronic granulomatous disease.

B. Severe, Malignant Osteopetrosis
Authorization of 12 months may be granted to delay time to disease progression in patients with severe, malignant osteopetrosis.

C. Mycosis Fungoides/Sezary Syndrome
Authorization of 12 months may be granted for treatment of mycosis fungoides or Sezary syndrome.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II who are experiencing benefit from therapy as evidenced by disease stability or disease improvement.

IV. REFERENCES

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PRIOR AUTHORIZATION CRITERIA

DRUG CLASS	**RETINOIDS (TOPICAL)**
BRAND NAME*	
(generic)	
	(adapalene)
	DIFFERIN
	(adapalene)
Status: CVS Caremark Criteria	
Type: Initial Prior Authorization with Quantity Limit	***Ref # 351-C***

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Differin Cream 0.1%, Adapalene Gel 0.1%, Adapalene Topical Solution 0.1% (swab), Adapalene Topical Solution 0.1%

Differin Cream 0.1%, Adapalene Gel 0.1%, Adapalene Topical Solution 0.1% (swab), and Adapalene Topical Solution 0.1% are indicated for the topical treatment of acne vulgaris.

Differin Gel 0.3%, Differin Lotion 0.1%

Differin Gel 0.3% and Differin Lotion 0.1% are indicated for the topical treatment of acne vulgaris in patients 12 years of age and older.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has a diagnosis of acne vulgaris
  AND
  - If additional quantities are being requested, then the requested drug is being prescribed to treat a body surface area that requires additional quantities

Quantity Limits apply.

QUANTITY LIMIT

PLEASE NOTE: Since manufacturer package sizes may vary, it is the discretion of the dispensing pharmacy to fill quantities per package size up to these quantity limits. In such cases the filling limit and day supply may be less than what is indicated.

Medication	COLUMN A (Lower Limit)	COLUMN B (Lower Limit)	COLUMN C (Upper Limit)	COLUMN D (Upper Limit)
	4 Week Limit*	12 Week Limit*	4 Week Limit*	12 Week Limit*
Adapalene topical solution	120 mL / 21 days	360 mL / 63 days	240 mL / 21 days	720 mL / 63 days
Adapalene topical solution (swab)	28 swabs / 21 days	84 swabs / 63 days	56 swabs / 21 days	168 swabs / 63 days
Differin cream 0.1% (adapalene cream)	45 grams / 21 days	135 grams / 63 days	90 grams / 21 days	270 grams / 63 days
Adapalene gel 0.1%	45 grams / 21 days	135 grams / 63 days	90 grams / 21 days	270 grams / 63 days

Differin gel 0.3% (adapalene gel)	45 grams / 21 days	135 grams / 63 days	90 grams / 21 days	270 grams / 63 days
Differin lotion 0.1% (adapalene lotion)	59 mL / 21 days	177 mL / 63 days	118 mL / 21 days	354 mL / 63 days
** The duration of 21 days is used for a 28-day fill period and 63 days is used for an 84-day fill period to allow time for refill processing.*				

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Adapalene is indicated for the topical treatment of acne vulgaris.[1-8]

The American Academy of Dermatology (AAD) guidelines state that the topical therapy of acne vulgaris includes the usage of agents that are available over the counter or via prescription. Therapy choice may be influenced by age of the patient, site of involvement, extent and severity of disease, and patient preference. Topical therapies may be used as monotherapy, in combination with other topical agents or in combination with oral agents in both initial control and maintenance. Commonly used topical acne therapies include benzoyl peroxide, salicylic acid, antibiotics, combination antibiotics with benzoyl peroxide, retinoids, retinoid with benzoyl peroxide, retinoid with antibiotic, azelaic acid, and sulfone agents. A topical retinoid alone is a first-line treatment option for mild acne vulgaris. Topical retinoids are also considered to be a first-line treatment option for mild, moderate or severe acne vulgaris when used as combination therapy with benzoyl peroxide, oral antibiotics, and/or topical antibiotics. Topical retinoids are important in addressing the development and maintenance of acne and are recommended as monotherapy in primarily comedonal acne, or in combination with topical or oral antimicrobials in patients with mixed or primarily inflammatory acne lesions. Using multiple topical agents that affect different aspects of acne pathogenesis can be useful; combination therapy should be used in the majority of patients with acne.[9]

The safety and effectiveness of adapalene in pediatric patients below the age of 12 have not been established.[1-6]
Per AAD guidelines, topical adapalene, tretinoin, and benzoyl peroxide can be safely used in the management of preadolescent acne in children. Current data show that retinoids in younger patients are effective and are not associated with increased irritation or risk.[9]

These criteria do not provide approval for cosmetic uses of this drug.

Adapalene Topical Solution 0.1%
Adapalene Topical Solution 0.1% should be applied once a day to affected areas. Adapalene Topical Solution 0.1% is available in a 120 mL glass bottle.

Adapalene Topical Solution 0.1% (swab)
Adapalene solution should be applied once a day to affected areas. Adapalene Topical Solution, 0.1% is available in 14-count unit-of-use 1.2 gram swabs.

Differin Cream 0.1%
Differin Cream 0.1% should be applied once daily to the affected area. Differin Cream 0.1% is available in a 45 gram tube.

Adapalene Gel 0.1%
Differin Gel 0.1% should be applied once a day to the affected area. Differin Gel 0.1% is available in a 45 gram tube.

Differin Gel 0.3%
Differin Gel 0.3% should be applied once daily to the entire face and other affected areas. Differin Gel 0.3% is available in a 45 gram tube.

Differin Lotion 0.1%
Differin Lotion 0.1% should be applied once daily to the entire face and other affected areas. Differin Lotion 0.1% is available in a 2 oz (59 mL) pump bottle.

The quantity limits take into consideration available packages sizes, including at least the smallest package size, and quantity sufficient for FDA-approved dosage for approximate body surface area (BSA) treated. The quantity for an application and the percent BSA were chosen based on estimations of the areas that may be affected following the fingertip method and rule of nines. Gels, creams, lotions, and solutions, will follow this approximation for determining the quantity limits. The dosing and duration of use for the target drugs varies. Since manufacturer package sizes may also vary, it is the discretion of the dispensing pharmacy to fill quantities per package size up to these quantity limits. In such cases the filling limit and day supply may be less than what is indicated.

No universal standard exists for quantity of application, although suggested methods include use of the adult fingertip unit (the amount from the distal interphalangeal joint to the fingertip, or approximately 0.5 grams (gm), being applied over an area equal to 2 adult palms), following the rule of 9's that measures the percent of affected area, and use of charts that propose amounts based on patient age and body site.[10] It is calculated by using the area from the wrist to the fingers and thumb of the hand closed together to represent 1% of the patient's BSA.[11]
In adults, the rule of nines is used as a rough indicator of % BSA. Palmar hand surface is approximately 1% BSA.[12]

Anatomic Surface	% of Body Surface
head and neck	9%
anterior trunk	18%
posterior trunk	18%
arms, including hands	9% each
legs, including feet	18% each
genitalia	1%

Quantity for 1% BSA, suggested AAD estimation
- Grams per application
  0.5 gm per application over 2 palms (1% BSA per palm) = 0.25gm per application over 1% BSA

Limit
- 45 gm / 0.25 gm per 1% BSA / 1 application per day / 28 days = 6.4% BSA
- 59 mL / 0.25 mL per 1% BSA / 1 application per day / 28 days = 8.4% BSA

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Written by: UM Development (LS)
Date Written: 10/1996
Revised: (LS) 12/1998, 11/1999, 09/2000; (JG) 10/2002; (MG) 10/2003; (TM) 10/2004; (NB) 09/2005, 09/2006; (AM) 08/2007; (MS) 08/2008; (AM) 09/2008; (SE) 09/2009; (MS) 08/2010; (CY) 07/2011; (MS) 08/2012, 10/2012 (extended duration), 06/2013, 06/2014; (RP) 06/2015 , (SF) 05/2016 (no clinical changes); (RP) 06/2017 (no clinical changes), 06/2018 (no clinical changes), 06/2019 (Added adapalene swab; renamed criteria to Adapalene; removed MDC-1 designation; shortened DOA to 12 months per Aetna Integration); (JK) (adjustment of target drug list to capture 0.1% solution bottle); (CJH) 07/2021 (no clinical changes); (PM) 10/2021 (added QL); (RZ) 07/2022 (no clinical changes)

QUANTITY LIMIT PRIOR AUTHORIZATION CRITERIA

DRUG CLASS	**SELECT INJECTABLE, INTRAVENOUS ANTIMICROBIALS**
BRAND NAME (generic)	
	ABELCET (amphotericin B lipid complex)
	AMBISOME (amphotericin B liposome)
	(amphotericin B)
	CANCIDAS (caspofungin)
	(ceftriaxone vials)
	COLY-MYCIN M (colistimethate)
	CUBICIN (daptomycin)
	CUBICIN RF (daptomycin)
	DALVANCE (dalbavancin)
	(daptomycin)
	DAPZURA RT (daptomycin)
	INVANZ (ertapenem)
	KIMYRSA (oritavancin)
	(levofloxacin injection)
	MERREM (meropenem)
	MYCAMINE (micafungin)

ORBACTIV
(oritavancin)

(streptomycin)

(tobramycin injection)

TYGACIL
(tigecycline)

(vancomycin injection vials, bottles)

VFEND IV
(voriconazole injection)

Status: CVS Caremark Criteria
Type: Quantity Limit; Post Limit Prior Authorization

POLICY

FDA-APPROVED INDICATIONS

Abelcet
Abelcet is indicated for the treatment of invasive fungal infections in patients who are refractory to or intolerant of conventional amphotericin B therapy. This is based on open-label treatment of patients judged by their physicians to be intolerant to or failing conventional amphotericin B therapy.

AmBisome
AmBisome is indicated for the following:
- Empirical therapy for presumed fungal infection in febrile, neutropenic patients.
- Treatment of Cryptococcal Meningitis in HIV-infected patients.
- Treatment of patients with Aspergillus species, Candida species and/or Cryptococcus species infections (see above for the treatment of Cryptococcal Meningitis) refractory to amphotericin B deoxycholate, or in patients where renal impairment or unacceptable toxicity precludes the use of amphotericin B deoxycholate.
- Treatment of visceral leishmaniasis. In immunocompromised patients with visceral leishmaniasis treated with AmBisome, relapse rates were high following initial clearance of parasites.

Amphotericin B
Amphotericin B for Injection USP should be administered primarily to patients with progressive, potentially life-threatening fungal infections. This potent drug should not be used to treat noninvasive fungal infections, such as oral thrush, vaginal candidiasis and esophageal candidiasis in patients with normal neutrophil counts.
Amphotericin B for Injection USP is specifically intended to treat potentially life threatening fungal infections: aspergillosis, cryptococcosis (torulosis), North American blastomycosis, systemic candidiasis, coccidioido-mycosis, histoplasmosis, zygomycosis including mucormycosis due to susceptible species of the genera Absidia, Mucor and Rhizopus, and infections due to related susceptible species of Conidiobolus and Basidiobolus, and sporotrichosis.
Amphotericin B may be useful in the treatment of American mucocutaneous leishmaniasis, but it is not the drug of choice as primary therapy.

Cancidas
Empirical Therapy for Presumed Fungal Infections in Febrile, Neutropenic Patients
Cancidas is indicated as empirical therapy for presumed fungal infections in febrile, neutropenic adult and pediatric patients (3 months of age and older).
Treatment of Candidemia and Other Candida Infections

Cancidas is indicated for the treatment of candidemia and the following candida infections: intraabdominal abscesses, peritonitis, and pleural space infections in adult and pediatric patients (3 months of age and older).
Limitations of Use: Cancidas has not been studied in endocarditis, osteomyelitis, and meningitis due to Candida.
Treatment of Esophageal Candidiasis
Cancidas is indicated for the treatment of esophageal candidiasis in adult and pediatric patients (3 months of age and older).
Limitations of Use: Cancidas has not been approved for the treatment of oropharyngeal candidiasis (OPC). In the study that evaluated the efficacy of caspofungin in the treatment of esophageal candidiasis, patients with concomitant OPC had higher relapse rate of the OPC.
Treatment of Invasive Aspergillosis in Patients Who Are Refractory to or Intolerant of Other Therapies
Cancidas is indicated for the treatment of invasive aspergillosis in adult and pediatric patients (3 months of age and older) who are refractory to or intolerant of other therapies.
Limitations of Use: Cancidas has not been studied as initial therapy for invasive aspergillosis.

Ceftriaxone
Before instituting treatment with Ceftriaxone appropriate specimens should be obtained for isolation of the causative organism and for determination of its susceptibility to the drug. Therapy may be instituted prior to obtaining results of susceptibility testing.
To reduce the development of drug-resistant bacteria and maintain the effectiveness of Ceftriaxone for injection, USP and other antibacterial drugs, Ceftriaxone for injection, USP should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.
Ceftriaxone for injection, USP is indicated for the treatment of the following infections when caused by susceptible organisms:
Lower Respiratory Tract Infections caused by Streptococcus pneumoniae, Staphylococcus aureus, Haemophilus influenzae, Haemophilus parainfluenzae, Klebsiella pneumoniae, Escherichia coli, Enterobacter aerogenes, Proteus mirabilis or Serratia marcescens.
Acute Bacterial Otitis Media caused by Streptococcus pneumoniae, Haemophilus influenzae (including beta-lactamase producing strains) or Moraxella catarrhalis (including beta-lactamase producing strains).
Note: In one study lower clinical cure rates were observed with a single dose of Ceftriaxone compared to 10 days of oral therapy. In a second study comparable cure rates were observed between single dose Ceftriaxone and the comparator. The potentially lower clinical cure rate of Ceftriaxone should be balanced against the potential advantages of parenteral therapy.
Skin and Skin Structure Infections caused by Staphylococcus aureus, Staphylococcus epidermidis, Streptococcus pyogenes, Viridans group streptococci, Escherichia coli, Enterobacter cloacae, Klebsiella oxytoca, Klebsiella pneumoniae, Proteus mirabilis, Morganella morganii,* Pseudomonas aeruginosa, Serratia marcescens, Acinetobacter calcoaceticus, Bacteroides fragilis* or Peptostreptococcus species.
Urinary Tract Infections (complicated and uncomplicated) caused by Escherichia coli, Proteus mirabilis, Proteus vulgaris, Morganella morganii or Klebsiella pneumoniae.
Uncomplicated Gonorrhea (cervical/urethral and rectal) caused by Neisseria gonorrhoeae, including both penicillinase- and nonpenicillinase-producing strains, and pharyngeal gonorrhea caused by nonpenicillinase-producing strains of Neisseria gonorrhoeae.
Pelvic Inflammatory Disease caused by Neisseria gonorrhoeae. Ceftriaxone sodium, like other cephalosporins, has no activity against Chlamydia trachomatis. Therefore, when cephalosporins are used in the treatment of patients with pelvic inflammatory disease and Chlamydia trachomatis is one of the suspected pathogens, appropriate antichlamydial coverage should be added.
Bacterial Septicemia caused by Staphylococcus aureus, Streptococcus pneumoniae, Escherichia coli, Haemophilus influenzae or Klebsiella pneumoniae.
Bone and Joint Infections caused by Staphylococcus aureus, Streptococcus pneumoniae, Escherichia coli, Proteus mirabilis, Klebsiella pneumoniae or Enterobacter species.
Intra-Abdominal Infections caused by Escherichia coli, Klebsiella pneumoniae, Bacteroides fragilis, Clostridium species (Note: most strains of Clostridium difficile are resistant) or Peptostreptococcus species.
Meningitis caused by Haemophilus influenzae, Neisseria meningitidis or Streptococcus pneumoniae. Ceftriaxone has also been used successfully in a limited number of cases of meningitis and shunt infection caused by Staphylococcus epidermidis* and Escherichia coli.*
* Efficacy for this organism in this organ system was studied in fewer than ten infections.
Surgical Prophylaxis: The preoperative administration of a single 1g dose of Ceftriaxone may reduce the incidence of postoperative infections in patients undergoing surgical procedures classified as contaminated or potentially contaminated

(e.g., vaginal or abdominal hysterectomy or cholecystectomy for chronic calculous cholecystitis in high-risk patients, such as those over 70 years of age, with acute cholecystitis not requiring therapeutic antimicrobials, obstructive jaundice or common duct bile stones) and in surgical patients for whom infection at the operative site would present serious risk (e.g., during coronary artery bypass surgery). Although Ceftriaxone has been shown to have been as effective as cefazolin in the prevention of infection following coronary artery bypass surgery, no placebo-controlled trials have been conducted to evaluate any cephalosporin antibiotic in the prevention of infection following coronary artery bypass surgery.
When administered prior to surgical procedures for which it is indicated, a single 1g dose of Ceftriaxone provides protection from most infections due to susceptible organisms throughout the course of the procedure.

Coly-Mycin M
Coly-Mycin M Parenteral is indicated for the treatment of acute or chronic infections due to sensitive strains of certain gram-negative bacilli. It is particularly indicated when the infection is caused by sensitive strains of Pseudomonas aeruginosa. This antibiotic is not indicated for infections due to Proteus or Neisseria. Coly-Mycin M Parenteral has proven clinically effective in treatment of infections due to the following gram-negative organisms: Enterobacter aerogenes, Escherichia coli, Klebsiella pneumoniae and Pseudomonas aeruginosa.
Coly-Mycin M Parenteral may be used to initiate therapy in serious infections that are suspected to be due to gram-negative organisms and in the treatment of infections due to susceptible gram-negative pathogenic bacilli.
To reduce the development of drug-resistant bacteria and maintain the effectiveness of Coly-Mycin M and other antibacterial drugs, Coly-Mycin M should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

Cubicin[8], Cubicin RF[9], Daptomycin 350mg[10,11,12], Daptomycin 500mg[11], Dapzura RT[13]
Complicated Skin and Skin Structure Infections (cSSSI) [8,9,10,11,12,13]
Cubicin, Cubicin RF, Daptomycin for Injection, and Dapzura RT are indicated for the treatment of adult[11] and pediatric patients (1 to 17 years of age) with complicated skin and skin structure infections (cSSSI) caused by susceptible isolates of the following Gram-positive bacteria: Staphylococcus aureus (including methicillin-resistant isolates), Streptococcus pyogenes, Streptococcus agalactiae, Streptococcus dysgalactiae subsp. equisimilis, and Enterococcus faecalis (vancomycin-susceptible isolates only).
Staphylococcus aureus Bloodstream Infections (Bacteremia) in Adult Patients, Including Those with Right-Sided Infective Endocarditis, Caused by Methicillin-Susceptible and Methicillin-Resistant Isolates [8,9,10,11,12,13]
Cubicin, Cubicin RF, Daptomycin for Injection, and Dapzura RT are indicated for the treatment of adult patients with Staphylococcus aureus bloodstream infections (bacteremia), including adult patients with right-sided infective endocarditis, caused by methicillin-susceptible and methicillin-resistant isolates.
Staphylococcus aureus Bloodstream Infections (Bacteremia) in Pediatric Patients (1 to 17 Years of Age)[8,9,10,12,13]
Cubicin, Cubicin RF, Daptomycin for Injection, and Dapzura RT are indicated for the treatment of pediatric patients (1 to 17 years of age) with Staphylococcus aureus bloodstream infections (bacteremia).
Limitations of Use [8,9,10,11,12,13]
Cubicin, Cubicin RF, Daptomycin for Injection, and Dapzura RT are not indicated for the treatment of pneumonia.
Cubicin, Cubicin RF, Daptomycin for Injection, and Dapzura RT are not indicated for the treatment of left-sided infective endocarditis due to S. aureus. The clinical trial of Cubicin, Cubicin RF, Daptomycin for Injection, and Dapzura RT in adult patients with S. aureus bloodstream infections included limited data from patients with left-sided infective endocarditis; outcomes in these patients were poor. Cubicin, Cubicin RF, Daptomycin for Injection, and Dapzura RT have not been studied in patients with prosthetic valve endocarditis.
Cubicin, Cubicin RF, Daptomycin for Injection, and Dapzura RT are not recommended in pediatric patients younger than 1 year of age due to the risk of potential effects on muscular, neuromuscular, and/or nervous systems (either peripheral and/or central) observed in neonatal dogs.[8,9,10,13]
Usage [8,9,10,11,12,13]
Appropriate specimens for microbiological examination should be obtained in order to isolate and identify the causative pathogens and to determine their susceptibility to daptomycin.
To reduce the development of drug-resistant bacteria and maintain the effectiveness of Cubicin, Cubicin RF, Daptomycin for Injection, Dapzura RT and other antibacterial drugs, Cubicin, Cubicin RF, Daptomycin for Injection, and Dapzura RT should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria.
When culture and susceptibility information is available, it should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy. Empiric therapy may be initiated while awaiting test results.

Dalvance
Dalvance is indicated for the treatment of adult and pediatric patients with acute bacterial skin and skin structure infections (ABSSSI), caused by designated susceptible strains of the following Gram-positive microorganisms: Staphylococcus aureus (including methicillin-susceptible and methicillin-resistant isolates), Streptococcus pyogenes, Streptococcus agalactiae, Streptococcus dysgalactiae, Streptococcus anginosus group (including S. anginosus, S. intermedius, S. constellatus) and Enterococcus faecalis (vancomycin susceptible strains).
Usage
To reduce the development of drug-resistant bacteria and maintain the effectiveness of Dalvance and other antibacterial agents, Dalvance should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

Invanz
Complicated Intra-Abdominal Infections
Invanz is indicated for the treatment of adult patients and pediatric patients (3 months of age and older) with complicated intra-abdominal infections due to Escherichia coli, Clostridium clostridiiforme, Eubacterium lentum, Peptostreptococcus species, Bacteroides fragilis, Bacteroides distasonis, Bacteroides ovatus, Bacteroides thetaiotaomicron, or Bacteroides uniformis.
Complicated Skin and Skin Structure Infections, Including Diabetic Foot Infections without Osteomyelitis
Invanz is indicated for the treatment of adult patients and pediatric patients (3 months of age and older) with complicated skin and skin structure infections, including diabetic foot infections without osteomyelitis due to Staphylococcus aureus (methicillin susceptible isolates only), Streptococcus agalactiae, Streptococcus pyogenes, Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis, Bacteroides fragilis, Peptostreptococcus species, Porphyromonas asaccharolytica, or Prevotella bivia. Invanz has not been studied in diabetic foot infections with concomitant osteomyelitis.
Community Acquired Pneumonia
Invanz is indicated for the treatment of adult patients and pediatric patients (3 months of age and older) with community acquired pneumonia due to Streptococcus pneumoniae (penicillin susceptible isolates only) including cases with concurrent bacteremia, Haemophilus influenzae (beta-lactamase negative isolates only), or Moraxella catarrhalis.
Complicated Urinary Tract Infections Including Pyelonephritis
Invanz is indicated for the treatment of adult patients and pediatric patients (3 months of age and older) with complicated urinary tract infections including pyelonephritis due to Escherichia coli, including cases with concurrent bacteremia, or Klebsiella pneumoniae.
Acute Pelvic Infections Including Postpartum Endomyometritis, Septic Abortion and Post Surgical Gynecologic Infections
Invanz is indicated for the treatment of adult patients and pediatric patients (3 months of age and older) with acute pelvic infections including postpartum endomyometritis, septic abortion and post surgical gynecological infections due to Streptococcus agalactiae, Escherichia coli, Bacteroides fragilis, Porphyromonas asaccharolytica, Peptostreptococcus species, or Prevotella bivia.
Prophylaxis of Surgical Site Infection Following Elective Colorectal Surgery
Invanz is indicated in adults for the prevention of surgical site infection following elective colorectal surgery.
Usage
To reduce the development of drug-resistant bacteria and maintain the effectiveness of Invanz and other antibacterial drugs, Invanz should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

Kimyrsa
Kimyrsa is indicated for the treatment of adult patients with acute bacterial skin and skin structure infections (ABSSSI) caused by susceptible isolates of the following Gram positive microorganisms:
Staphylococcus aureus (including methicillin-susceptible and methicillin-resistant isolates), Streptococcus pyogenes, Streptococcus agalactiae, Streptococcus dysgalactiae, Streptococcus anginosus group (includes S. anginosus, S. intermedius, and S. constellatus), and Enterococcus faecalis (vancomycin-susceptible isolates only).
Usage
To reduce the development of drug-resistant bacteria and maintain the effectiveness of Kimyrsa and other antibacterial drugs, Kimyrsa should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in

selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

Levofloxacin injection
Levofloxacin injection is indicated for the treatment of adults (≥18 years of age) with mild, moderate, and severe infections caused by susceptible isolates of the designated microorganisms in the conditions listed in this section. Levofloxacin injection is indicated when intravenous administration offers a route of administration advantageous to the patient (e.g., patient cannot tolerate an oral dosage form).
Nosocomial Pneumonia
Levofloxacin injection is indicated for the treatment of nosocomial pneumonia due to methicillin-susceptible Staphylococcus aureus, Pseudomonas aeruginosa, Serratia marcescens, Escherichia coli, Klebsiella pneumoniae, Haemophilus influenzae, or Streptococcus pneumoniae. Adjunctive therapy should be used as clinically indicated. Where Pseudomonas aeruginosa is a documented or presumptive pathogen, combination therapy with an anti-pseudomonal β-lactam is recommended.
Community-Acquired Pneumonia: 7- to 14-day Treatment Regimen
Levofloxacin injection is indicated for the treatment of community-acquired pneumonia due to methicillin-susceptible Staphylococcus aureus, Streptococcus pneumoniae (including multi-drug-resistant Streptococcus pneumoniae [MDRSP]), Haemophilus influenzae, Haemophilus parainfluenzae, Klebsiella pneumoniae, Moraxella catarrhalis, Chlamydophila pneumoniae, Legionella pneumophila, or Mycoplasma pneumoniae.
MDRSP isolates are isolates resistant to two or more of the following antibacterials: penicillin (MIC ≥2 mcg/mL), second generation cephalosporins, e.g., cefuroxime, macrolides, tetracyclines and trimethoprim/sulfamethoxazole.
Community-Acquired Pneumonia: 5-day Treatment Regimen
Levofloxacin injection is indicated for the treatment of community-acquired pneumonia due to Streptococcus pneumoniae (excluding multi-drug-resistant isolates [MDRSP]), Haemophilus influenzae, Haemophilus parainfluenzae, Mycoplasma pneumoniae, or Chlamydophila pneumoniae.
Complicated Skin and Skin Structure Infections
Levofloxacin injection is indicated for the treatment of complicated skin and skin structure infections due to methicillin-susceptible Staphylococcus aureus, Enterococcus faecalis, Streptococcus pyogenes, or Proteus mirabilis.
Uncomplicated Skin and Skin Structure Infections
Levofloxacin injection is indicated for the treatment of uncomplicated skin and skin structure infections (mild to moderate) including abscesses, cellulitis, furuncles, impetigo, pyoderma, wound infections, due to methicillin-susceptible Staphylococcus aureus, or Streptococcus pyogenes.
Chronic Bacterial Prostatitis
Levofloxacin injection is indicated for the treatment of chronic bacterial prostatitis due to Escherichia coli, Enterococcus faecalis, or methicillin-susceptible Staphylococcus epidermidis.
Inhalational Anthrax (Post-Exposure)
Levofloxacin injection is indicated for inhalational anthrax (post-exposure) to reduce the incidence or progression of disease following exposure to aerosolized Bacillus anthracis. The effectiveness of levofloxacin is based on plasma concentrations achieved in humans, a surrogate endpoint reasonably likely to predict clinical benefit. Levofloxacin injection has not been tested in humans for the post-exposure prevention of inhalation anthrax. The safety of levofloxacin injection in adults for durations of therapy beyond 28 days or in pediatric patients for durations of therapy beyond 14 days has not been studied. Prolonged levofloxacin injection therapy should only be used when the benefit outweighs the risk.
Plague
Levofloxacin injection is indicated for treatment of plague, including pneumonic and septicemic plague, due to Yersinia pestis (Y. pestis) and prophylaxis for plague in adults and pediatric patients, 6 months of age and older. Efficacy studies of levofloxacin injection could not be conducted in humans with plague for ethical and feasibility reasons. Therefore, approval of this indication was based on an efficacy study conducted in animals.
Complicated Urinary Tract Infections: 5-day Treatment Regimen
Levofloxacin injection is indicated for the treatment of complicated urinary tract infections due to Escherichia coli, Klebsiella pneumoniae, or Proteus mirabilis.
Complicated Urinary Tract Infections: 10-day Treatment Regimen
Levofloxacin injection is indicated for the treatment of complicated urinary tract infections (mild to moderate) due to Enterococcus faecalis, Enterobacter cloacae, Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis, or Pseudomonas aeruginosa.
Acute Pyelonephritis: 5- or 10-day Treatment Regimen
Levofloxacin injection is indicated for the treatment of acute pyelonephritis caused by Escherichia coli, including cases with concurrent bacteremia.
Uncomplicated Urinary Tract Infections

Levofloxacin injection is indicated for the treatment of uncomplicated urinary tract infections (mild to moderate) due to Escherichia coli, Klebsiella pneumoniae, or Staphylococcus saprophyticus.
Because fluoroquinolones, including levofloxacin injection, have been associated with serious adverse reactions and for some patients uncomplicated urinary tract infection is self-limiting, reserve levofloxacin injection for treatment of uncomplicated urinary tract infections in patients who have no alternative treatment options.
Acute Bacterial Exacerbation of Chronic Bronchitis
Levofloxacin injection is indicated for the treatment of acute bacterial exacerbation of chronic bronchitis (ABECB) due to methicillin-susceptible Staphylococcus aureus, Streptococcus pneumoniae, Haemophilus influenzae, Haemophilus parainfluenzae, or Moraxella catarrhalis.
Because fluoroquinolones, including levofloxacin injection, have been associated with serious adverse reactions [see Warnings and Precautions (5.1 to 5.15)] and for some patients ABECB is self-limiting, reserve levofloxacin for treatment of ABECB in patients who have no alternative treatment options.
Acute Bacterial Sinusitis: 5-day and 10–14 day Treatment Regimens
Levofloxacin injection is indicated for the treatment of acute bacterial sinusitis (ABS) due to Streptococcus pneumoniae, Haemophilus influenzae, or Moraxella catarrhalis.
Because fluoroquinolones, including levofloxacin injection, have been associated with serious adverse reactions and for some patients ABS is self-limiting, reserve levofloxacin for treatment of ABS in patients who have no alternative treatment options.
Usage
To reduce the development of drug-resistant bacteria and maintain the effectiveness of levofloxacin and other antibacterial drugs, levofloxacin should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.
Culture and susceptibility testing
Appropriate culture and susceptibility tests should be performed before treatment in order to isolate and identify organisms causing the infection and to determine their susceptibility to levofloxacin. Therapy with levofloxacin injection may be initiated before results of these tests are known; once results become available, appropriate therapy should be selected.
As with other drugs in this class, some isolates of Pseudomonas aeruginosa may develop resistance fairly rapidly during treatment with levofloxacin injection. Culture and susceptibility testing performed periodically during therapy will provide information about the continued susceptibility of the pathogens to the antimicrobial agent and also the possible emergence of bacterial resistance.

Merrem
Complicated Skin and Skin Structure Infections (Adult Patients and Pediatric Patients 3 Months of Age and Older Only)
Merrem IV is indicated for the treatment of complicated skin and skin structure infections (cSSSI) due to Staphylococcus aureus (methicillin-susceptible isolates only), Streptococcus pyogenes, Streptococcus agalactiae, viridans group streptococci, Enterococcus faecalis (vancomycin-susceptible isolates only), Pseudomonas aeruginosa, Escherichia coli, Proteus mirabilis, Bacteroides fragilis, and Peptostreptococcus species.
Complicated Intra-abdominal Infections (Adult and Pediatric Patients)
Merrem IV is indicated for the treatment of complicated appendicitis and peritonitis caused by viridans group streptococci, Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, Bacteroides fragilis, B. thetaiotaomicron, and Peptostreptococcus species.
Bacterial Meningitis (Pediatric Patients 3 Months of Age and Older Only)
Merrem IV is indicated for the treatment of bacterial meningitis caused by Haemophilus influenzae, Neisseria meningitidis and penicillin-susceptible isolates of Streptococcus pneumoniae.
Merrem IV has been found to be effective in eliminating concurrent bacteremia in association with bacterial meningitis.
Usage
To reduce the development of drug-resistant bacteria and maintain the effectiveness of Merrem IV and other antibacterial drugs, Merrem IV should only be used to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

Mycamine
Mycamine is indicated for:
- Treatment of Candidemia, Acute Disseminated Candidiasis, Candida Peritonitis and Abscesses in adult and pediatric patients 4 months of age and older.

- Treatment of Candidemia, Acute Disseminated Candidiasis, Candida Peritonitis and Abscesses without meningoencephalitis and/or ocular dissemination in pediatric patients younger than 4 months of age.
- Treatment of Esophageal Candidiasis in adult and pediatric patients 4 months of age and older.
- Prophylaxis of Candida Infections in adult and pediatric patients 4 months of age and older undergoing hematopoietic stem cell transplantation.

Limitations of Use

- The safety and effectiveness of Mycamine have not been established for the treatment of candidemia with meningoencephalitis and/or ocular dissemination in pediatric patients younger than 4 months of age as a higher dose may be needed.
- Mycamine has not been adequately studied in patients with endocarditis, osteomyelitis and meningoencephalitis due to Candida.
- The efficacy of Mycamine against infections caused by fungi other than Candida has not been established.

Orbactiv

Orbactiv (oritavancin) is indicated for the treatment of adult patients with acute bacterial skin and skin structure infections (ABSSSI) caused by susceptible isolates of the following Gram-positive microorganisms:
Staphylococcus aureus (including methicillin-susceptible and methicillin–resistant isolates), Streptococcus pyogenes, Streptococcus agalactiae, Streptococcus dysgalactiae, Streptococcus anginosus group (includes S. anginosus, S. intermedius, and S. constellatus), and Enterococcus faecalis (vancomycin susceptible isolates only).

Usage

To reduce the development of drug-resistant bacteria and maintain the effectiveness of Orbactiv and other antibacterial drugs, Orbactiv should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

Streptomycin

Streptomycin is indicated for the treatment of individuals with moderate to severe infections caused by susceptible strains of microorganisms in the specific conditions listed below:

1. Mycobacterium tuberculosis: The Advisory Council for the Elimination of Tuberculosis, the American Thoracic Society, and the Center for Disease Control recommend that either streptomycin or ethambutol be added as a fourth drug in a regimen containing isoniazid (INH), rifampin and pyrazinamide for initial treatment of tuberculosis unless the likelihood of INH or rifampin resistance is very low. The need for a fourth drug should be reassessed when the results of susceptibility testing are known. In the past when the national rate of primary drug resistance to isoniazid was known to be less than 4% and was either stable or declining, therapy with two and three drug regimens was considered adequate. If community rates of INH resistance are currently less than 4%, an initial treatment regimen with less than four drugs may be considered. Streptomycin is also indicated for therapy of tuberculosis when one or more of the above drugs is contraindicated because of toxicity or intolerance. The management of tuberculosis has become more complex as a consequence of increasing rates of drug resistance and concomitant HIV infection. Additional consultation from experts in the treatment of tuberculosis may be desirable in those settings.
2. Non-tuberculosis infections: The use of streptomycin should be limited to the treatment of infections caused by bacteria which have been shown to be susceptible to the antibacterial effects of streptomycin and which are not amenable to therapy with less potentially toxic agents.
    a. Pasteurella pestis (plague),
    b. Francisella tularensis (tularemia),
    c. Brucella,
    d. Calymmatobacterium granulomatis (donovanosis, granuloma inguinale),
    e. H. ducreyi (chancroid),
    f. H. influenzae (in respiratory, endocardial, and meningeal infections-concomitantly with another antibacterial agent),
    g. K. pneumoniae pneumonia (concomitantly with another antibacterial agent),
    h. E.coli, Proteus, A. aerogenes, K. pneumoniae, and Enterococcus faecalis in urinary tract infections,
    i. Streptococcus viridans, Enterococcus faecalis (in endocardial infections -concomitantly with penicillin),
    j. Gram-negative bacillary bacteremia (concomitantly with another antibacterial agent).

Tobramycin injection

Tobramycin is indicated for the treatment of serious bacterial infections caused by susceptible strains of the designated microorganisms in the diseases listed below:

Septicemia in the pediatric patient and adult caused by P. aeruginosa, E. coli, and Klebsiella sp.

Lower respiratory tract infections caused by P. aeruginosa, Klebsiella sp, Enterobacter sp, Serratia sp, E. coli, and S. aureus (penicillinase- and non-penicillinase-producing strains).
Serious central-nervous-system infections (meningitis) caused by susceptible organisms.
Intra-abdominal infections, including peritonitis, caused by E. coli, Klebsiella sp, and Enterobacter sp.
Skin, bone, and skin-structure infections caused by P. aeruginosa, Proteus sp, E. coli, Klebsiella sp, Enterobacter sp, and S. aureus.
Complicated and recurrent urinary tract infections caused by P. aeruginosa, Proteus sp (indole-positive and indole-negative), E. coli, Klebsiella sp, Enterobacter sp, Serratia sp, S. aureus, Providencia sp, and Citrobacter sp.

Aminoglycosides, including tobramycin sulfate, are not indicated in uncomplicated initial episodes of urinary tract infections unless the causative organisms are not susceptible to antibiotics having less potential toxicity. Tobramycin may be considered in serious staphylococcal infections when penicillin or other potentially less toxic drugs are contraindicated and when bacterial susceptibility testing and clinical judgment indicate its use.

Bacterial cultures should be obtained prior to and during treatment to isolate and identify etiologic organisms and to test their susceptibility to tobramycin. If susceptibility tests show that the causative organisms are resistant to tobramycin, other appropriate therapy should be instituted. In patients in whom a serious life-threatening gram-negative infection is suspected, including those in whom concurrent therapy with a penicillin or cephalosporin and an aminoglycoside may be indicated, treatment with tobramycin sulfate may be initiated before the results of susceptibility studies are obtained. The decision to continue therapy with tobramycin should be based on the results of susceptibility studies, the severity of the infection, and the important additional concepts discussed in the warnings box.

To reduce the development of drug-resistant bacteria and maintain the effectiveness of tobramycin and other antibacterial drugs, tobramycin should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antimicrobial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

Tygacil

Complicated Skin and Skin Structure Infections

Tygacil is indicated in patients 18 years of age and older for the treatment of complicated skin and skin structure infections caused by susceptible isolates of Escherichia coli, Enterococcus faecalis (vancomycin-susceptible isolates), Staphylococcus aureus (methicillin-susceptible and -resistant isolates), Streptococcus agalactiae, Streptococcus anginosus grp. (includes S. anginosus, S. intermedius, and S. constellatus), Streptococcus pyogenes, Enterobacter cloacae, Klebsiella pneumoniae, and Bacteroides fragilis.

Complicated Intra-abdominal Infections

Tygacil is indicated in patients 18 years of age and older for the treatment of complicated intra-abdominal infections caused by susceptible isolates of Citrobacter freundii, Enterobacter cloacae, Escherichia coli, Klebsiella oxytoca, Klebsiella pneumoniae, Enterococcus faecalis (vancomycin-susceptible isolates), Staphylococcus aureus (methicillin-susceptible and -resistant isolates), Streptococcus anginosus grp. (includes S. anginosus, S. intermedius, and S. constellatus), Bacteroides fragilis, Bacteroides thetaiotaomicron, Bacteroides uniformis, Bacteroides vulgatus, Clostridium perfringens, and Peptostreptococcus micros.

Community-Acquired Bacterial Pneumonia

Tygacil is indicated in patients 18 years of age and older for the treatment of community-acquired bacterial pneumonia caused by susceptible isolates of Streptococcus pneumoniae (penicillin-susceptible isolates), including cases with concurrent bacteremia, Haemophilus influenzae, and Legionella pneumophila.

Limitations of Use

Tygacil is not indicated for the treatment of diabetic foot infections. A clinical trial failed to demonstrate non-inferiority of Tygacil for treatment of diabetic foot infections.

Tygacil is not indicated for the treatment of hospital-acquired or ventilator-associated pneumonia. In a comparative clinical trial, greater mortality and decreased efficacy were reported in Tygacil treated patients.

Usage

To reduce the development of drug-resistant bacteria and maintain the effectiveness of Tygacil and other antibacterial drugs, Tygacil should be used only to treat infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

Appropriate specimens for bacteriological examination should be obtained in order to isolate and identify the causative organisms and to determine their susceptibility to tigecycline. Tygacil may be initiated as empiric monotherapy before results of these tests are known.

Vancomycin injection

Septicemia
Vancomycin Hydrochloride for Injection is indicated in adults and pediatric patients (neonates and older) for the treatment of septicemia due to:

- Susceptible isolates of methicillin-resistant Staphylococcus aureus (MRSA) and coagulase negative staphylococci.
- Methicillin-susceptible staphylococci in penicillin-allergic patients, or those patients who cannot receive or who have failed to respond to other drugs, including penicillins or cephalosporins

Infective Endocarditis
Vancomycin Hydrochloride for Injection is indicated in adults and pediatric patients (neonates and older) for the treatment of infective endocarditis due to:

- Susceptible isolates of MRSA.
- Viridans group streptococci Streptococcus gallolyticus (previously known as Streptococcus bovis), Enterococcus species and Corynebacterium species. For enterococcal endocarditis, use Vancomycin Hydrochloride for Injection in combination with an aminoglycoside.
- Methicillin-susceptible staphylococci in penicillin-allergic patients, or those patients who cannot receive or who have failed to respond to other drugs, including penicillins or cephalosporins.

Vancomycin Hydrochloride for Injection is indicated in adults and pediatric patients (neonates and older) for the treatment of early-onset prosthetic valve endocarditis caused by Staphylococcus epidermidis in combination with rifampin and an aminoglycoside.
Skin and Skin Structure Infections
Vancomycin Hydrochloride for Injection is indicated in adults and pediatric patients (neonates and older) for the treatment of skin and skin structure infections due to:

- Susceptible isolates of MRSA and coagulase negative staphylococci.
- Methicillin-susceptible staphylococci in penicillin-allergic patients, or those patients who cannot receive or who have failed to respond to other drugs, including penicillins or cephalosporins.

Bone Infections
Vancomycin Hydrochloride for Injection is indicated in adults and pediatric patients (neonates and older) for the treatment of bone infections due to:

- Susceptible isolates of MRSA and coagulase negative staphylococci.
- Methicillin-susceptible staphylococci in penicillin-allergic patients, or those patients who cannot receive or who have failed to respond to other drugs, including penicillins or cephalosporins.

Lower Respiratory Tract Infections
Vancomycin Hydrochloride for Injection is indicated in adults and pediatric patients (neonates and older) for the treatment of lower respiratory tract infections due to:

- Susceptible isolates of MRSA
- Methicillin-susceptible staphylococci in penicillin-allergic patients, or those patients who cannot receive or who have failed to respond to other drugs, including penicillins or cephalosporins.

Usage
To reduce the development of drug-resistant bacteria and maintain the effectiveness of Vancomycin Hydrochloride for Injection and other antibacterial drugs, Vancomycin Hydrochloride for Injection should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.
The parenteral form of vancomycin hydrochloride for injection, USP may be administered orally for treatment of antibiotic-associated pseudomembranous colitis produced by C. difficile and for staphylococcal enterocolitis. Parenteral administration of vancomycin hydrochloride alone is of unproven benefit for these indications. Vancomycin is not effective by the oral route for other types of infections.

Vfend IV
Invasive Aspergillosis
Vfend is indicated in adults and pediatric patients (2 years of age and older) for the treatment of invasive aspergillosis (IA). In clinical trials, the majority of isolates recovered were Aspergillus fumigatus. There was a small number of cases of culture-proven disease due to species of Aspergillus other than A. fumigatus.
Candidemia in Non-neutropenic Patients and Other Deep Tissue Candida Infections
Vfend is indicated in adults and pediatric patients (2 years of age and older) for the treatment of candidemia in non-neutropenic patients and the following Candida infections: disseminated infections in skin and infections in abdomen, kidney, bladder wall, and wounds.
Esophageal Candidiasis

Vfend is indicated in adults and pediatric patients (2 years of age and older) for the treatment of esophageal candidiasis (EC) in adults and pediatric patients 2 years of age and older.

Scedosporiosis and Fusariosis

Vfend is indicated for the treatment of serious fungal infections caused by Scedosporium apiospermum (asexual form of Pseudallescheria boydii) and Fusarium spp. including Fusarium solani, in adults and pediatric patients (2 years of age and older) intolerant of, or refractory to, other therapy.

Usage

Specimens for fungal culture and other relevant laboratory studies (including histopathology) should be obtained prior to therapy to isolate and identify causative organism(s). Therapy may be instituted before the results of the cultures and other laboratory studies are known. However, once these results become available, antifungal therapy should be adjusted accordingly.

INITIAL QUANTITY LIMIT*

Duration limits (Column A) and Daily dose limits (Column B) apply for each drug.

LIMIT CRITERIA

Limits do not accumulate together; patient is allowed the maximum limit for each drug and strength

PLEASE NOTE: Since manufacturer package sizes may vary, it is the discretion of the dispensing pharmacy to fill quantities per package size up to these quantity limits. In such cases the filling limit and day supply may be less than what is indicated.

		Column A	**Column B**	
Medication	usual/maximum recommended dose (139.9kg allows for 95th percentile dosing)[32]	**Duration per 365 days**	**Daily dose**	**package size**
Abelcet (amphotericin B lipid complex)	5mg/kg/day *5mgx139.9kg = 699.5mg/day* *699.5mg/day/100mg/vial = 7vials/day* *7vialsx20mL/vial = 140mL*	14 days	140mL	5mg/mL 20mL per vial (100mg per vial)
AmBisome (amphotericin B liposome)	6mg/kg/day, *6mgx139.9kg = 839.4mg/day* *839.4mg/day/50mg/vial = 16.8vials/day*	14 days	17 vials	50mg per vial
Amphotericin B	1 mg/kg/day *1mgx139.9kg/day = 139.9mg/day* *139.9mg/day/50mg/vial = 2.8vials/day*	14 days	3 vials	50mg per vial
Cancidas (caspofungin)	50mg/day or 70mg/day *= 1vial/day*	14 days	1 vial	50mg per vial 70mg per vial
Ceftriaxone vials, bottles	1 to 2 gm once a day (or divided doses twice a day) The total daily dose should not exceed 4gm *1vial/dosex2doses/day = 2vials/day*	14 days	2 vials	250mg per vial 500mg per vial 1gm per vial 2gm per vial
			0.5 bottle	10gm per bottle
Coly-Mycin M (colistimethate)	5mg/kg/day in 2 to 4 divided doses *5mgx139.9kg = 699.5mg/day,* *699.5mg/4doses/day = 174.9mg/dose* *174.9mg/dose/150mg/vial = 1.2vials/dose* *2vials/dosex4doses/day = 8vials/day*	14 days	8 vials	150mg per vial
Cubicin, Cubicin RF (daptomycin)	6mg/kg once every 24 hours *6mgx139.9kg = 839.4/day* *839.4mg/day/500mg/vial = 1.7vials/day*	14 days	2 vials	500mg per vial
Dapzura RT (daptomycin)				
Daptomycin 500mg				
Daptomycin 350mg	6mg/kg once every 24 hours *6mgx139.9kg = 839.4mg/day* *839.4mg/day/350mg/vial = 2.4vials/day*	14 days	3 vials	350mg per vial
Dalvance (dalbavancin)	1500mg as single dose or divided *1500mg/dose/500mg/vialx1dose = 3 vials*	1 day	3 vials	500mg per vial
Invanz (ertapenem)	Adult: 1g given once a day *1vial/dosex1dose/day = 1vial/day*	14 days	2 vials	1gm per vial

	Pediatric: 15mg/kg twice daily (not to exceed 1g/day), *1vial/dosex2doses/day = 2vials/day*			
Kimyrsa (oritavancin)	1200mg (one dose) *1200mg/dose/1200mg/vialx1dose = 1 vial*	1 day	1 vial	1200mg per vial
Levofloxacin inj	Adult: 750mg every 24 hours *750mg/day/25mg/mL = 30mL/day* *30mL/day/30mL/vial = 1 vial/day* Pediatric: 250mg every 12 hours *250mg/dose/25mg/mL = 10mL/dose* *10mL/dose/20mL/vial = 0.5vials/dose* *1vial/dosex2doses/day = 2vials/day* *2vials/dayx20mL/vial = 40mL/day*	14 days	40mL	25mg/mL 20mL per vial =500mg / 20mL vial
				25mg/mL 30mL per vial =750mg / 30mL vial
Merrem (meropenem)	2gm every 8 hours *2gm/dose/500mg/vial = 4vials/dose* *4vials/dosex3doses/day = 12vials/day* *2gm/dose/1gm/vial = 2vials/dose* *2vials/dosex3doses/day = 6vials/day*	14 days	12 vials	500mg per vial
			6 vials	1gm per vial
Mycamine (micafungin)	150mg once daily *150mg/day/50mg/vial = 3vials/day* *150mg/day/100mg/vial = 2vials/day*	14 days	3 vials	50mg per vial
			2 vials	100mg per vial
Orbactiv (oritavancin)	1200mg (one dose) *1200mg/dose/400mg/vialx1dose = 3 vials*	1 day	3 vials	400mg per vial
Streptomycin	1 to 2 gm in divided doses *1gm/vialx2doses/day = 2 vials/day*	14 days	2 vials	1gm per vial
Tobramycin inj	10mg/kg/day in 3 equal doses or in 4 equal doses. *10mgx139.9kg = 1399kg/day* *1399mg/day/4doses/day = 349.8mg/dose* *349.8mg/dose/40mg/mL = 8.7mL/dose* *9mL/dosex4doses/day = 36mL/day*	10 days	36mL	10mg/mL 2mL per vial (20mg / 2mL vial)
				80mg/2mL 2mL per vial (40mg / mL vial)
				40mg/mL 30mL per vial (1200mg / 30mL vial)
				40mg/mL 50mL per vial (2000mg / 50mL vial)
			2 vials	1.2gm powd per vial
Tygacil (tigecycline)	Initial dose of 100mg *100mg/dose/50mg/vialx1dose = 2 vials* Followed by 50mg every 12 hours *50mg/dose/50mg/vial = 1vial/dose* *1vial/dosex2doses/day = 2vials/day* **2vials initial dose + followed by 1vial = 3vials 1st day*	14 days	3 vials* **Daily limit allows for maximum quantity needed for first day of treatment*	50mg per vial
Vancomycin inj vials, bottles	2 grams divided either as 500mg every 6 hours *4doses/dayx1vial/dose = 4vials/day* or 1 g every 12 hours *2doses/dayx1vial/dose = 2vials/day* [oral: 125mg to 2gm in four divided doses for ten days]	14 days	4 vials	250mg per vial 500mg per vial 750mg per vial
			2 vials	1gm per vial 1.25gm per vial 1.5gm per vial
			0.3 bottles	5gm per bottle 10gm per bottle
Vfend IV (voriconazole inj)	Loading dose 6mg/kg every 12 hours for the first 24 hours *6mgx139.9kg/dose = 839.4mg/dose* *839.4mg/dose/200mg/vial = 4.2vials/dose* *5vials/dosex2doses = 10 vials 1st day* Maintenance dose 4mg/kg every 12 hours *4mgx139.9kg/dose = 559.6mg/dose* *559.6mg/dose/200mg/vial = 2.8vials/dose* *3vials/dosex2doses/day = 6vials/day*	14 days	10 vials* **Daily limit allows for maximum quantity needed for first day of treatment*	200mg per vial

**If the patient is requesting more than the initial quantity limit, the claim will reject with a message indicating that a prior authorization is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug will not be used intranasally or in a footbath

AND

- The requested drug is being used for an FDA-approved indication or an indication supported in the compendia of current literature (examples: AHFS, Micromedex, current accepted guidelines)

AND

- The requested drug is being used to treat an infection proven or strongly suspected to be caused by susceptible microorganisms

AND

- The patient is unable to switch to oral therapy

  OR

- The request is for vancomycin to be taken orally for the treatment of C. difficile associated diarrhea or for staphylococcal enterocolitis

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External Review: 02/2004, 12/2004, 12/2005, 12/2006, 02/2008, 04/2009, 12/2009, 02/2011, 02/2012, 12/2012, 10/2013, 10/2014, 10/2015, 10/2016, 10/2017, 10/2018, 10/2019, 10/2020, 10/2021, 03/2022, 10/2022

CRITERIA FOR APPROVAL

1	Does the patient have a diagnosis of acne vulgaris? [If yes, go to 2. If no, then no further questions.]	Yes	No
2	Is the requested drug being prescribed to treat a body surface area that requires more than any of the following per 4 weeks: A) 120 milliliters of adapalene topical solution, B) 45 grams of Differin cream or gel (adapalene cream, gel), C) 59 milliliters of Differin lotion (adapalene lotion), D) 28 swabs of adapalene topical solution? [If yes, go to 3. If no, then no further questions.]	Yes	No
3	Does the patient require MORE than the plan allowance per 4 weeks of any of the following: A) 240 milliliters of adapalene topical solution, B) 90 grams of Differin cream or gel (adapalene cream, gel), C) 118 milliliters of Differin lotion (adapalene lotion), D) 56 swabs of adapalene topical solution? [No further questions] [RPh Note: If yes, then deny and enter a partial approval per Quantity Limit Chart.]	Yes	No

Mapping Instructions			
	Yes	**No**	**DENIAL REASONS**
1.	Go to 2	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have acne vulgaris. Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]
2.	Go to 3	Approve, 12 Months, See Quantity Limit Chart Column A for a 4 week limit Column B for a 12 week limit	
3.	Deny, RPh Note: For the denial verbiage, only include the requested drug. Remove all the other drugs from the verbiage.	Approve, 12 Months, See Quantity Limit Chart Column C for a 4 week limit	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to: - 240 mL per month of adapalene topical solution - 90 grams per month of Differin cream (adapalene cream) - 90 grams per month of Differin gel (adapalene gel) - 118 mL per month of Differin lotion (adapalene lotion) - 56 swabs per month of adapalene topical solution (swab) Your request has been partially approved. You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity]

STEP THERAPY CRITERIA

CATEGORY **ANTIDIABETIC AGENTS**

DRUG CLASS
BRAND NAME
(generic)

AMYLIN ANALOG:

SYMLINPEN
(pramlintide acetate)

GLUCAGON-LIKE PEPTIDE-1 (GLP-1) RECEPTOR AGONIST:

ADLYXIN
(lixisenatide)

BYDUREON BCISE
(exenatide extended-release)

BYETTA
(exenatide)

OZEMPIC
(semaglutide)

RYBELSUS
(semaglutide)

TRULICITY
(dulaglutide)

VICTOZA
(liraglutide)

GLUCOSE-DEPENDENT INSULINOTROPIC POLYPEPTIDE (GIP) RECEPTOR AND GLUCAGON-LIKE PEPTIDE-1 (GLP-1) RECEPTOR AGONIST:

MOUNJARO
(tirzepatide)

SODIUM-GLUCOSE COTRANSPORTER 2 (SGLT2) INHIBITOR:

BRENZAVVY
(bexagliflozin)

FARXIGA
(dapagliflozin)

INVOKANA
(canagliflozin)

JARDIANCE
(empagliflozin)

STEGLATRO
(ertugliflozin)

SGLT2 INHIBITOR / METFORMIN:

INVOKAMET
(canagliflozin / metformin HCl)

INVOKAMET XR
(canagliflozin /metformin HCl extended-release)

SEGLUROMET
(ertugliflozin / metformin HCl)

SYNJARDY
(empagliflozin / metformin HCl)

SYNJARDY XR
(empagliflozin / metformin HCl extended-release)

XIGDUO XR
(dapagliflozin / metformin HCl)

SGLT2 INHIBITOR / DIPEPTIDYL PEPTIDASE-4 (DPP-4) INHIBITOR:

GLYXAMBI
(empagliflozin / linagliptin)

QTERN
(dapagliflozin / saxagliptin)

STEGLUJAN
(ertugliflozin / sitagliptin)

SGLT2 INHIBITOR / DPP4 INHIBITOR / METFORMIN:

TRIJARDY XR
(empagliflozin / linagliptin / metformin HCl extended-release)

LONG ACTING INSULIN/GLP-1 RECEPTOR AGONIST:

SOLIQUA

(insulin glargine / lixisenatide injection)

XULTOPHY
(insulin degludec / liraglutide injection)

Status: CVS Caremark® Criteria
Type: Initial Step Therapy; Post Step Therapy Prior Authorization

POLICY

FDA APPROVED INDICATIONS

AMYLIN ANALOG:

SymlinPen

SymlinPen is indicated as an adjunctive treatment in patients with type 1 or type 2 diabetes who use mealtime insulin therapy and who have failed to achieve desired glucose control despite optimal insulin therapy.

GLP-1 RECEPTOR AGONIST:

Adlyxin

Adlyxin is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Limitations of Use

- Adlyxin has not been studied in patients with chronic pancreatitis or a history of unexplained pancreatitis. Consider other antidiabetic therapies in patients with a history of pancreatitis.
- Adlyxin should not be used in patients with type 1 diabetes mellitus.
- Adlyxin has not been studied in patients with gastroparesis and is not recommended in patients with gastroparesis.

Bydureon BCise

Bydureon BCise is indicated as an adjunct to diet and exercise to improve glycemic control in adults and pediatric patients aged 10 years and older with type 2 diabetes mellitus.

Limitations of Use

- Bydureon BCise is not recommended as first-line therapy for patients who have inadequate glycemic control on diet and exercise because of the uncertain relevance of the rat thyroid C-cell tumor findings to humans.
- Bydureon BCise is not indicated for use in patients with type 1 diabetes mellitus.
- Bydureon BCise is an extended-release formulations of exenatide and should not be used with other products containing the active ingredient exenatide.
- Bydureon BCise has not been studied in patients with a history of pancreatitis. Consider other antidiabetic therapies in patients with a history of pancreatitis.

Byetta

Byetta is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Limitations of Use

- Byetta is not indicated for use in patients with type 1 diabetes.
- Byetta contains exenatide and should not be used with other products containing the active ingredient exenatide. Byetta has not been studied in patients with a history of pancreatitis. Consider other antidiabetic therapies in patients with a history of pancreatitis.

Ozempic

Ozempic is indicated:

- as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.
- to reduce the risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction or non-fatal stroke) in adults with type 2 diabetes mellitus and established cardiovascular disease.

Limitations of Use

- Ozempic has not been studied in patients with a history of pancreatitis. Consider other antidiabetic therapies in patients with a history of pancreatitis.
- Ozempic is not indicated for use in patients with type 1 diabetes mellitus.

Rybelsus

Rybelsus is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Limitations of Use

- Rybelsus has not been studied in patients with a history of pancreatitis. Consider other antidiabetic therapies in patients with a history of pancreatitis.
- Rybelsus is not indicated for use in patients with type 1 diabetes mellitus.

Trulicity

Trulicity is indicated:

- As an adjunct to diet and exercise to improve glycemic control in adults and pediatric patients 10 years of age and older with type 2 diabetes mellitus.
- To reduce the risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke) in adults with type 2 diabetes mellitus who have established cardiovascular disease or multiple cardiovascular risk factors.

Limitations of Use

- Trulicity has not been studied in patients with a history of pancreatitis. Consider other antidiabetic therapies in patients with a history of pancreatitis.
- Trulicity should not be used in patients with type 1 diabetes mellitus.
- Trulicity has not been studied in patients with severe gastrointestinal disease, including severe gastroparesis and is therefore not recommended in these patients.

Victoza

Victoza is indicated:

- as an adjunct to diet and exercise to improve glycemic control in patients 10 years and older with type 2 diabetes mellitus.
- to reduce the risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke) in adults with type 2 diabetes mellitus and established cardiovascular disease.

Limitations of Use

- Victoza should not be used in patients with type 1 diabetes mellitus.
- Victoza contains liraglutide and should not be coadministered with other liraglutide-containing products.

GIP/GLP-1 RECEPTOR AGONIST:

Mounjaro

Mounjaro is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Limitations of Use

- Mounjaro has not been studied in patients with a history of pancreatitis.
- Mounjaro is not indicated for use in patients with type 1 diabetes mellitus.

SGLT2 INHIBITOR:

Brenzavvy

Brenzavvy is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Limitations of Use

Brenzavvy is not recommended in patients with type 1 diabetes mellitus. It may increase the risk of diabetic ketoacidosis in these patients.

Farxiga

Farxiga (dapagliflozin) is indicated:

- To reduce the risk of sustained eGFR decline, end-stage kidney disease, cardiovascular death, and hospitalization for heart failure in adults with chronic kidney disease at risk of progression.

- To reduce the risk of cardiovascular death, hospitalization for heart failure, and urgent heart failure visits in adults with heart failure.
- To reduce the risk of hospitalization for heart failure in adults with type 2 diabetes mellitus and either established cardiovascular disease or multiple cardiovascular risk factors.
- As an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Limitations of Use

- Farxiga is not recommended for patients with type 1 diabetes mellitus. It may increase the risk of diabetic ketoacidosis in these patients
- Farxiga is not recommended for use to improve glycemic control in adults with type 2 diabetes mellitus with an eGFR less than 45 mL/min/1.73 m^2. Farxiga is likely to be ineffective in this setting based upon its mechanism of action.
- Farxiga is not recommended for the treatment of chronic kidney disease in patients with polycystic kidney disease or patients requiring or with a recent history of immunosuppressive therapy for kidney disease. Farxiga is not expected to be effective in these populations.

Invokana

Invokana (canagliflozin) is indicated:

- as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.
- to reduce the risk of major adverse cardiovascular events (cardiovascular death, nonfatal myocardial infarction and nonfatal stroke) in adults with type 2 diabetes mellitus and established cardiovascular disease (CVD).
- to reduce the risk of end-stage kidney disease (ESKD), doubling of serum creatinine, cardiovascular (CV) death, and hospitalization for heart failure in adults with type 2 diabetes mellitus and diabetic nephropathy with albuminuria greater than 300 mg/day.

Limitations of Use

Invokana is not recommended in patients with type 1 diabetes mellitus. It may increase the risk of diabetic ketoacidosis in these patients.

Invokana is not recommended for use to improve glycemic control in adults with type 2 diabetes mellitus with an eGFR less than 30 mL/min/1.73m^2. Invokana is likely to be ineffective in this setting based upon its mechanism of action.

Jardiance

Jardiance is indicated:

- to reduce the risk of cardiovascular death and hospitalization for heart failure in adults with heart failure.
- to reduce the risk of cardiovascular death in adult patients with type 2 diabetes mellitus and established cardiovascular disease.
- as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus,

Limitation of Use

Jardiance is not recommended in patients with type 1 diabetes mellitus. It may increase the risk of diabetic ketoacidosis in these patients.

Jardiance is not recommended for use to improve glycemic control in adults with type 2 diabetes mellitus with an eGFR less than 30 mL/min/1.73 m2. Jardiance is likely to be ineffective in this setting based upon its mechanism of action.

Steglatro

Steglatro is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Limitations of Use

Not recommended in patients with type 1 diabetes mellitus. It may increase the risk of diabetic ketoacidosis in these patients.

SGLT2 INHIBITOR / METFORMIN:

Invokamet, Invokamet XR

Invokamet and Invokamet XR are a combination of canagliflozin and metformin hydrochloride (HCl) indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Canagliflozin is indicated to reduce the risk of major adverse cardiovascular events (cardiovascular death, nonfatal myocardial infarction and nonfatal stroke) in adults with type 2 diabetes mellitus and established cardiovascular disease (CVD).

Canagliflozin is indicated to reduce the risk of end-stage kidney disease (ESKD), doubling of serum creatinine, cardiovascular (CV) death, and hospitalization for heart failure in adults with type 2 diabetes mellitus and diabetic nephropathy with albuminuria greater than 300 mg/day.

Limitations of Use
Invokamet/Invokamet XR is not recommended in patients with type 1 diabetes mellitus. It may increase the risk of diabetic ketoacidosis in these patients.

Segluromet

Segluromet is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Limitations of Use
Not recommended in patients with type 1 diabetes mellitus. It may increase the risk of diabetic ketoacidosis in these patients.

Synjardy, Synjardy XR

Synjardy and Synjardy XR are a combination of empagliflozin and metformin hydrochloride (HCl) indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.
Empagliflozin, when used as a component of Synjardy/Synjardy XR, is indicated in adults with type 2 diabetes mellitus to reduce the risk of:

- Cardiovascular death in adults with established cardiovascular disease.
- Cardiovascular death and hospitalization for heart failure in adults with heart failure.

Limitation of Use

- Synjardy/Synjardy XR are not recommended for patients with type 1 diabetes mellitus. It may increase the risk of diabetic ketoacidosis in these patients.
- Because of the metformin component, Synjardy/Synjardy XR is not recommended for use in patients with heart failure without type 2 diabetes mellitus.

Xigduo XR

Xigduo XR is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.
Dapagliflozin is indicated to reduce:

- the risk of hospitalization for heart failure in adults with type 2 diabetes mellitus and established cardiovascular disease (CVD) or multiple cardiovascular (CV) risk factors.
- the risk of cardiovascular death and hospitalization for heart failure in adults with heart failure (NYHA class II-IV) with reduced ejection fraction.
- the risk of sustained estimated glomerular filtration rate decline, end-stage kidney disease, cardiovascular death, and hospitalization for heart failure in adults with chronic kidney disease at risk of progression.

Limitation of Use

- Xigduo XR is not recommended for patients with type 1 diabetes mellitus. It may increase the risk of diabetic ketoacidosis in these patients.
- Because of the metformin component, the use of Xigduo XR is limited to adults with type 2 diabetes for all indications.
- Xigduo XR is not recommended for the treatment of chronic kidney disease in patients with polycystic kidney disease or patients requiring or with a recent history of immunosuppressive therapy for kidney disease. Xigduo XR is not expected to be effective in these populations.

SGLT2 INHIBITOR / DPP-4 INHIBITOR:

Glyxambi

Glyxambi is a combination of empagliflozin and linagliptin indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.
Empagliflozin is indicated to reduce the risk of cardiovascular death in adults with type 2 diabetes mellitus and established cardiovascular disease.

Limitations of Use
Glyxambi is not recommended for patients with type 1 diabetes mellitus. It may increase the risk of diabetic ketoacidosis in these patients.
Glyxambi has not been studied in patients with a history of pancreatitis. It is unknown whether patients with a history of pancreatitis are at an increased risk for the development of pancreatitis while using Glyxambi.
Glyxambi is not recommended for use to improve glycemic control in adults with type 2 diabetes mellitus with an eGFR less than 30 ml/min/1.73m2. Glyxambi is likely to be ineffective in this setting based upon its mechanism of action.

Qtern

Qtern is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.
Limitations of Use
Qtern is not recommended for patients with type 1 diabetes mellitus. It may increase the risk of diabetic ketoacidosis in these patients.

Steglujan

Steglujan is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.
Limitations of Use

- Not recommended in patients with type 1 diabetes mellitus. It may increase the risk of diabetic ketoacidosis in these patients.
- Has not been studied in patients with a history of pancreatitis. It is unknown whether patients with a history of pancreatitis are at increased risk for the development of pancreatitis while using Steglujan.

SGLT2 INHIBITOR / DPP-4 INHIBITOR / METFORMIN:

Trijardy XR

Trijardy XR is a combination of empagliflozin, linagliptin, and metformin hydrochloride (HCl) indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.
Empagliflozin is indicated to reduce the risk of cardiovascular death in adults with type 2 diabetes mellitus and established cardiovascular disease.
Limitations of Use
Trijardy XR is not recommended for patients with type 1 diabetes mellitus. It may increase the risk of diabetic ketoacidosis in these patients.
Trijardy XR has not been studied in patients with a history of pancreatitis. It is unknown whether patients with a history of pancreatitis are at an increased risk for the development of pancreatitis while using Trijardy XR.

LONG ACTING INSULIN / GLP-1 RECEPTOR AGONIST:

Soliqua

Soliqua 100/33 is a combination of insulin glargine and lixisenatide and is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.
Limitations of Use:

- Soliqua 100/33 has not been studied in patients with a history of pancreatitis. Consider other antidiabetic therapies in patients with a history of pancreatitis.
- Soliqua 100/33 is not recommended for use in combination with any other product containing a GLP-1 receptor agonist.
- Soliqua 100/33 is not indicated for use in patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis.
- Soliqua 100/33 has not been studied in patients with gastroparesis and is not recommended in patients with gastroparesis.
- Soliqua 100/33 has not been studied in combination with prandial insulin.

Xultophy

Xultophy 100/3.6 is a combination of insulin degludec and liraglutide and is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.
Limitations of Use:

- Xultophy 100/3.6 is not recommended as first-line therapy for patients who have inadequate glycemic control on diet and exercise because of the uncertain relevance of the rodent C-cell tumor findings to humans.
- Xultophy 100/3.6 is not recommended for use in combination with any other product containing liraglutide or another GLP-1 receptor agonist.
- Xultophy 100/3.6 is not indicated for use in patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis.
- Xultophy 100/3.6 has not been studied in combination with prandial insulin.

INITIAL STEP THERAPY*

**Include Rx and OTC products unless otherwise stated.*

INITIAL STEP THERAPY For AMYLIN ANALOGS (SymlinPen):
If the patient has filled a prescription for at least a 30-day supply of a rapid-acting insulin or short-acting insulin or pre-mixed insulin [e.g., insulin aspart (Novolog), insulin glulisine (Apidra), insulin lispro (Humalog), insulin regular R (Afrezza, Humulin R, Novolin R)] within the past 120 days under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit. If the patient does not meet the initial step therapy criteria, then the claim will reject with a message indicating that a prior authorization (PA) is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

INITIAL STEP THERAPY For ALL OTHER TARGET DRUGS:
If the patient has filled a prescription for at least a 30-day supply of metformin within the past 180 days under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit. If the patient does not meet the initial step therapy criteria, then the claim will reject with a message indicating that a prior authorization (PA) is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

COVERAGE CRITERIA
The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has a diagnosis of type 2 diabetes mellitus **AND**
  - The patient has NOT been receiving a stable maintenance dose of the requested drug for at least 3 months **AND**
    - The patient experienced an inadequate treatment response, intolerance, or has a contraindication to metformin

    OR
    - The patient requires combination therapy AND has an A1C of 7.5 percent or greater

    OR
    - The request is for Farxiga (dapagliflozin), Invokana (canagliflozin), Jardiance (empagliflozin), Ozempic (semaglutide), Trulicity (dulaglutide), or Victoza (liraglutide) AND the patient has established cardiovascular disease

    OR
    - The request is for Invokana (canagliflozin) AND the patient has diabetic nephropathy with albuminuria greater than 300 mg per day

    OR
    - The request is for Trulicity (dulaglutide) or Farxiga (dapagliflozin) AND the patient has multiple cardiovascular risk factors

    OR
    - The request is for Farxiga (dapagliflozin) or Jardiance (empagliflozin) **AND**
      - The patient has a diagnosis of heart failure

    OR
    - The request is for Farxiga (dapagliflozin) **AND**
      - The patient has chronic kidney disease at risk of progression **AND**
        - The patient has an estimated glomerular filtration rate (eGFR) of 25 to 75 mL/min/1.73m2

        OR
        - The patient has a urine albumin creatinine ratio (UACR) between 200 and 5000 mg/g

        OR
        - The patient has an estimated glomerular filtration rate (eGFR) less than 25 mL/min/1.73m2 AND the request is for continuation of therapy

  OR
  - The patient has been receiving a stable maintenance dose of the requested drug for at least 3 months **AND**
    - The patient has demonstrated a reduction in A1C since starting this therapy

    OR

- The request is for Farxiga (dapagliflozin), Invokana (canagliflozin), Jardiance (empagliflozin), Ozempic (semaglutide), Trulicity (dulaglutide), or Victoza (liraglutide) AND the patient has established cardiovascular disease

OR

- The request is for Invokana (canagliflozin) AND the patient has diabetic nephropathy with albuminuria greater than 300 mg per day

OR

- The request is for Trulicity (dulaglutide) or Farxiga (dapagliflozin) AND the patient has multiple cardiovascular risk factors

OR

- The request is for Farxiga (dapagliflozin) or Jardiance (empagliflozin) **AND**
  - The patient has a diagnosis of heart failure

OR

- The request is for Farxiga (dapagliflozin) **AND**
  - The patient has chronic kidney disease at risk of progression **AND**
    - The patient has an estimated glomerular filtration rate (eGFR) of 25 to 75 mL/min/1.73m2

    OR
    - The patient has a urine albumin creatinine ratio (UACR) between 200 and 5000 mg/g

    OR
    - The patient has patient has an estimated glomerular filtration rate (eGFR) less than 25 mL/min/1.73m2 AND the request is for continuation of therapy

OR

- The request is for SymlinPen (pramlintide acetate) AND the patient has a diagnosis of type 1 or type 2 diabetes mellitus **AND**
  - The patient has NOT been receiving a stable maintenance dose of the requested drug for at least 3 months **AND**
    - The patient has failed to achieve desired glucose control despite receiving optimal insulin therapy, including mealtime insulin

  OR
  - The patient has been receiving a stable maintenance dose of the requested drug for at least 3 months **AND**
    - The patient has demonstrated a reduction in A1C since starting this therapy

OR

- The request is for Farxiga (dapagliflozin) **AND**
  - The patient has a diagnosis of heart failure

  OR
  - The patient has chronic kidney disease at risk of progression **AND**
    - The patient has an estimated glomerular filtration rate (eGFR) of 25 to 75 mL/min/1.73m2

    OR
    - The patient has a urine albumin creatinine ratio (UACR) between 200 and 5000 mg/g

    OR
    - The patient has an estimated glomerular filtration rate (eGFR) less than 25 mL/min/1.73m2 AND the request is for continuation of therapy

OR

- The request is for Jardiance (empagliflozin) **AND**
  - The patient has a diagnosis of heart failure

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QUANTITY LIMIT CRITERIA

DRUG CLASS **ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD) AGENTS**

BRAND NAME*
(generic)

AMPHETAMINES:

ADZENYS (ALL PRODUCTS)
(amphetamine)

DYANAVEL (ALL PRODUCTS)
(amphetamine)

EVEKEO (ALL PRODUCTS)
(amphetamine)

AMPHETAMINE MIXTURES:

ADDERALL (ALL PRODUCTS)
(amphetamine mixture)

MYDAYIS (ALL PRODUCTS)
(amphetamine mixture)

DEXMETHYLPHENIDATES:

AZSTARYS (ALL PRODUCTS)
(serdexmethylphenidate / dexmethylphenidate)

FOCALIN (ALL PRODUCTS)
(dexmethylphenidate)

DEXTROAMPHETAMINES:

DEXEDRINE (ALL PRODUCTS)
(dextroamphetamine)

(dextroamphetamine) (ALL PRODUCTS)

PROCENTRA (ALL PRODUCTS)
(dextroamphetamine)

XELSTRYM (ALL PRODUCTS)
(dextroamphetamine)

ZENZEDI (ALL PRODUCTS)
(dextroamphetamine)

LISDEXAMFETAMINES:

VYVANSE (ALL PRODUCTS)
(lisdexamfetamine)

METHAMPHETAMINES:

DESOXYN (ALL PRODUCTS)
(methamphetamine)

METHYLPHENIDATES:

ADHANSIA (ALL PRODUCTS)
(methylphenidate)

APTENSIO (ALL PRODUCTS)
(methylphenidate)

CONCERTA (ALL PRODUCTS)
(methylphenidate)

COTEMPLA (ALL PRODUCTS)
(methylphenidate)

DAYTRANA (ALL PRODUCTS)
(methylphenidate)

JORNAY (ALL PRODUCTS)
(methylphenidate)

METHYLIN (ALL PRODUCTS)
(methylphenidate)

(methylphenidate) (ALL PRODUCTS)

QUILLICHEW (ALL PRODUCTS)
(methylphenidate)

QUILLIVANT (ALL PRODUCTS)
(methylphenidate)

RELEXXII (ALL PRODUCTS)
(methylphenidate)

RITALIN (ALL PRODUCTS)
(methylphenidate)

SELECTIVE NOREPINEPHRINE REUPTAKE INHIBITORS:
QELBREE (ALL PRODUCTS)
(viloxazine)

STRATTERA (ALL PRODUCTS)
(atomoxetine)

Status: CVS Caremark Criteria
Type: Quantity Limit ***Ref # 682-H***

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Adderall XR, Daytrana, Focalin, Focalin XR, Methylphenidate CD, QuilliChew ER, Quillivant XR, Strattera
These products are indicated for the treatment of Attention Deficit Hyperactivity Disorder (ADHD).

Adderall
These products are indicated for the treatment of Attention Deficit Hyperactivity Disorder (ADHD) and Narcolepsy.

Adhansia XR, Adzenys ER, Adzenys XR-ODT, Aptensio XR, Azstarys, Dyanavel XR, Jornay PM
These products are indicated for the treatment of Attention Deficit Hyperactivity Disorder (ADHD) in patients 6 years and older.

Concerta, Methylphenidate Osmotic Extended-Release
These products are indicated for the treatment of Attention Deficit Hyperactivity Disorder (ADHD) in children 6 years of age and older, adolescents, and adults up to the age of 65.

Cotempla XR-ODT
Cotempla XR-ODT is indicated for the treatment of Attention Deficit Hyperactivity Disorder (ADHD) in pediatric patients 6 to 17 years of age.

Desoxyn
Desoxyn tablets are indicated for Attention Deficit Disorder with Hyperactivity (ADHD) as an integral part of a total treatment program which typically includes other remedial measures (psychological, educational, social) for a stabilizing effect in children over 6 years of age with a behavioral syndrome characterized by the following group of developmentally inappropriate symptoms: moderate to severe distractibility, short attention span, hyperactivity, emotional lability, and impulsivity.

Dexedrine Spansule
Narcolepsy
Attention Deficit Disorder with Hyperactivity (ADHD) as an integral part of a total treatment program that typically includes other measures (psychological, educational, social) for patients (ages 6 years to 16 years) with this syndrome.

Evekeo
Narcolepsy
Attention Deficit Disorder with Hyperactivity (ADHD) as an integral part of a total treatment program which typically includes other remedial measures (psychological, educational, social) for a stabilizing effect in children with a behavioral syndrome characterized by the following group of developmentally inappropriate symptoms: moderate to severe distractibility, short attention span, hyperactivity, emotional lability, and impulsivity.
Exogenous Obesity as a short term (a few weeks) adjunct in a regimen of weight reduction based on caloric restriction for patients refractory to alternative therapy, e.g., repeated diets, group programs, and other drugs. The limited usefulness of amphetamines should be weighed against possible risks inherent in use of the drug.

Evekeo ODT
Evekeo ODT is indicated for the treatment of Attention Deficit Hyperactivity Disorder (ADHD) in pediatric patients 3 to 17 years of age.

Methylin Oral Solution, Methylphenidate, Methylphenidate Extended-Release, Ritalin/Ritalin SR
Attention Deficit Hyperactivity Disorders (ADHD) in pediatric patients 6 years and older and adults.
Narcolepsy

Methylphenidate Chewable Tablets
Narcolepsy
Attention Deficit Disorders as an integral part of a total treatment program which typically includes other remedial measures (psychological, educational, social) for a stabilizing effect in children with a behavioral syndrome characterized by the following group of developmentally inappropriate symptoms: moderate to severe distractibility, short attention span, hyperactivity, emotional lability, and impulsivity.

Mydayis
Mydayis is indicated for the treatment of Attention Deficit Hyperactivity Disorder (ADHD) in patients 13 years and older.
Limitations of Use
Pediatric patients 12 years and younger experienced higher plasma exposure than patients 13 years and older at the same dose, and experienced higher rates of adverse reactions, mainly insomnia and decreased appetite.

Dextroamphetamine Tablets, ProCentra, Zenzedi
Narcolepsy
Attention Deficit Disorder with Hyperactivity (ADHD) as an integral part of a total treatment program which typically includes other remedial measures (psychological, educational, social) for a stabilizing effect in pediatric patients (ages 3 to 16 years) with a behavioral syndrome characterized by the following group of developmentally inappropriate symptoms: moderate to severe distractibility, short attention span, hyperactivity, emotional lability, and impulsivity.

Qelbree
Qelbree is indicated for the treatment of Attention Deficit Hyperactivity Disorder (ADHD) in adults and pediatric patients 6 years and older.

Relexxii
Relexxii is indicated for the treatment of Attention Deficit Hyperactivity Disorder (ADHD) in adults (up to the age of 65 years) and pediatric patients 6 years of age and older.

Ritalin LA
Ritalin LA is indicated for the treatment of Attention Deficit Hyperactivity Disorder (ADHD) in pediatric patients 6 to 12 years of age.

Vyvanse
Vyvanse is indicated for the treatment of:

- Attention Deficit Hyperactivity Disorder (ADHD) in adults and pediatric patients 6 years and older
- Moderate to Severe Binge-Eating Disorder (BED) in adults
- Limitation of Use
  Pediatric patients with ADHD younger than 6 years of age experienced more long-term weight loss than patients 6 years and older.
  Vyvanse is not indicated or recommended for weight loss. Use of other sympathomimetic drugs for weight loss has been associated with serious cardiovascular adverse events. The safety and effectiveness of Vyvanse for the treatment of obesity have not been established.

Xelstrym
Xelstrym is indicated for the treatment of Attention Deficit Hyperactivity Disorder (ADHD) in adults and pediatric patients 6 years and older.

Limitations of Use
Pediatric patients younger than 6 years of age experienced more long-term weight loss than patients 6 years and older.

LIMIT CRITERIA
Limits do not accumulate together, patient is allowed the maximum limit for each drug and strength

Drug	Maximum Dose/24 hours (ADHD only)[1-39]	1 Month Limit*	3 Month Limit*
Adderall 5 mg, 7.5 mg, 10 mg, 12.5 mg	40 mg	90 tabs/25 days	270 tabs/75 days
Adderall 15 mg, 20 mg		60 tabs/25 days	180 tabs/75 days
Adderall 30 mg		30 tabs/25 days	90 tabs/75 days
Adderall XR 5 mg, 10 mg	30 mg	90 caps/25 days	270 caps/75 days
Adderall XR 15 mg, 20 mg, 25 mg, 30 mg		30 caps/25 days	90 caps/75 days
Adhansia XR 25 mg, 35 mg, 45 mg	100 mg	60 caps/25 days	180 caps/75 days
Adhansia XR 55 mg, 70 mg, 85 mg		30 caps/25 days	90 caps/75 days
Adzenys ER oral suspension 1.25 mg/mL	18.8 mg	450 mL/25 days	1350 mL/75 days
Adzenys XR-ODT 3.1 mg, 6.3 mg, 9.4 mg	18.8 mg	60 tabs/25 days	180 tabs/75 days
Adzenys XR-ODT 12.5 mg, 15.7 mg. 18.8 mg		30 tabs/25 days	90 tabs/75 days
Aptensio XR 10 mg, 15 mg, 20 mg, 30 mg	60 mg	60 caps/25 days	180 caps/75 days
Aptensio XR 40 mg, 50 mg, 60 mg		30 caps/25 days	90 caps/75 days
Azstarys 26.1 mg/5.2 mg, 39.2 mg/7.8 mg, 52.3 mg/10.4 mg	52.3 mg/10.4 mg	30 caps/25 days	90 caps/75 days
Concerta 18 mg, 27 mg, 36 mg	72 mg	60 tabs/25 days	180 tabs/75 days
Concerta 54 mg		30 tabs/25 days	90 tabs/75 days
Cotempla XR 8.6 mg, 17.3 mg, 25.9 mg	51.8 mg	60 tabs/25 days	180 tabs/75 days
Daytrana Patch 10 mg, 15 mg, 20 mg, 30 mg	30 mg	30 patches/25 days	90 patches/75 days
Desoxyn 5 mg	25 mg	150 tabs/25 days	450 tabs/75 days
Dexedrine Spansule 5 mg, 10 mg	40 mg	120 caps/25 days	360 caps/75 days
Dexedrine Spansule 15 mg		60 caps/25 days	180 caps/75 days
Dextroamphetamine 5 mg, 10 mg	40 mg	120 tabs/25 days	360 tabs/75 days

Dyanavel XR oral suspension 2.5 mg/mL	20 mg	240 mL/25 days	720 mL/75 days
Dyanavel XR tablets 5 mg, 10 mg		60 tabs/25 days	180 tabs/75 days
Dyanavel XR tablets 15 mg, 20 mg		30 tabs/25 days	90 tabs/75 days
Evekeo 5 mg, 10 mg	40 mg	120 tabs/25 days	360 tabs/75 days
Evekeo ODT 2.5 mg, 5 mg, 10 mg	40 mg	120 tabs/25 days	360 tabs/75 days
Evekeo ODT 15 mg, 20 mg		60 tabs/25 days	180 tabs/75 days
Focalin 2.5 mg, 5 mg	20 mg	120 tabs/25 days	360 tabs/75 days
Focalin 10 mg		60 tabs/25 days	180 tabs/75 days
Focalin XR 5 mg, 10 mg, 15 mg, 20 mg	40 mg	60 caps/25 days	180 caps/75 days
Focalin XR 25 mg, 30 mg, 35 mg, 40 mg		30 caps/25 days	90 caps/75 days
Jornay PM 20 mg, 40 mg	100 mg	60 caps/25 days	180 caps/75 days
Jornay PM 60 mg, 80 mg, 100 mg		30 caps/25 days	90 caps/75 days
Methylphenidate CD 10 mg, 20 mg, 30 mg	60 mg	60 caps/25 days	180 caps/75 days
Methylphenidate CD 40 mg, 50 mg, 60 mg		30 caps/25 days	90 caps/75 days
Methylphenidate chewable tablets 2.5 mg, 5 mg, 10 mg	60 mg	180 tabs/25 days	540 tabs/75 days
Methylphenidate 5 mg, 10 mg	60 mg	180 tabs/25 days	540 tabs/75 days
Methylphenidate 20 mg		90 tabs/25 days	270 tabs/75 days
Methylphenidate ER 10 mg, 20 mg	60 mg	90 tabs/25 days	270 tabs/75 days
Methylphenidate oral solution 5 mg/5 mL	60 mg	1800 mL/25 days	5400 mL/75 days
Methylphenidate oral solution 10 mg/5 mL		900 mL/25 days	2,700 mL/75 days
Methylphenidate osmotic ER 45 mg, 63 mg, 72 mg	72 mg	30 tabs/25 days	90 tabs/75 days
Mydayis 12.5 mg, 25 mg	50 mg	60 caps/25 days	180 caps/75 days
Mydayis 37.5 mg, 50 mg		30 caps/25 days	90 caps/75 days
ProCentra oral solution 5 mg/5 mL	40 mg	1200 mL/25 days	3600 mL/75 days
Qelbree 100 mg, 150 mg, 200 mg	600 mg	90 caps/25 days	270 caps/75 days
QuilliChew ER 20 mg, 30 mg	60 mg	60 tabs/25 day	180 tabs/75 days

QuilliChew ER 40 mg		30 tabs/25 days	90 tabs/75 days
Quillivant XR oral suspension 25 mg/5 mL (5 mg/1 mL)	60 mg	360 mL/25 days	1080 mL/75 days
Relexxii 18 mg, 27 mg, 36 mg	72 mg	60 tabs/25 days	180 tabs/75 days
Relexxii 45 mg, 54 mg, 63 mg, 72 mg		30 tabs/25 days	90 tabs/75 days
Ritalin LA 10 mg, 20 mg, 30 mg	60 mg	60 caps/25 days	180 caps/75 days
Ritalin LA 40 mg, 60 mg		30 caps/25 days	90 caps/75 days
Strattera 10 mg, 18 mg, 25 mg	100 mg	120 caps/25 days	360 caps/75 days
Strattera 40 mg		60 caps/25 days	180 caps/75 days
Strattera 60 mg, 80 mg, 100 mg		30 caps/25 days	90 caps/75 days
Vyvanse 10 mg, 20 mg, 30 mg	70 mg	60 units/25 days	180 units/75 days
Vyvanse 40 mg, 50 mg, 60 mg, 70 mg		30 units/25 days	90 units/75 days
Xelstrym 4.5 mg, 9 mg, 13.5 mg, 18 mg	18 mg	30 transdermal systems/25 days	90 transdermal systems/75 days
Zenzedi 2.5 mg, 5 mg, 7.5 mg, 10 mg	40 mg	120 tabs/25 days	360 tabs/75 days
Zenzedi 15 mg, 20 mg		60 tabs/25 days	180 tabs/75 days
Zenzedi 30 mg		30 tabs/25 days	90 tabs/75 days
**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*			

RATIONALE

Amphetamines are indicated for the treatment of Attention-Deficit/Hyperactivity Disorder (ADHD) and for the treatment of narcolepsy; except for Adderall XR, Adzenys ER, Adzenys XR-ODT, Dyanavel XR, Evekeo ODT, Mydayis, Vyvanse, and Xelstrym which are not indicated for narcolepsy. Dexmethylphenidates are indicated for the treatment of ADHD. Methylphenidates are indicated for the treatment of ADHD and for the treatment of narcolepsy; except for Adhansia XR, Aptensio XR, Concerta, Cotempla XR-ODT, Daytrana, Jornay PM, methylphenidate CD, methylphenidate osmotic extended-release, QuilliChew ER, Quillivant XR, Relexxii, and Ritalin LA which are not indicated for narcolepsy. Desoxyn, Strattera, and Qelbree are indicated for the treatment of ADHD.[1-37]
Evekeo is also indicated for exogenous obesity as a short term (a few weeks) adjunct in a regimen of weight reduction based on caloric restriction for patients refractory to alternative therapy, e.g., repeated diets, group programs, and other drugs. The limited usefulness of amphetamines should be weighed against possible risks inherent in use of the drug.[15]

Vyvanse is also indicated for moderate to severe Binge-Eating Disorder (BED).[35]

Both the amphetamine and methylphenidate products are classified as Schedule II controlled substances by Federal regulation and have a high potential for abuse and misuse. The lowest effective doses are recommended.[1-39]

These initial limit criteria allow up to the FDA-approved maximum dose of the included products for the diagnosis of ADHD only. The limits are set to accommodate varying dosages utilizing higher strengths available at maximum recommended dosage. All applicable strengths have been included on the limit criteria. However, due to the availability of higher strengths, not all lower strengths reach the maximum daily dose. The initial quantity limits for methylphenidate immediate-

release, methylphenidate chewable tablets, methylphenidate extended-release (Ritalin SR) are the same for the FDA maximum approved daily doses for narcolepsy (60 mg). The initial quantity limits for Vyvanse are sufficient for quantities indicated to treat moderate-to-severe BED (70 mg/day). The initial quantity limit for Evekeo is sufficient for the short-term (i.e., a few weeks) treatment of exogenous obesity (30 mg/day).[1-37]

If the patient is requesting more than the initial quantity limit, then the system will reject with a message indicating that a prior authorization is required.

Additional post limit quantities are established for:

- Products that have off-label doses above the FDA maximum approved daily doses for ADHD
- Products that are indicated for narcolepsy, up to FDA maximum approved daily doses

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Written by:	UM Development (JK)
Date Written:	07/2011
Revised:	(MS) 11/2011, (JK) 04/2012; (MS) 11/2012; (RP) 08/2013 (added Zenzedi strengths); (MS) 11/2013, 05/2014 (added Zenzedi [dextroamphetamine] strengths 15 mg, 20 mg, 30 mg); (CF) 11/2014, 01/2015 (added Vyvanse 10 mg, added BED indication for Vyvanse), 02/2015 (added Evekeo), 05/2015 (added Aptensio XR), 05/2015 (added Ritalin LA 60 mg), 06/2015 (rationale), 10/2015 (added Dyanavel XR), 11/2015 (no clinical changes), 12/2015 (added QuilliChew ER), 01/2016 (added Adzenys XR-ODT); (KM) 11/2016 (no clinical changes, created separate entry for Zenzedi in target drug box and limit chart), 06/2017 (added Cotempla XR, Mydayis), 10/2017 (Added Adzenys ER); 11/2017 (no clinical changes), 01/2018 (added methylphenidate osmotic extended-release 72 mg), 08/2018 (added Jornay PM), 11/2018 (no clinical changes), 03/2019 (Added Adhansia XR), 07/2019 (Added Evekeo ODT); (RP) 11/2019 (no clinical changes), 11/2020 (no clinical changes), 03/2021 (Added Azstarys), 04/2021 (Added Qelbree, Evekeo ODT 2.5mg); (RZ) 11/2021 (added Dyanavel XR tablets), 11/2021 (removed brand Metadate), 04/2022 (Added Xelstrym, updated Qelbree limit); (MRS) 07/2022 (added new strengths of Relexxii), 11/2022 (added new strengths of methylphenidate osmotic ER to limit chart)
Reviewed:	Medical Affairs (KP) 08/2011, 11/2011; (LS) 11/2012; (DC) 08/2013; (LB) 11/2013; (SS) 05/2014; (DNC) 11/2014; (SES) 02/2015; (DNC) 05/2015; (ADA) 05/2015; (MM) 10/2015; (GAD) 12/2015; (AM) 07/2017, 10/2017, 01/2018; (GAD) 08/2018, 04/2019, (ME) 07/2019; (CHART) 11/27/2019, 12/03/2020, 03/18/2021, 04/22/2021, 12/02/2021, 04/14/2022, 05/19/2022, 08/04/2022, 12/01/2022 External Review: 08/2011, 02/2012, 02/2013, 02/2014, 02/2015, 02/2016, 02/2017, 08/2017, 10/2017, 12/2017, 02/2018, 10/2018, 02/2019, 06/2019 (FYI), 08/2019 (FYI), 02/2020, 02/2021, 03/2021, 05/2021, 02/2022, 06/2022 (FYI), 02/2023 (FYI)

QUANTITY LIMIT CRITERIA

BRAND NAME*
(generic)

AKYNZEO CAPSULES
(netupitant/palonosetron)

AKYNZEO INJECTION
(fosnetupitant/palonosetron)

Status: CVS Caremark Criteria
Type: Quantity Limit ***Ref # 1211-H***

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Akynzeo capsules is indicated in combination with dexamethasone in adults for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of cancer chemotherapy, including, but not limited to, highly emetogenic chemotherapy. Akynzeo capsules is a combination of palonosetron and netupitant: palonosetron prevents nausea and vomiting during the acute phase and netupitant prevents nausea and vomiting during both the acute and delayed phase after cancer chemotherapy.

Akynzeo for injection and Akynzeo injection are indicated in combination with dexamethasone in adults for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy. Akynzeo for injection is a combination of palonosetron and fosnetupitant, a prodrug of netupitant: palonosetron prevents nausea and vomiting during the acute phase and fosnetupitant prevents nausea and vomiting during both the acute and delayed phase after cancer chemotherapy.

Limitations of Use

Akynzeo for injection and Akynzeo injection have not been studied for the prevention of nausea and vomiting associated with anthracycline plus cyclophosphamide chemotherapy.

INITIAL LIMIT QUANTITY

Limits do not accumulate together; patient is allowed the maximum limit for each drug and strength

Drug	4 Week Limit*	12 Week Limit*
Akynzeo capsules (netupitant/palonosetron)	2 capsules / 21 days	Does Not Apply**
Akynzeo for injection (fosnetupitant/palonosetron lyophilized powder in single-dose vial for reconstitution)	2 vials / 21 days	Does Not Apply**
Akynzeo injection (fosnetupitant/palonosetron solution in single dose 20 mL vial)	40 mL / 21 days	Does Not Apply**

** The duration of 21 days is used for a 28-day fill period to allow time for refill processing.*
** These drugs are for short-term acute use; therefore, the mail limit will be the same as the retail limit. The intent is for prescriptions of the requested drug to be filled one month at a time, even if filled at mail order; there should be no 3 month supplies filled.*

RATIONALE

Akynzeo capsules is indicated in combination with dexamethasone in adults for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of cancer chemotherapy, including, but not limited to, highly emetogenic chemotherapy. Akynzeo for injection and Akynzeo injection are indicated in combination with dexamethasone in adults for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy.[1-3]

The recommended oral dosage in adults for highly emetogenic chemotherapy, including cisplatin-based chemotherapy, is one capsule of Akynzeo administered approximately 1 hour prior to the start of chemotherapy with dexamethasone 12 mg administered 30 minutes prior to chemotherapy on day 1; followed by dexamethasone 8 mg once daily on days 2 to 4. The recommended dosage in adults for anthracyclines and cyclophosphamide-based chemotherapy and chemotherapy not considered highly emetogenic is one capsule of Akynzeo approximately 1 hour prior to the start of chemotherapy with dexamethasone 12 mg administered 30 minutes prior to chemotherapy on day 1. Administration of dexamethasone on days 2 to 4 is not necessary.[1-3]

The recommended injection dosage in adults for highly emetogenic chemotherapy, including cisplatin-based chemotherapy, is one vial of Akynzeo administered approximately 30 minutes prior to the start of chemotherapy with dexamethasone 12 mg administered 30 minutes prior to chemotherapy on day 1; followed by dexamethasone 8 mg once daily on days 2 to 4. Akynzeo for injection and Akynzeo injection have not been studied for the prevention of nausea and vomiting associated with anthracycline plus cyclophosphamide chemotherapy.[1-3]

The limit allows a quantity sufficient for two chemotherapy cycles per month (i.e., one chemotherapy cycle every 2 weeks). If the patient is requesting more than the initial quantity limit, then the claim will reject with a message indicating that a prior authorization is required.

REFERENCES

1. Akynzeo [package insert]. Iselin, NJ: Helsinn Therapeutics (U.S.), Inc.; June 2021.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2022; Accessed November 14, 2022.
3. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed November 11, 2022.

Written by:	UM Development (RP)
Date Written:	10/2014
Revised:	01/2015; (MS) 01/2016 (no clinical changes), 01/2017 (no clinical changes), (ME) 01/2018 (no clinical changes), 05/2018 (added injection), 01/2019 (no clinical changes), 01/2020 (no clinical changes), 01/2021 (no clinical changes), (VS) 01/2022 (added Akynzeo injection and updated QL), (TM/KJ) 12/2022 (no clinical changes)
Reviewed:	Medical Affairs (SES) 10/2014, 01/2015; (JG) 01/2017, (ME) 05/2018, (CHART) 01/30/20, (CHART) 1/28/01, (CHART) 02/03/2022, 12/29/2022 External Review: 11/2014, 04/2015, 04/2016, 04/2017, 04/2018, 06/2018, 04/2019, 04/2020, 04/2021, 04/2022, 04/2023

PRIOR AUTHORIZATION CRITERIA

BRAND NAME
(generic)

AKYNZEO CAPSULES
(netupitant/palonosetron)

AKYNZEO INJECTION
(fosnetupitant/palonosetron)

Status: CVS Caremark Criteria
Type: Post Limit Prior Authorization

POLICY

FDA-APPROVED INDICATIONS

Akynzeo capsules is indicated in combination with dexamethasone in adults for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of cancer chemotherapy, including, but not limited to, highly emetogenic chemotherapy. Akynzeo capsules is a combination of palonosetron and netupitant: palonosetron prevents nausea and vomiting during the acute phase and netupitant prevents nausea and vomiting during both the acute and delayed phase after cancer chemotherapy.

Akynzeo for injection and Akynzeo injection are indicated in combination with dexamethasone in adults for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy. Akynzeo for injection is a combination of palonosetron and fosnetupitant, a prodrug of netupitant: palonosetron prevents nausea and vomiting during the acute phase and fosnetupitant prevents nausea and vomiting during both the acute and delayed phase after cancer chemotherapy.

Limitations of Use
Akynzeo for injection and Akynzeo injection have not been studied for the prevention of nausea and vomiting associated with anthracycline plus cyclophosphamide chemotherapy.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of cancer chemotherapy

Quantity Limits apply.
4 capsules of Akynzeo per 21 days*; 4 vials of Akynzeo for injection per 21 days*; 80 mL of Akynzeo injection per 21 days*. No 3 month supplies should be filled.
** The duration of 21 days is used for a 28-day fill period to allow time for refill processing.*
** These drugs are for short-term acute use; therefore, the mail limit will be the same as the retail limit. The intent is for prescriptions of the requested drug to be filled one month at a time, even if filled at mail order; there should be no 3 month supplies filled.*

REFERENCES

1. Akynzeo [package insert]. Iselin, NJ: Helsinn Therapeutics (U.S.), Inc.; June 2021.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2022; Accessed November 14, 2022.
3. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed November 11, 2022.

4. National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology. Antiemesis. Version 2.2022. Available at: https://www.nccn.org/professionals/physician_gls/pdf/antiemesis.pdf. Accessed November 16, 2022.
5. American Society of Clinical Oncology. What is Chemotherapy? https://www.cancer.net/navigating-cancer-care/how-cancer-treated/chemotherapy/what-chemotherapy. May 2022. Accessed November 16, 2022.
6. American Cancer Society. How is Chemotherapy Used to Treat Cancer? https://www.cancer.org/treatment/treatments-and-side-effects/treatment-types/chemotherapy/how-is-chemotherapy-used-to-treat-cancer.html November 2019. Accessed November 16, 2022.

Written by:	UM Development (RP)
Date Written:	10/2014
Revised:	01/2015, 05/2015 (added denial reasons); (MS) 01/2016 (no clinical changes), 01/2017, (ME) 01/2018 (no clinical changes) (ME) 05/2018 (added injection), (ME) 01/2019 (no clinical changes), 01/2020 (no clinical changes), 01/2021 (no clinical changes); (PM) 08/2021 (updated denial verbiage), (VS) 01/2021 (added Akynzeo injection and updated QL), (TM/KJ) 12/2022 (no clinical changes)
Reviewed:	Medical Affairs (SES) 10/2014, 01/2015; (JG) 01/2017, (ME) 05/2018, (CHART) 01/30/20, (CHART) 1/28/01, (CHART) 02/03/2022, 12/29/2022 External Review: 11/2014, 04/2015, 04/2016, 04/2017, 04/2018, 06/2018, 04/2019, 04/2020, 04/2021, 04/2022, 04/2023

PRIOR AUTHORIZATION CRITERIA

DRUG CLASS **ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD) AGENTS**

BRAND NAME*
(generic)

AMPHETAMINES:

ADZENYS (ALL PRODUCTS)
(amphetamine)

DYANAVEL (ALL PRODUCTS)
(amphetamine)

EVEKEO (ALL PRODUCTS)
(amphetamine)

AMPHETAMINE MIXTURES:

ADDERALL (ALL PRODUCTS)
(amphetamine mixture)

MYDAYIS (ALL PRODUCTS)
(amphetamine mixture)

DEXMETHYLPHENIDATES:

AZSTARYS (ALL PRODUCTS)
(serdexmethylphenidate / dexmethylphenidate)

FOCALIN (ALL PRODUCTS)
(dexmethylphenidate)

DEXTROAMPHETAMINES:

DEXEDRINE (ALL PRODUCTS)
(dextroamphetamine)

(dextroamphetamine) (ALL PRODUCTS)

PROCENTRA (ALL PRODUCTS)
(dextroamphetamine)

XELSTRYM (ALL PRODUCTS)
(dextroamphetamine)

ZENZEDI (ALL PRODUCTS)
(dextroamphetamine)

LISDEXAMFETAMINES:

VYVANSE (ALL PRODUCTS)
(lisdexamfetamine)

METHAMPHETAMINES:

DESOXYN (ALL PRODUCTS)
(methamphetamine)

METHYLPHENIDATES:

ADHANSIA (ALL PRODUCTS)
(methylphenidate)

APTENSIO (ALL PRODUCTS)
(methylphenidate)

CONCERTA (ALL PRODUCTS)
(methylphenidate)

COTEMPLA (ALL PRODUCTS)
(methylphenidate)

DAYTRANA (ALL PRODUCTS)
(methylphenidate)

JORNAY (ALL PRODUCTS)
(methylphenidate)

METHYLIN (ALL PRODUCTS)
(methylphenidate)

(methylphenidate) (ALL PRODUCTS)

QUILLICHEW (ALL PRODUCTS)
(methylphenidate)

QUILLIVANT (ALL PRODUCTS)
(methylphenidate)

RELEXXII (ALL PRODUCTS)
(methylphenidate)

RITALIN (ALL PRODUCTS)
(methylphenidate)

SELECTIVE NOREPINEPHRINE REUPTAKE INHIBITORS:

QELBREE (ALL PRODUCTS)

(viloxazine)

STRATTERA (ALL PRODUCTS)
(atomoxetine)

Status: CVS Caremark Criteria ***Ref # 1218-J***
Type: Post Limit Prior Authorization ***Ref # MMT 683-J***

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Adderall XR, Daytrana, Focalin, Focalin XR, Methylphenidate CD, QuilliChew ER, Quillivant XR, Strattera
These products are indicated for the treatment of Attention Deficit Hyperactivity Disorder (ADHD).

Adderall
These products are indicated for the treatment of Attention Deficit Hyperactivity Disorder (ADHD) and Narcolepsy.

Adhansia XR, Adzenys ER, Adzenys XR-ODT, Aptensio XR, Azstarys, Dyanavel XR, Jornay PM
These products are indicated for the treatment of Attention Deficit Hyperactivity Disorder (ADHD) in patients 6 years and older.

Concerta, Methylphenidate Osmotic Extended-Release
These products are indicated for the treatment of Attention Deficit Hyperactivity Disorder (ADHD) in children 6 years of age and older, adolescents, and adults up to the age of 65.

Cotempla XR-ODT
Cotempla XR-ODT is indicated for the treatment of Attention Deficit Hyperactivity Disorder (ADHD) in pediatric patients 6 to 17 years of age.

Desoxyn
Desoxyn tablets are indicated for Attention Deficit Disorder with Hyperactivity (ADHD) as an integral part of a total treatment program which typically includes other remedial measures (psychological, educational, social) for a stabilizing effect in children over 6 years of age with a behavioral syndrome characterized by the following group of developmentally inappropriate symptoms: moderate to severe distractibility, short attention span, hyperactivity, emotional lability, and impulsivity.

Dexedrine Spansule
Narcolepsy
Attention Deficit Disorder with Hyperactivity (ADHD) as an integral part of a total treatment program that typically includes other measures (psychological, educational, social) for patients (ages 6 years to 16 years) with this syndrome.

Evekeo
Narcolepsy
Attention Deficit Disorder with Hyperactivity (ADHD) as an integral part of a total treatment program which typically includes other remedial measures (psychological, educational, social) for a stabilizing effect in children with a behavioral syndrome characterized by the following group of developmentally inappropriate symptoms: moderate to severe distractibility, short attention span, hyperactivity, emotional lability, and impulsivity.
Exogenous Obesity as a short term (a few weeks) adjunct in a regimen of weight reduction based on caloric restriction for patients refractory to alternative therapy, e.g., repeated diets, group programs, and other drugs. The limited usefulness of amphetamines should be weighed against possible risks inherent in use of the drug.

Evekeo ODT

Evekeo ODT is indicated for the treatment of Attention Deficit Hyperactivity Disorder (ADHD) in pediatric patients 3 to 17 years of age.

Methylin Oral Solution, Methylphenidate, Methylphenidate Extended-Release, Ritalin/Ritalin SR
Attention Deficit Hyperactivity Disorders (ADHD) in pediatric patients 6 years and older and adults.
Narcolepsy

Methylphenidate Chewable Tablets
Narcolepsy
Attention Deficit Disorders as an integral part of a total treatment program which typically includes other remedial measures (psychological, educational, social) for a stabilizing effect in children with a behavioral syndrome characterized by the following group of developmentally inappropriate symptoms: moderate to severe distractibility, short attention span, hyperactivity, emotional lability, and impulsivity.

Mydayis
Mydayis is indicated for the treatment of Attention Deficit Hyperactivity Disorder (ADHD) in patients 13 years and older.
Limitations of Use
Pediatric patients 12 years and younger experienced higher plasma exposure than patients 13 years and older at the same dose, and experienced higher rates of adverse reactions, mainly insomnia and decreased appetite.

Dextroamphetamine Tablets, ProCentra, Zenzedi
Narcolepsy
Attention Deficit Disorder with Hyperactivity (ADHD) as an integral part of a total treatment program which typically includes other remedial measures (psychological, educational, social) for a stabilizing effect in pediatric patients (ages 3 to 16 years) with a behavioral syndrome characterized by the following group of developmentally inappropriate symptoms: moderate to severe distractibility, short attention span, hyperactivity, emotional lability, and impulsivity.

Qelbree
Qelbree is indicated for the treatment of Attention Deficit Hyperactivity Disorder (ADHD) in adults and pediatric patients 6 years and older.

Relexxii
Relexxii is indicated for the treatment of Attention Deficit Hyperactivity Disorder (ADHD) in adults (up to the age of 65 years) and pediatric patients 6 years of age and older.

Ritalin LA
Ritalin LA is indicated for the treatment of Attention Deficit Hyperactivity Disorder (ADHD) in pediatric patients 6 to 12 years of age.

Vyvanse
Vyvanse is indicated for the treatment of:
- Attention Deficit Hyperactivity Disorder (ADHD) in adults and pediatric patients 6 years and older
- Moderate to Severe Binge-Eating Disorder (BED) in adults
- **Limitation of Use**
  Pediatric patients with ADHD younger than 6 years of age experienced more long-term weight loss than patients 6 years and older.

Vyvanse is not indicated or recommended for weight loss. Use of other sympathomimetic drugs for weight loss has been associated with serious cardiovascular adverse events. The safety and effectiveness of Vyvanse for the treatment of obesity have not been established.

Xelstrym
Xelstrym is indicated for the treatment of Attention Deficit Hyperactivity Disorder (ADHD) in adults and pediatric patients 6 years and older.
Limitations of Use
Pediatric patients younger than 6 years of age experienced more long-term weight loss than patients 6 years and older.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has a diagnosis of Attention-Deficit Hyperactivity Disorder (ADHD) or Attention Deficit Disorder (ADD)
  AND
- If 5 years of age or younger, the patient continues to have Attention-Deficit Hyperactivity Disorder (ADHD) or Attention Deficit Disorder (ADD) symptoms despite participating in evidence-based behavioral therapy (e.g., parent training in behavior management (PTBM), behavioral classroom interventions)
  AND
- The diagnosis has been appropriately documented (e.g., evaluated by a complete clinical assessment, using DSM-5, standardized rating scales, interviews/questionnaires)

OR

- The patient has a diagnosis of narcolepsy
  AND
- The diagnosis has been confirmed by a sleep study
  AND
- This request is NOT for amphetamine extended-release (Adzenys ER, Adzenys XR-ODT), amphetamine extended-release mixture (Adderall XR, Mydayis), amphetamine sulfate orally disintegrating tablet (Evekeo ODT), methylphenidate chewable tablet, methylphenidate immediate release, methylphenidate extended-release (Aptensio XR, Concerta, Cotempla XR-ODT, methylphenidate CD, Methylphenidate Osmotic Extended-Release, QuilliChew ER, Quillivant XR, Relexxii, Ritalin LA), dexmethylphenidate (Focalin), or dexmethylphenidate extended-release (Focalin XR)

Quantity Limits apply.

QUANTITY LIMIT CHART for ADHD**

Drug	Quantity/25 days*	Quantity/75 days*
Adderall 5 mg, 7.5 mg, 10 mg, 12.5 mg	120 tablets	360 tablets
Adderall 15 mg, 20 mg	90 tablets	270 tablets
Adderall 30 mg	60 tablets	180 tablets
Adderall XR 5 mg, 10 mg	120 capsules	360 capsules
Adderall XR 15 mg, 20 mg, 25 mg, 30 mg	60 capsules	180 capsules
Adzenys ER oral suspension 1.25 mg/ml	900 ml	2700 ml
Adzenys XR-ODT 3.1 mg, 6.3 mg, 9.4 mg	120 tablets	360 tablets
Adzenys XR-ODT 12.5 mg, 15.7 mg, 18.8 mg	60 capsules	180 capsules
Aptensio XR 10 mg, 15 mg, 20 mg, 30 mg**	90 capsules	270 capsules
Aptensio XR 40 mg, 50 mg**	60 capsules	180 capsules
Concerta 18 mg, 27 mg, 36 mg	90 tablets	270 tablets
Concerta 54 mg	60 tablets	180 tablets
Cotempla XR-ODT 8.6 mg, 17.3 mg	120 tablets	360 tablets
Cotempla XR-ODT 25.9 mg	90 tablets	270 tablets
Dextroamphetamine 5 mg, 10 mg	180 tablets	540 tablets
Dexedrine Spansule 5 mg, 10 mg	150 capsules	450 capsules
Dexedrine Spansule 15 mg	120 capsules	360 capsules
Evekeo 5 mg, 10 mg	180 tablets	540 tablets
Evekeo ODT 2.5mg, 5 mg, 10 mg	180 tablets	540 tablets
Evekeo ODT 15 mg, 20 mg	90 tablets	270 tablets
Focalin 2.5 mg, 5 mg, 10 mg	150 tablets	450 tablets
Focalin XR 5 mg, 10 mg, 15 mg**	90 capsules	270 capsules
Focalin XR 25 mg**	60 capsules	180 capsules
Methylphenidate CD 10 mg, 20 mg, 30 mg**	90 capsules	270 capsules
Methylphenidate CD 40 mg, 50 mg**	60 capsules	180 capsules

Methylphenidate chewable tablets 2.5 mg, 5 mg, 10 mg	300 tablets	900 tablets
Methylphenidate 5 mg, 10 mg	210 tablets	630 tablets
Methylphenidate 20 mg	150 tablets	450 tablets
Methylphenidate Osmotic Extended-Release 45 mg**	60 tablets	180 tablets
Methylphenidate oral solution 5 mg/5 ml	3,000 ml	9,000 ml
Methylphenidate oral solution 10 mg/5 ml	1,500 ml	4,500 ml
Methylphenidate ER 10 mg, 20 mg	150 tablets	450 tablets
Mydayis 12.5 mg**	90 capsules	270 capsules
ProCentra oral solution 5mg/5ml	1,800 ml	5,400 ml
QuilliChew ER 20 mg	150 tablets	450 tablets
QuilliChew ER 30 mg	90 tablets	270 tablets
QuilliChew ER 40 mg	60 tablets	180 tablets
Quillivant XR oral suspension 25 mg/5 mL (5 mg/1 ml)	600 ml	1,800 ml
Relexxii 18 mg, 27 mg, 36 mg	90 tablets	270 tablets
Relexxii 45 mg, 54 mg	60 tablets	180 tablets
Ritalin LA 10 mg, 20 mg**	150 capsules	450 capsules
Ritalin LA 30 mg**	90 capsules	270 capsules
Ritalin LA 40 mg**	60 capsules	180 capsules
Zenzedi (dextroamphetamine) 2.5 mg, 5 mg, 7.5 mg, 10 mg	180 tablets	540 tablets
Zenzedi (dextroamphetamine) 15 mg	120 tablets	360 tablets
Zenzedi (dextroamphetamine) 20 mg	90 tablets	270 tablets
Zenzedi (dextroamphetamine) 30 mg	60 tablets	180 tablets
**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*		

** Aptensio XR 60 mg, Focalin XR 20mg, 30 mg, 35 mg, and 40 mg, Methylphenidate CD 60 mg, Methylphenidate Osmotic Extended-Release 63 mg and 72 mg, Mydayis 25 mg, 37.5 mg, and 50 mg, Methylphenidate LA (Ritalin LA) 60 mg strengths are not included in the post limit because a quantity that is greater than the initial limit would result in exceeding the off-label maximum daily dose.
***The initial limits for Adhansia XR, Azstarys, Daytrana, Desoxyn, Dyanavel XR, Jornay PM, Qelbree, Strattera, Vyvanse, and Xelstrym are set at the off-label maximum daily dose for ADHD or there is no established off-label maximum daily dosage; therefore, no post limit quantities will be available for these drugs for the diagnosis of ADHD.

QUANTITY LIMIT CHART for NARCOLEPSY**

Drug	**Quantity/25 days***	**Quantity/75 days***
Adderall 5 mg, 7.5 mg, 10 mg, 12.5 mg	120 tablets	360 tablets
Adderall 15 mg, 20 mg	90 tablets	270 tablets
Adderall 30 mg	60 tablets	180 tablets
Dextroamphetamine 5 mg, 10 mg	180 tablets	540 tablets
Dexedrine Spansule 5 mg, 10 mg	150 capsules	450 capsules
Dexedrine Spansule 15 mg	120 capsules	360 capsules
Evekeo 5 mg, 10 mg	180 tablets	540 tablets
ProCentra oral solution 5 mg/5 ml	1,800 ml	5,400 ml
Zenzedi (dextroamphetamine) 2.5 mg, 5 mg, 7.5 mg, 10 mg	180 tablets	540 tablets
Zenzedi (dextroamphetamine) 15 mg	120 tablets	360 tablets
Zenzedi (dextroamphetamine) 20 mg	90 tablets	270 tablets
Zenzedi (dextroamphetamine) 30 mg	60 tablets	180 tablets
**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*		

**The initial limits for methylphenidate immediate-release, methylphenidate extended-release, and methylphenidate chewable tablets are set at the FDA maximum approved daily doses for narcolepsy; therefore, no post limit quantities will be available for these drugs for the diagnosis of narcolepsy.

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Amphetamines are indicated for the treatment of Attention-Deficit/Hyperactivity Disorder (ADHD) and for the treatment of narcolepsy; except for Adderall XR, Adzenys ER, Adzenys XR-ODT, Desoxyn, Dyanavel XR, Evekeo ODT, Mydayis, Vyvanse, and Xelstrym which are not indicated for narcolepsy. Dexmethylphenidates are indicated for the treatment of ADHD. Methylphenidates are indicated for the treatment of ADHD and for the treatment of narcolepsy; except for Adhansia XR, Aptensio XR, Concerta, Cotempla XR-ODT, Daytrana, Jornay PM, methylphenidate CD, methylphenidate osmotic extended-release, QuilliChew ER, Quillivant XR, Relexxii, and Ritalin LA which are not indicated for narcolepsy. Desoxyn, Strattera, and Qelbree are indicated for ADHD.[1-37]

Evekeo is also indicated for exogenous obesity as a short term (a few weeks) adjunct in a regimen of weight reduction based on caloric restriction for patients refractory to alternative therapy, e.g., repeated diets, group programs, and other drugs. The limited usefulness of amphetamines should be weighed against possible risks inherent in use of the drug.[15]

Vyvanse is also indicated for moderate to severe Binge-Eating Disorder (BED).[35]

Both the amphetamine and methylphenidate products are classified as Schedule II controlled substances by Federal regulation and have a high potential for abuse and misuse. The lowest effective doses are recommended.[1-39]

Stimulants (e.g., methylphenidate, amphetamines) remain the drugs of choice for the management of ADHD.[38-40] The American Academy of Pediatrics Clinical Practice Guideline states that stimulant medications are highly effective for most children in reducing core symptoms of ADHD. Preschool-aged children (age 4 years to the 6th birthday) with ADHD should be prescribed evidence-based behavioral parent training in behavior management (PTBM) and/or behavioral classroom interventions as the first line of treatment, if available. Methylphenidate may be considered if these behavioral interventions do not provide significant improvement and there is moderate-to-severe continued disturbance in the 4- through 5-year-old child's functioning. Elementary and middle school-aged children (age 6 years to the 12th birthday) with ADHD should be prescribed US Food and Drug Administration (FDA)-approved medications for ADHD, along with PTBM and/or behavioral classroom intervention.[41] Stimulants have been used effectively in the management of ADHD in adolescents and adults, but experience is far less extensive than in children.[39] However, the definition of attention-deficit/hyperactivity disorder (ADHD) has been updated in the fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5) to more accurately characterize the experience of affected adults. This revision is based on nearly two decades of research showing that ADHD, although a disorder that begins in childhood, can continue through adulthood for some people. Individuals were tracked for years or even decades after their initial childhood diagnosis and the results showed that ADHD does not fade at a specific age.[42]

For patients with a diagnosis of narcolepsy, confirmation should be made by multiple sleep studies.[43]

The initial limits are set to allow up to the FDA-approved maximum doses for the diagnosis of ADHD. These Post Limit criteria are established for products that have established doses above the FDA maximum approved daily doses for ADHD[40] and for products that are indicated for narcolepsy, up to the FDA maximum approved daily doses.[39] The limits are set to accommodate varying dosages utilizing higher strengths available at maximum recommended dosage.

Additional post limit quantities will NOT be available for the following:

- Adhansia XR, Azstarys, Daytrana, Desoxyn, Dyanavel XR, Jornay PM, Qelbree, Strattera, Vyvanse, and Xelstrym are neither indicated for narcolepsy nor have established doses above the FDA maximum approved daily doses for ADHD.[3,7,10,11,14,19,28,34,35,36] Therefore, no additional post limit quantities will be available for these products.
    - Azstarys should not be substituted for other methylphenidate products on a milligram-per-milligram basis because these products have different pharmacokinetic profiles from Azstarys and may have different methylphenidate base composition.[7] Therefore the off-label maximum daily dose used for other methylphenidate or dexmethylphenidate products cannot be applied to Azstarys.
    - Dyanavel XR should not be substituted for other amphetamine products on a milligram-per-milligram basis because of different amphetamine base compositions and differing pharmacokinetic profiles.[14] Therefore, the 60 mg off-label maximum daily dose used for other amphetamine products cannot be applied to Dyanavel XR.

- Jornay PM should not be substituted for other methylphenidate products on a milligram-per-milligram basis because these products have different pharmacokinetic profiles from Jornay PM and may have different methylphenidate base composition.[19] Therefore, the off-label maximum daily dose used for other methylphenidate extended-release products cannot be applied to Jornay PM.
- Only one Xelstrym transdermal system should be applied at one time, and not for more than 9 hours. Only one Xelstrym patch should be used in a 24-hour period. Xelstrym should not be substituted for other amphetamine products on a milligram-per-milligram basis because of different amphetamine base compositions and differing pharmacokinetic profiles.[36] Therefore, the 60 mg off-label maximum daily dose used for other amphetamine and dextroamphetamine products cannot be applied to Xelstrym.

- Quantities that are greater than the initial limit for Aptensio XR 60 mg, Focalin XR 20 mg, 30 mg, 35 mg, and 40 mg, methylphenidate CD 60 mg, Methylphenidate Osmotic Extended-Release 63 mg and 72 mg, Mydayis 25 mg, 37.5 mg, and 50 mg, Relexxii 63 mg and 72 mg, Ritalin LA 60 mg would exceed the established off-label maximum daily dose for ADHD.[40] Therefore, no post limit quantities will be available for these drugs for the diagnosis of ADHD.
- The initial quantity limits for methylphenidate immediate-release, methylphenidate chewable tablets, methylphenidate extended-release (Ritalin SR, Metadate ER) allow for the FDA maximum approved daily doses for narcolepsy (60 mg).[22-23,24,32] Therefore, no additional post limit quantities will be available for these products for the diagnosis of narcolepsy.
- The initial quantity limits for Vyvanse are sufficient for quantities indicated to treat moderate-to-severe BED (70 mg/day).[35] Therefore, no additional post limit quantities will be available for BED.
- The initial quantity limit for Evekeo is sufficient for the short-term (i.e., a few weeks) treatment of exogenous obesity (30 mg/day).[15] Therefore, no additional post limit quantities will be available for obesity.
- According to the National Comprehensive Cancer Network guidelines for cancer-related fatigue (CRF), pharmacologic interventions include consideration of the psychostimulant methylphenidate after ruling out other causes of fatigue.[44] The American Society of Clinical Oncology, evidence suggests that psychostimulants (e.g., methylphenidate) can be effectively used to manage fatigue in patients with advanced disease or those receiving active treatment.[45] However, because optimal dosing has not been established for cancer-related fatigue, no additional post limit quantities will be available for CRF.

The chart below details dosing for the drugs targeted by this criteria document.

Brand Name	Generic Name	Maximum Dose/24 hours[1-37]	Off-Label Maximum Dose/24 hours (ADHD)[40]
Adderall	amphetamine mixture	40 mg for ADHD; 60 mg for Narcolepsy	60 mg
Adderall XR	amphetamine extended-release mixture	30 mg	60 mg
Adhansia XR	methylphenidate extended-release	100 mg	N/A
Adzenys ER	amphetamine extended-release oral suspension	18.8 mg	37.6 mg
Adzenys XR-ODT	amphetamine extended-release orally disintegrating tablets	18.8 mg	37.6 mg
Aptensio XR	methylphenidate extended release	60 mg	100 mg
Azstarys	serdexmethylphenidate/dexmethylphenidate	52.3 mg/10.4 mg	N/A
Concerta	methylphenidate extended-release	72 mg	108 mg
Cotempla XR-ODT	methylphenidate extended-release orally disintegrating tablets	51.8 mg	100 mg
Daytrana	methylphenidate transdermal system	30 mg	N/A
Desoxyn	methamphetamine	25 mg	N/A
N/A	dextroamphetamine	40 mg for ADHD; 60 mg for Narcolepsy	60 mg

Dexedrine Spansule	dextroamphetamine sustained release	40 mg for ADHD; 60 mg for Narcolepsy	60 mg
Dyanavel XR	amphetamine extended release oral suspension, tablets	20 mg	N/A
Evekeo	amphetamine sulfate	40 mg for ADHD; 60 mg for Narcolepsy	60 mg
Evekeo ODT	amphetamine sulfate orally disintegrating tablets	40 mg	60 mg
Focalin	dexmethylphenidate	20 mg	50 mg
Focalin XR	dexmethylphenidate extended release	40 mg	50 mg
Jornay PM	methylphenidate extended-release	100 mg	N/A
Methylphenidate CD	methylphenidate extended release	60 mg	100 mg
Methylin oral solution, Methylphenidate (Ritalin), Methylphenidate ER (Ritalin SR, Metadate ER), Methylphenidate chewable tablets	methylphenidate/methylphenidate extended release*	60 mg for ADHD, Narcolepsy	100 mg
Methylphenidate osmotic extended-release	methylphenidate extended-release	72 mg	108 mg
Mydayis	amphetamine extended-release mixture	50 mg	60 mg
ProCentra oral solution	dextroamphetamine	40 mg for ADHD; 60 mg for Narcolepsy	60 mg
Qelbree	viloxazine extended-release capsules	600 mg	N/A
QuilliChew ER	methylphenidate extended-release chewable tablet	60 mg	100 mg
Quillivant XR oral suspension	methylphenidate extended-release oral suspension	60 mg	100 mg
Relexxii	Methylphenidate extended-release	72 mg	108 mg
Ritalin LA	methylphenidate extended release	60 mg	100 mg
Strattera	atomoxetine	100 mg	N/A
Vyvanse	lisdexamfetamine	70 mg for ADHD; 70 mg for BED	N/A
Xelstrym	dextroamphetamine transdermal system	18 mg	N/A
Zenzedi	dextroamphetamine	40 mg for ADHD; 60 mg for Narcolepsy	60 mg

*The initial limits for methylphenidate immediate-release, methylphenidate extended-release, and methylphenidate chewable tablets are set at the FDA maximum approved daily doses for narcolepsy; therefore, no post limit quantities will be available for these drugs for the diagnosis of narcolepsy.

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Written by:	UM Development (JK)
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Revised:	(MS) 11/2011 (added ProCentra to question 1), 01/2012, 02/2012, (JK) 04/2012, 10/2012 (extended duration); (MS) 11/2012; (JK) 12/2012 (shortened duration); (MS) 01/2013; (CS) 08/2013 (removed MAOI and MD questions); (RP) 08/2013 (added Zenzedi PI); 10/2013 (operational change) ; (MS) 11/2013 (added Quillivant XR, reordered questions), 04/2014 (added Adderall XR 20 mg to the target list), 05/2014 (added Zenzedi [dextroamphetamine] strengths 15 mg, 20 mg, 30 mg); (CF) 11/2014 (created 1218-J with 36 month DOA), 02/2015 (added Evekeo), 03/2015 (increased qty of Focalin XR 5 mg, 10 mg, 15 mg), 05/2015 (added Aptensio XR), 05/2015 (updated for Ritalin LA 60 mg strength – not included), 07/2015 (added Metadate CD strengths), (NB) 10/2015 (updated denial reason for question #4); (CF) 10/2015 (updated rationale), 11/2015 (no clinical changes), 12/2015 (added QuilliChew ER),

01/2016 (added Adzenys XR-ODT); (KM) 11/2016 (no clinical changes, created separate entry for Zenzedi and methylphenidate oral solution 5 mg/5 ml on limit chart, added partial approval questions, added ADHD meds with no post limit quantity to target list), 06/2017 (added Cotempla XR, Mydayis), 10/2017 (Added Adzenys ER), 11/2017 (no clinical changes, combined MMT and commercial documents), 01/2018 (added methylphenidate osmotic extended-release 72 mg), 08/2018 (added Jornay PM), 11/2018 (no clinical changes), 03/2019 (Added Adhansia XR), 07/2019 (Added Evekeo ODT); (RP) 11/2019 (no clinical changes), 12/2019 (Created two new Ref#s [from 1218-J & 683-J] for DAW-9 Strategy for Brand only Adderall XR, Concerta), 11/2020 (no clinical changes), 03/2021 (Added Azstarys), 04/2021 (Added Qelbree, Evekeo ODT 2.5mg); (PM) 08/2021 (updated denial verbiage); (RZ) 11/2021 (added Dyanavel XR tablets), 11/2021 (removed brand Metadate), 03/2022 (added Xelstrym, updated document title from DAW to BOG, updated Qelbree); (MRS) 03/2022 (added continued symptoms despite evidence-based behavioral therapy for ADHD/ADD in patients 5 and younger to coverage criteria; additional internal notes), 07/2022 (added new strengths of Relexxii), 09/2022 (removed BOG 3454-J and BOG 3455-J due to retirement), 11/2022 (added Methylphenidate Osmotic ER 45 mg to limit chart and 63 mg to question 1)

Reviewed: Medical Affairs (KP) 08/2011, 11/2011, 01/2012, 02/2012, 10/2012; (LS) 11/2012; (DR) 08/2013; (DC) 08/2013; (LB) 11/2013; (SS) 04/2014, 05/2014; (DNC) 11/2014; (SES) 02/2015; (DNC) 03/2015, 05/2015; (ADA) 05/2015; (MM) 10/2015; (GAD) 12/2015; (AM) 07/2017, 10/2017, (AN) 01/2018, (GAD) 08/2018, 04/2019, (ME) 07/2019; (CHART) 11/27/2019, (EPA) 12/2019, (CHART) 12/03/2020, 3/18/2021, 04/22/2021, 12/02/2021, 3/17/2022, 4/14/2022, 05/19/2022, 08/04/2022, 12/01/2022
External Review: 08/2011, 02/2012, 02/2013, 08/2013, 02/2014, 02/2015, 02/2016, 02/2017, 08/2017, 10/2017, 12/2017, 02/2018, 10/2018, 02/2019, 06/2019 (FYI), 08/2019 (FYI), 02/2020 (FYI), 02/2020, 02/2021, 03/2021, 05/2021, 02/2022, 06/2022 (FYI), 10/2022 (FYI), 02/2023 (FYI)

CRITERIA FOR APPROVAL

1	Is this request for one of the following: A) Adhansia XR, B) Aptensio XR 60 mg, C) Azstarys, D) Daytrana, E) Desoxyn, F) Dyanavel XR, G) Focalin XR 20 mg, 30 mg, 35 mg, or 40 mg, H) Jornay PM, I) Methylphenidate CD 60 mg, J) Methylphenidate Osmotic Extended-Release 63 mg, 72 mg, K) Mydayis 25 mg, 37.5 mg, or 50 mg, L) Qelbree, M) Relexxii 63 mg, 72 mg, N) Ritalin LA 60 mg, O) Strattera, P) Vyvanse, Q) Xelstrym? [If yes, then no further questions.] [RPh Note: If yes, then deny. No override is required because no additional quantities are available with this post limit criteria.]	Yes	No
2	Does the patient have a diagnosis of Attention-Deficit Hyperactivity Disorder (ADHD) or Attention Deficit Disorder (ADD)? [If no, then skip to question 22.]	Yes	No
3	Is the patient 5 years of age or younger? [If no, then skip to question 5.]	Yes	No
4	Does the patient continue to have ADHD/ADD (Attention Deficit Hyperactivity Disorder / Attention Deficit Disorder) symptoms despite participating in evidence-based behavioral therapy (e.g., parent training in behavior management (PTBM), behavioral classroom interventions)? [If no, then no further questions.]	Yes	No
5	Has the diagnosis been appropriately documented (e.g., evaluated by a complete clinical assessment, using DSM-5, standardized rating scales, interviews/questionnaires)? [If no, then no further questions.]	Yes	No
6	Which drug is being requested (applies to brand or generic)? [Note: Please check which drug (applies to brand or generic).] [] Adderall (amphetamine mixture) (if checked, go to 7) [] Adderall XR (amphetamine extended-release mixture) (if checked, go to 7) [] Adzenys ER (amphetamine extended-release oral suspension) (if checked, go to 8) [] Adzenys XR-ODT (amphetamine extended-release orally disintegrating tablets) (if checked, go to 8)		

[] Aptensio XR (methylphenidate extended-release) (if checked, go to 9)
[] Concerta (methylphenidate extended-release) (if checked, go to 10)
[] Cotempla XR (methylphenidate extended-release orally disintegrating tablet) (if checked, go to 11)
[] Dexedrine Spansule (dextroamphetamine sustained-release) (if checked, go to 12)
[] dextroamphetamine (if checked, go to 12)
[] Evekeo (amphetamine sulfate) (if checked, go to 13)
[] Evekeo ODT (amphetamine sulfate orally disintegrating tablet) (if checked, go to 13)
[] Focalin (dexmethylphenidate) (if checked, go to 14)
[] Focalin XR (dexmethylphenidate extended-release) (if checked, go to 14)
[] methylphenidate CD (methylphenidate extended-release) (if checked, go to 15)
[] methylphenidate chewable tablet (if checked, go to 16)
[] methylphenidate tablets (if checked, go to 16)
[] Methylin (methylphenidate) oral solution (if checked, go to 17)
[] methylphenidate extended-release (if checked, go to 15)
[] Methylphenidate Osmotic Extended-Release (if checked, go to 10)
[] Mydayis (amphetamine extended-release mixture) (if checked, go to 18)
[] ProCentra (dextroamphetamine sulfate oral solution) (if checked, go to 19)
[] QuilliChew ER (methylphenidate extended-release chewable tablets) (if checked, go to 20)
[] Quillivant XR (methylphenidate hydrochloride extended-release oral suspension) (if checked, go to 21)
[] Relexxii (methylphenidate hydrochloride extended-release tablets) (if checked, go to 10)
[] Ritalin LA (methylphenidate extended-release) (if checked, go to 15)
[] Zenzedi (dextroamphetamine) (if checked, go to 12)

7	Does the patient require use of MORE than any of the following PER MONTH: A) 120 units of Adderall 5 mg, 7.5 mg, 10 mg, 12.5 mg OR Adderall XR 5 mg, 10 mg, B) 90 units of Adderall 15 mg, 20 mg, C) 60 units of Adderall 30 mg OR Adderall XR 15 mg, 20 mg, 25 mg, 30 mg? [No further questions.] [RPh Note: If yes, then deny and enter a partial approval per Quantity Limit Chart for ADHD.]	Yes	No
8	Does the patient require use of MORE than any of the following PER MONTH: A) 900 ml of Adzenys ER, B) 120 tablets of Adzenys XR-ODT 3.1 mg, 6.3 mg, 9.4 mg, C) 60 tablets of Adzenys XR-ODT 12.5 mg, 15.7 mg, 18.8 mg? [No further questions.] [RPh Note: If yes, then deny and enter a partial approval per Quantity Limit Chart for ADHD.]	Yes	No
9	Does the patient require use of MORE than any of the following PER MONTH: A) 90 capsules of Aptensio XR 10 mg, 15 mg, 20 mg, 30 mg, B) 60 capsules of Aptensio XR 40 mg, 50 mg? [No further questions.] [RPh Note: If yes, then deny and enter a partial approval per Quantity Limit Chart for ADHD.]	Yes	No
10	Does the patient require use of MORE than any of the following PER MONTH: A) 90 tablets of Concerta 18 mg, 27 mg, 36 mg OR Relexxii 18 mg, 27 mg, 36 mg, B) 60 tablets	Yes	No

	of Concerta 54 mg OR Methylphenidate Osmotic Extended-Release 45 mg OR Relexxii 45 mg, 54 mg? [No further questions.] [RPh Note: If yes, then deny and enter a partial approval per Quantity Limit Chart for ADHD.]		
11	Does the patient require use of MORE than any of the following PER MONTH: A) 120 tablets of Cotempla XR 8.6 mg, 17.3 mg, B) 90 tablets of Cotempla XR 25.9 mg? [No further questions.] [RPh Note: If yes, then deny and enter a partial approval per Quantity Limit Chart for ADHD.]	Yes	No
12	Does the patient require use of MORE than any of the following PER MONTH: A) 180 tablets of dextroamphetamine 5 mg, 10 mg OR Zenzedi 2.5 mg, 5 mg, 7.5 mg, 10 mg, B) 150 capsules of Dexedrine Spansule 5 mg, 10 mg, C) 120 units of Dexedrine Spansule 15 mg OR Zenzedi 15 mg, D) 90 tablets of Zenzedi 20 mg, E) 60 tablets of Zenzedi 30 mg? [No further questions.] [RPh Note: If yes, then deny and enter a partial approval per Quantity Limit Chart for ADHD.]	Yes	No
13	Does the patient require use of MORE than any of the following PER MONTH: A) 180 tablets of Evekeo 5 mg, 10 mg OR Evekeo ODT 2.5 mg, 5 mg, 10 mg, B) 90 tablets of Evekeo ODT 15 mg, 20 mg? [No further questions.] [RPh Note: If yes, then deny and enter a partial approval per Quantity Limit Chart for ADHD.]	Yes	No
14	Does the patient require use of MORE than any of the following PER MONTH: A) 150 tablets of Focalin 2.5 mg, 5 mg, 10 mg, B) 90 capsules of Focalin XR 5 mg, 10 mg, 15 mg, C) 60 capsules of Focalin XR 25 mg? [No further questions.] [RPh Note: If yes, then deny and enter a partial approval per Quantity Limit Chart for ADHD.]	Yes	No
15	Does the patient require use of MORE than any of the following PER MONTH: A) 150 units of methylphenidate ER 10 mg, 20 mg OR Ritalin LA 10 mg, 20 mg, B) 90 capsules of methylphenidate CD 10 mg, 20 mg, 30 mg OR Ritalin LA 30 mg, C) 60 capsules of methylphenidate CD 40 mg, 50 mg OR Ritalin LA 40 mg? [No further questions.] [RPh Note: If yes, then deny and enter a partial approval per Quantity Limit Chart for ADHD.]	Yes	No
16	Does the patient require use of MORE than any of the following PER MONTH: A) 300 tablets of methylphenidate chewable 2.5 mg, 5 mg, 10 mg, B) 210 tablets of methylphenidate 5 mg, 10 mg, C) 150 tablets of methylphenidate 20 mg? [No further questions.]	Yes	No

	[RPh Note: If yes, then deny and enter a partial approval per Quantity Limit Chart for ADHD.]		
17	Does the patient require use of MORE than any of the following PER MONTH: A) 3,000 ml of Methylin (methylphenidate) oral solution 5 mg/5 ml, B) 1,500 ml of Methylin (methylphenidate) oral solution 10 mg/5 ml? [No further questions.] [RPh Note: If yes, then deny and enter a partial approval per Quantity Limit Chart for ADHD.]	Yes	No
18	Does the patient require use of MORE than 90 capsules PER MONTH of Mydayis 12.5 mg? [No further questions.] [RPh Note: If yes, then deny and enter a partial approval per Quantity Limit Chart for ADHD.]	Yes	No
19	Does the patient require use of MORE than 1,800 ml PER MONTH of ProCentra oral solution 5 mg/5 ml? [No further questions.] [RPh Note: If yes, then deny and enter a partial approval per Quantity Limit Chart for ADHD.]	Yes	No
20	Does the patient require use of MORE than any of the following PER MONTH: A) 150 tablets of QuilliChew ER 20 mg, B) 90 tablets of QuilliChew ER 30 mg, C) 60 tablets of QuilliChew ER 40 mg? [No further questions.] [RPh Note: If yes, then deny and enter a partial approval per Quantity Limit Chart for ADHD.]	Yes	No
21	Does the patient require use of MORE than 600 ml PER MONTH of Quillivant XR oral suspension 25 mg/5 ml (5 mg/1 ml)? [No further questions.] [RPh Note: If yes, then deny and enter a partial approval per Quantity Limit Chart for ADHD.]	Yes	No
22	Does the patient have a diagnosis of narcolepsy? [If no, then no further questions.]	Yes	No
23	Has the diagnosis been confirmed by a sleep study? [If no, then no further questions.]	Yes	No
24	Is this request for amphetamine extended-release (Adzenys ER, Adzenys XR-ODT), amphetamine extended-release mixture (Adderall XR, Mydayis), amphetamine sulfate orally disintegrating tablet (Evekeo ODT), methylphenidate chewable tablet, methylphenidate immediate-release, methylphenidate extended-release (Aptensio XR, Concerta, Cotempla XR-ODT, methylphenidate CD, methylphenidate osmotic extended-release, QuilliChew ER, Quillivant XR, Relexxii, Ritalin LA), dexmethylphenidate (Focalin), or dexmethylphenidate extended-release (Focalin XR)? [If yes, then no further questions.]	Yes	No

25 Which drug is being requested (applies to brand or generic)?
[Note: Please check which drug (applies to brand or generic).]

[] Adderall (amphetamine mixture) (if checked, go to 26)
[] Dexedrine Spansule (dextroamphetamine sustained-release) (if checked, go to 27)
[] dextroamphetamine (if checked, go to 27)
[] Evekeo (amphetamine sulfate) (if checked, go to 28)
[] ProCentra (dextroamphetamine sulfate oral solution) (if checked, go to 29)
[] Zenzedi (dextroamphetamine) (if checked, go to 27)

26 Does the patient require use of MORE than any of the following PER MONTH: A) 120 tablets of Adderall 5 mg, 7.5 mg, 10 mg, 12.5 mg, B) 90 tablets of Adderall 15 mg, 20 mg, C) 60 tablets of Adderall 30 mg? Yes No
[No further questions.]

[RPh Note: If yes, then deny and enter a partial approval per the Quantity Limit Chart for Narcolepsy.]

27 Does the patient require use of MORE than any of the following PER MONTH: A) 180 tablets of dextroamphetamine 5 mg, 10 mg OR Zenzedi 2.5 mg, 5 mg, 7.5 mg, 10 mg, B) 150 capsules of Dexedrine Spansule 5 mg, 10 mg, C) 120 units of Dexedrine Spansule 15 mg OR Zenzedi 15 mg, D) 90 tablets of Zenzedi 20 mg, E) 60 tablets of Zenzedi 30 mg? Yes No

[RPh Note: If yes, then deny and enter a partial approval per the Quantity Limit Chart for Narcolepsy.]

28 Does the patient require use of MORE than 180 tablets PER MONTH of Evekeo 5 mg or 10 mg? Yes No
[No further questions.]

[RPh Note: If yes, then deny and enter a partial approval per the Quantity Limit Chart for Narcolepsy.]

29 Does the patient require use of MORE than 1,800 ml PER MONTH of ProCentra oral solution 5 mg/5 ml? Yes No

[RPh Note: If yes, then deny and enter a partial approval per the Quantity Limit Chart for Narcolepsy.]

Mapping Instructions (1218-J)			
	Yes	**No**	**DENIAL REASONS – DO NOT USE FOR MEDICARE PART D**
1.	Deny No override required. (No additional quantities are available on this post limit.)	Go to 2	You do not meet the requirements of your plan. Your plan covers a sufficient quantity of the requested drug to treat Attention-Deficit Hyperactivity Disorder (ADHD) / Attention Deficit Disorder (ADD) up to a maximum of: - 30 capsules per month of Adhansia XR 55 mg, 70 mg, 85 mg - 60 capsules per month of Adhansia XR 25 mg, 35 mg, 45 mg - 30 capsules per month of Aptensio XR 60 mg - 30 capsules per month of Azstarys 26.1 mg/5.2 mg, 39.2 mg/7.8 mg, 52.3 mg/10.4 mg - 30 patches per month of Daytrana 10 mg, 15 mg, 20 mg, 30 mg

	For the denial verbiage, only include the requested drug. Remove all the other drugs from the verbiage.		- 150 tablets per month of Desoxyn 5 mg - 240 ml per month of Dyanavel XR oral suspension - 60 tablets per month of Dyanavel XR 5 mg, 10 mg - 30 tablets per month of Dyanavel XR 15 mg, 20 mg - 60 capsules per month of Focalin XR 20 mg - 30 capsules per month of Focalin XR 30 mg, 35 mg, 40 mg - 60 capsules per month of Jornay PM 20 mg, 40 mg - 30 capsules per month of Jornay PM 60 mg, 80 mg, 100 mg - 30 capsules per month of methylphenidate CD 60 mg - 30 tablets per month of Methylphenidate Osmotic Extended-Release 63 mg, 72 mg - 60 capsules per month of Mydayis 25 mg - 30 capsules per month of Mydayis 37.5 mg, 50 mg - 90 capsules per month of Qelbree 100 mg, 150 mg, 200 mg - 30 tablets per month of Relexxii 63 mg, 72 mg - 30 capsules per month of Ritalin LA 60 mg - 120 capsules per month of Strattera 10 mg, 18 mg, 25 mg - 60 capsules per month of Strattera 40 mg - 30 capsules per month of Strattera 60 mg, 80 mg, 100 mg - 30 transdermal systems per month of Xelstrym 4.5 mg, 9 mg, 13.5 mg, 18 mg Your plan also covers a sufficient quantity of Vyvanse to treat Attention-Deficit Hyperactivity Disorder (ADHD) / Attention Deficit Disorder (ADD) or Binge-Eating Disorder (BED) up to a maximum of: - 60 capsules or chewable tablets per month of Vyvanse 10 mg, 20 mg, 30 mg - 30 capsules or chewable tablets per month of Vyvanse 40 mg, 50 mg, 60 mg, 70 mg Your request for additional quantities of the requested drug and strength has been denied. [Short Description: No post limit available]
2.	Go to 3	Go to 22	
3.	Go to 4	Go to 5	
4.	Go to 5	Deny	You do not meet the requirements of your plan. Your plan covers this drug if you are under 6 years of age and: -You have Attention-Deficit Hyperactivity Disorder (ADHD)/Attention Deficit Disorder (ADD) -You have tried and failed behavioral therapy Your request has been denied based on the information we have. [Short Description: No failure of behavioral therapy under 6]
5.	Go to 6	Deny	You do not meet the requirements of your plan. Your plan covers additional quantities of this drug when Attention-Deficit Hyperactivity Disorder (ADHD)/Attention Deficit Disorder (ADD) has been confirmed by your doctor. Your request has been denied based on the information we have. [Short Description: No confirmation of diagnosis (e.g., complete clinical assessment using DSM-5)]
6.	1=7; 2=7; 3=8; 4=8; 5=9; 6=10;	N/A	

	7=11; 8=12; 9=12; 10=13; 11=13, 12=14; 13=14; 14=15; 15=16; 16=16; 17=17; 18=15; 19=10; 20=18; 21=19; 22=20; 23=21; 24=10; 25=15; 26=12		
7.	Deny For the denial verbiage, only include the requested drug. Remove all the other drugs from the verbiage.	Approve, 36 Months, See Quantity Limit Chart for ADHD	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to: - 120 tablets per month of Adderall 5 mg, 7.5 mg, 10 mg, 12.5 mg - 90 tablets per month of Adderall 15 mg, 20 mg - 60 tablets per month of Adderall 30 mg - 120 capsules per month of Adderall XR 5 mg, 10 mg - 60 capsules per month of Adderall XR 15 mg, 20 mg, 25 mg, 30 mg Your request has been partially approved. You have been approved for the maximum quantity that your plan covers for a duration of 36 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity Adderall]
8.	Deny For the denial verbiage, only include the requested drug. Remove all the other drugs from the verbiage.	Approve, 36 Months, See Quantity Limit Chart for ADHD	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to: - 900 ml per month of Adzenys ER - 120 tablets per month of Adzenys XR-ODT 3.1 mg, 6.3 mg, 9.4 mg - 60 tablets per month of Adzenys XR-ODT 12.5 mg, 15.7 mg, 18.8 mg Your request has been partially approved. You have been approved for the maximum quantity that your plan covers for a duration of 36 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity Adzenys]
9.	Deny For the denial verbiage, only include the requested drug. Remove all the other drugs from the verbiage.	Approve, 36 Months, See Quantity Limit Chart for ADHD	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to: - 90 capsules per month of Aptensio XR 10 mg, 15 mg, 20 mg, 30 mg - 60 capsules per month of Aptensio XR 40 mg, 50 mg Your request has been partially approved. You have been approved for the maximum quantity that your plan covers for a duration of 36 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity Aptensio]

10.	Deny For the denial verbiage, only include the requested drug. Remove all the other drugs from the verbiage.	Approve, 36 Months, See Quantity Limit Chart for ADHD	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to: - 90 tablets per month of Concerta 18 mg, 27 mg, 36 mg - 60 tablets per month of Concerta 54 mg - 60 tablets per month of Methylphenidate Osmotic Extended-Release 45 mg - 90 tablets per month of Relexxii 18 mg, 27 mg, 36 mg - 60 tablets per month of Relexxii 45 mg, 54 mg Your request has been partially approved. You have been approved for the maximum quantity that your plan covers for a duration of 36 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity Concerta, Methylphenidate Osmotic Extended-Release, Relexxii]
11.	Deny For the denial verbiage, only include the requested drug. Remove all the other drugs from the verbiage.	Approve, 36 Months, See Quantity Limit Chart for ADHD	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to: - 120 tablets per month of Cotempla XR-ODT 8.6 mg, 17.3 mg - 90 tablets per month of Cotempla XR-ODT 25.9 mg Your request has been partially approved. You have been approved for the maximum quantity that your plan covers for a duration of 36 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity Cotempla]
12.	Deny For the denial verbiage, only include the requested drug. Remove all the other drugs from the verbiage.	Approve, 36 Months, See Quantity Limit Chart for ADHD	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to: - 150 capsules per month of Dexedrine Spansule 5 mg, 10 mg - 120 capsules per month of Dexedrine Spansule 15 mg - 180 tablets per month of dextroamphetamine 5 mg, 10 mg - 180 tablets per month of Zenzedi (dextroamphetamine) 2.5 mg, 5 mg, 7.5 mg, 10 mg - 120 tablets per month of Zenzedi (dextroamphetamine)15 mg - 90 tablets per month of Zenzedi (dextroamphetamine) 20 mg - 60 tablets per month of Zenzedi (dextroamphetamine) 30 mg Your request has been partially approved. You have been approved for the maximum quantity that your plan covers for a duration of 36 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity Dexedrine, dextroamphetamine, Zenzedi]
13.	Deny For the denial verbiage, only include the requested drug. Remove all the other drugs from the verbiage.	Approve, 36 Months, See Quantity Limit Chart for ADHD	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to: - 180 tablets per month of Evekeo 5 mg, 10 mg - 180 tablets per month of Evekeo ODT 2.5 mg, 5 mg, 10 mg - 90 tablets per month of Evekeo ODT 15 mg, 20 mg Your request has been partially approved. You have been approved for the maximum quantity that your plan covers for a duration of 36 months. Your request for additional quantities of the requested drug and strength has been denied.

			[Short Description: Over max quantity Evekeo]
14.	Deny For the denial verbiage, only include the requested drug. Remove all the other drugs from the verbiage.	Approve, 36 Months, See Quantity Limit Chart for ADHD	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to: - 150 tablets per month of Focalin 2.5 mg, 5 mg, 10 mg - 90 capsules per month of Focalin XR 5 mg, 10 mg, 15 mg - 60 capsules per month of Focalin XR 25 mg Your request has been partially approved. You have been approved for the maximum quantity that your plan covers for a duration of 36 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity Focalin]
15.	Deny For the denial verbiage, only include the requested drug. Remove all the other drugs from the verbiage.	Approve, 36 Months, See Quantity Limit Chart for ADHD	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to: - 90 capsules per month of methylphenidate CD 10 mg, 20 mg, 30 mg - 60 capsules per month of methylphenidate CD 40 mg, 50 mg - 150 tablets per month of methylphenidate ER 10 mg, 20 mg - 150 capsules per month of Ritalin LA 10 mg, 20 mg - 90 capsules per month of Ritalin LA 30 mg - 60 capsules per month of Ritalin LA 40 mg Your request has been partially approved. You have been approved for the maximum quantity that your plan covers for a duration of 36 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity Ritalin LA, methylphenidate CD/ER]
16.	Deny For the denial verbiage, only include the requested drug. Remove all the other drugs from the verbiage.	Approve, 36 Months, See Quantity Limit Chart for ADHD	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to: - 300 tablets per month of methylphenidate chewable 2.5 mg, 5 mg, 10 mg - 210 tablets per month of methylphenidate 5 mg, 10 mg - 150 tablets per month of methylphenidate 20 mg Your request has been partially approved. You have been approved for the maximum quantity that your plan covers for a duration of 36 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity methylphenidate]
17.	Deny For the denial verbiage, only include the requested drug. Remove all the other drugs from the verbiage.	Approve, 36 Months, See Quantity Limit Chart for ADHD	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to: - 3000 ml per month of Methylin (methylphenidate) oral solution 5 mg/5 ml - 1500 ml per month of Methylin (methylphenidate) oral solution 10 mg/5 ml Your request has been partially approved. You have been approved for the maximum quantity that your plan covers for a duration of 36 months. Your request for additional quantities of the requested drug and strength has been denied.

			[Short Description: Over max quantity Methylin]
18.	Deny	Approve, 36 Months, See Quantity Limit Chart for ADHD	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 90 capsules per month of Mydayis 12.5 mg. Your request has been partially approved. You have been approved for the maximum quantity that your plan covers for a duration of 36 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity Mydayis]
19.	Deny	Approve, 36 Months, See Quantity Limit Chart for ADHD	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 1800 ml per month of ProCentra. Your request has been partially approved. You have been approved for the maximum quantity that your plan covers for a duration of 36 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity ProCentra]
20.	Deny For the denial verbiage, only include the requested drug. Remove all the other drugs from the verbiage.	Approve, 36 Months, See Quantity Limit Chart for ADHD	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to: - 150 tablets per month of QuilliChew ER 20 mg - 90 tablets per month of QuilliChew ER 30 mg - 60 tablets per month of QuilliChew ER 40 mg Your request has been partially approved. You have been approved for the maximum quantity that your plan covers for a duration of 36 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity QuilliChew]
21.	Deny	Approve, 36 Months, See Quantity Limit Chart for ADHD	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 600 ml per month of Quillivant XR. Your request has been partially approved. You have been approved for the maximum quantity that your plan covers for a duration of 36 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity Quillivant]
22.	Go to 23	Deny	You do not meet the requirements of your plan. Your plan covers additional quantities of this drug when you have any of these conditions: - Attention-Deficit Hyperactivity Disorder (ADHD) - Attention Deficit Disorder (ADD) - Narcolepsy and the drug you are requesting is Adderall (amphetamine mixture), Dexedrine Spansule (dextroamphetamine sustained-release), dextroamphetamine, Evekeo (amphetamine), ProCentra (dextroamphetamine sulfate oral solution), or Zenzedi (dextroamphetamine) Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]
23.	Go to 24	Deny	You do not meet the requirements of your plan. Your plan covers additional quantities of this drug when you meet the following conditions: - Narcolepsy is confirmed by a sleep study and the drug you are requesting is Adderall (amphetamine mixture), Dexedrine Spansule

			(dextroamphetamine sustained-release), dextroamphetamine, Evekeo (amphetamine), ProCentra (dextroamphetamine sulfate oral solution), or Zenzedi (dextroamphetamine) Your request has been denied based on the information we have. [Short Description: No sleep study]
24.	Deny	Go to 25	You do not meet the requirements of your plan. Your plan does not cover additional quantities of this drug for the diagnosis of narcolepsy. Your request has been denied based on the information we have. [Short Description: Over max quantity for narcolepsy diagnosis]
25.	1=26; 2=27; 3=27; 4=28; 5=29; 6=27	N/A	
26.	Deny For the denial verbiage, only include the requested drug. Remove all the other drugs from the verbiage.	Approve, 36 Months, See Quantity Limit Chart for Narcolepsy	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to: - 120 tablets per month of Adderall 5 mg, 7.5 mg, 10 mg, 12.5 mg - 90 tablets per month of Adderall 15 mg, 20 mg - 60 tablets per month of Adderall 30mg Your request has been partially approved. You have been approved for the maximum quantity that your plan covers for a duration of 36 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity narcolepsy Adderall]
27.	Deny For the denial verbiage, only include the requested drug. Remove all the other drugs from the verbiage.	Approve, 36 Months, See Quantity Limit Chart for Narcolepsy	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to: - 150 capsules per month of Dexedrine Spansule 5 mg, 10 mg - 120 capsules per month of Dexedrine Spansule 15 mg - 180 tablets per month of dextroamphetamine 5 mg,10 mg - 180 tablets per month of Zenzedi (dextroamphetamine) 2.5 mg, 5 mg, 7.5 mg, 10 mg - 120 tablets per month of Zenzedi (dextroamphetamine) 15 mg - 90 tablets per month of Zenzedi (dextroamphetamine) 20 mg - 60 tablets per month of Zenzedi (dextroamphetamine) 30 mg Your request has been partially approved. You have been approved for the maximum quantity that your plan covers for a duration of 36 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity narcolepsy Dexedrine, dextroamphetamine, Zenzedi]
28.	Deny For the denial verbiage, only include the requested drug. Remove all the other drugs from the verbiage.	Approve, 36 Months, See Quantity Limit Chart for Narcolepsy	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 180 tablets per month of Evekeo 5 mg or 10 mg. Your request has been partially approved. You have been approved for the maximum quantity that your plan covers for a duration of 36 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity narcolepsy Evekeo]
29.	Deny For the denial verbiage, only include the	Approve, 36 Months, See Quantity Limit	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 1800 ml per month of ProCentra. Your request has been partially approved. You have been approved for the maximum quantity that your plan covers for a duration of

	requested drug. Remove all the other drugs from the verbiage.	Chart for Narcolepsy	36 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity narcolepsy ProCentra]

Mapping Instructions (MMT 683-J)			
	Yes	**No**	**DENIAL REASONS – DO NOT USE FOR MEDICARE PART D**
1.	Deny No override required. (No additional quantities are available on this post limit.) For the denial verbiage, only include the requested drug. Remove all the other drugs from the verbiage.	Go to 2	You do not meet the requirements of your plan. Your plan covers a sufficient quantity of the requested drug to treat Attention- Deficit Hyperactivity Disorder (ADHD) / Attention Deficit Disorder (ADD) up to a maximum of: - 30 capsules per month of Adhansia XR 55 mg, 70 mg, 85 mg - 60 capsules per month of Adhansia XR 25 mg, 35 mg, 45 mg - 30 capsules per month of Aptensio XR 60 mg - 30 capsules per month of Azstarys 26.1 mg/5.2 mg, 39.2 mg/7.8 mg, 52.3 mg/10.4 mg - 30 patches per month of Daytrana 10 mg, 15 mg, 20 mg, 30 mg - 150 tablets per month of Desoxyn 5 mg - 240 ml per month of Dyanavel XR oral suspension - 60 tablets per month of Dyanavel XR 5 mg, 10 mg - 30 tablets per month of Dyanavel XR 15 mg, 20 mg - 60 capsules per month of Focalin XR 20 mg - 30 capsules per month of Focalin XR 30 mg, 35 mg, 40 mg - 60 capsules per month of Jornay PM 20 mg, 40 mg - 30 capsules per month of Jornay PM 60 mg, 80 mg, 100 mg - 30 capsules per month of methylphenidate CD 60 mg - 30 tablets per month of Methylphenidate Osmotic Extended-Release 63 mg, 72 mg - 60 capsules per month of Mydayis 25 mg - 30 capsules per month of Mydayis 37.5 mg, 50 mg - 90 capsules per month of Qelbree 100 mg, 150 mg, 200 mg - 30 tablets per month of Relexxii 63 mg, 72 mg - 30 capsules per month of Ritalin LA 60 mg - 120 capsules per month of Strattera 10 mg, 18 mg, 25 mg - 60 capsules per month of Strattera 40 mg - 30 capsules per month of Strattera 60 mg, 80 mg, 100 mg - 30 transdermal systems per month of Xelstrym 4.5 mg, 9 mg, 13.5 mg, 18 mg Your plan also covers a sufficient quantity of Vyvanse to treat Attention-Deficit Hyperactivity Disorder (ADHD) / Attention Deficit Disorder (ADD) or Binge-Eating Disorder (BED) up to a maximum of: - 60 capsules or chewable tablets per month of Vyvanse 10 mg, 20 mg, 30 mg - 30 capsules or chewable tablets per month of Vyvanse 40 mg, 50 mg, 60 mg, 70 mg Your request for additional quantities of the requested drug and strength has been denied. [Short Description: No post limit available]
2.	Go to 3	Go to 22	
3.	Go to 4	Go to 5	

4.	Go to 5	Deny	You do not meet the requirements of your plan. Your plan covers this drug if you are under 6 years of age and: -You have Attention-Deficit Hyperactivity Disorder (ADHD)/Attention Deficit Disorder (ADD) -You have tried and failed behavioral therapy Your request has been denied based on the information we have. [Short Description: No failure of behavioral therapy under 6]
5.	Go to 6	Deny	You do not meet the requirements of your plan. Your plan covers additional quantities of this drug when Attention-Deficit Hyperactivity Disorder (ADHD)/Attention Deficit Disorder (ADD) has been confirmed by your doctor. Your request has been denied based on the information we have. [Short Description: No confirmation of diagnosis (e.g., complete clinical assessment using DSM-5)]
6.	1=7; 2=7; 3=8; 4=8; 5=9; 6=10; 7=11; 8=12; 9=12; 10=13; 11=13, 12=14; 13=14; 14=15; 15=16; 16=16; 17=17; 18=15; 19=10; 20=18; 21=19; 22=20; 23=21; 24=10; 25=15; 26=12	N/A	
7.	Deny For the denial verbiage, only include the requested drug. Remove all the other drugs from the verbiage.	Approve, 12 Months, See Quantity Limit Chart for ADHD	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to: - 120 tablets per month of Adderall 5 mg, 7.5 mg, 10 mg, 12.5 mg - 90 tablets per month of Adderall 15 mg, 20 mg - 60 tablets per month of Adderall 30 mg - 120 capsules per month of Adderall XR 5 mg, 10 mg - 60 capsules per month of Adderall XR 15 mg, 20 mg, 25 mg, 30 mg Your request has been partially approved. You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity Adderall]
8.	Deny For the denial verbiage, only include the requested drug. Remove	Approve, 12 Months, See Quantity Limit Chart for ADHD	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to: - 900 ml per month of Adzenys ER - 120 tablets per month of Adzenys XR-ODT 3.1 mg, 6.3 mg, 9.4 mg

	all the other drugs from the verbiage.		- 60 tablets per month of Adzenys XR-ODT 12.5 mg, 15.7 mg, 18.8 mg Your request has been partially approved. You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity Adzenys]
9.	Deny For the denial verbiage, only include the requested drug. Remove all the other drugs from the verbiage.	Approve, 12 Months, See Quantity Limit Chart for ADHD	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to: - 90 capsules per month of Aptensio XR 10 mg, 15 mg, 20 mg, 30 mg - 60 capsules per month of Aptensio XR 40 mg, 50 mg Your request has been partially approved. You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity Aptensio]
10.	Deny For the denial verbiage, only include the requested drug. Remove all the other drugs from the verbiage.	Approve, 12 Months, See Quantity Limit Chart for ADHD	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to: - 90 tablets per month of Concerta 18 mg, 27 mg, 36 mg - 60 tablets per month of Concerta 54 mg - 60 tablets per month of Methylphenidate Osmotic Extended-Release 45 mg - 90 tablets per month of Relexxii 18 mg, 27 mg, 36 mg - 60 tablets per month of Relexxii 45 mg, 54 mg Your request has been partially approved. You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity Concerta, Methylphenidate Osmotic Extended-Release Relexxii]
11.	Deny For the denial verbiage, only include the requested drug. Remove all the other drugs from the verbiage.	Approve, 12 Months, See Quantity Limit Chart for ADHD	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to: - 120 tablets per month of Cotempla XR-ODT 8.6 mg, 17.3 mg - 90 tablets per month of Cotempla XR-ODT 25.9 mg Your request has been partially approved. You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity Cotempla]
12.	Deny For the denial verbiage, only include the requested drug. Remove all the other drugs from the verbiage.	Approve, 12 Months, See Quantity Limit Chart for ADHD	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to: - 150 capsules per month of Dexedrine Spansule 5 mg, 10 mg - 120 capsules per month of Dexedrine Spansule 15 mg - 180 tablets per month of dextroamphetamine 5 mg, 10 mg - 180 tablets per month of Zenzedi (dextroamphetamine) 2.5 mg, 5 mg, 7.5 mg, 10 mg - 120 tablets per month of Zenzedi (dextroamphetamine) 15 mg

			- 90 tablets per month of Zenzedi (dextroamphetamine) 20 mg - 60 tablets per month of Zenzedi (dextroamphetamine) 30 mg Your request has been partially approved. You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity Dexedrine, dextroamphetamine, Zenzedi]
13.	Deny For the denial verbiage, only include the requested drug. Remove all the other drugs from the verbiage.	Approve, 12 Months, See Quantity Limit Chart for ADHD	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to: - 180 tablets per month of Evekeo 5 mg, 10 mg - 180 tablets per month of Evekeo ODT 2.5 mg, 5 mg, 10 mg - 90 tablets per month of Evekeo ODT 15 mg, 20 mg Your request has been partially approved. You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity Evekeo]
14.	Deny For the denial verbiage, only include the requested drug. Remove all the other drugs from the verbiage.	Approve, 12 Months, See Quantity Limit Chart for ADHD	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to: - 150 tablets per month of Focalin 2.5 mg, 5 mg, 10 mg - 90 capsules per month of Focalin XR 5 mg, 10 mg, 15 mg - 60 capsules per month of Focalin XR 25 mg Your request has been partially approved. You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity Focalin]
15.	Deny For the denial verbiage, only include the requested drug. Remove all the other drugs from the verbiage.	Approve, 12 Months, See Quantity Limit Chart for ADHD	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to: - 90 capsules per month of methylphenidate CD 10 mg, 20 mg, 30 mg - 60 capsules per month of methylphenidate CD 40 mg, 50 mg - 150 tablets per month of methylphenidate ER 10 mg, 20 mg - 150 capsules per month of Ritalin LA 10 mg, 20 mg - 90 capsules per month of Ritalin LA 30 mg - 60 capsules per month of Ritalin LA 40 mg Your request has been partially approved. You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity Ritalin LA, methylphenidate CD/ER]
16.	Deny For the denial verbiage, only include the requested drug. Remove	Approve, 12 Months, See Quantity Limit Chart for ADHD	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to: - 300 tablets per month of methylphenidate chewable 2.5 mg, 5 mg, 10 mg - 210 tablets per month of methylphenidate 5 mg, 10 mg

	all the other drugs from the verbiage.		- 150 tablets per month of methylphenidate 20 mg Your request has been partially approved. You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity methylphenidate]
17.	Deny For the denial verbiage, only include the requested drug. Remove all the other drugs from the verbiage.	Approve, 12 Months, See Quantity Limit Chart for ADHD	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to: - 3000 ml per month of Methylin (methylphenidate) oral solution 5 mg/5 ml - 1500 ml per month of Methylin (methylphenidate) oral solution 10 mg/5 ml Your request has been partially approved. You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity Methylin]
18.	Deny	Approve, 12 Months, See Quantity Limit Chart for ADHD	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 90 capsules per month of Mydayis 12.5 mg. Your request has been partially approved. You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity Mydayis]
19.	Deny	Approve, 12 Months, See Quantity Limit Chart for ADHD	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 1800 ml per month of ProCentra. Your request has been partially approved. You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity ProCentra]
20.	Deny For the denial verbiage, only include the requested drug. Remove all the other drugs from the verbiage.	Approve, 12 Months, See Quantity Limit Chart for ADHD	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to: - 150 tablets per month of QuilliChew ER 20 mg - 90 tablets per month of QuilliChew ER 30 mg - 60 tablets per month of QuilliChew ER 40 mg Your request has been partially approved. You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity QuilliChew]
21.	Deny	Approve, 12 Months, See Quantity Limit Chart for ADHD	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 600 ml per month of Quillivant XR. Your request has been partially approved. You have been approved for the maximum quantity that your plan covers for a duration of 12 months.

			Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity Quillivant]
22.	Go to 23	Deny	You do not meet the requirements of your plan. Your plan covers additional quantities of this drug when you have any of these conditions: - Attention-Deficit Hyperactivity Disorder (ADHD) - Attention Deficit Disorder (ADD) - Narcolepsy and the drug you are requesting is Adderall (amphetamine mixture), Dexedrine Spansule (dextroamphetamine sustained-release), dextroamphetamine, Evekeo (amphetamine), ProCentra (dextroamphetamine sulfate oral solution), or Zenzedi (dextroamphetamine) Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]
23.	Go to 24	Deny	You do not meet the requirements of your plan. Your plan covers additional quantities of this drug when you meet the following conditions: - Narcolepsy is confirmed by a sleep study and the drug you are requesting is Adderall (amphetamine mixture), Dexedrine Spansule (dextroamphetamine sustained-release), dextroamphetamine, Evekeo (amphetamine), ProCentra (dextroamphetamine sulfate oral solution), or Zenzedi (dextroamphetamine) Your request has been denied based on the information we have. [Short Description: No sleep study]
24.	Deny	Go to 25	You do not meet the requirements of your plan. Your plan does not cover additional quantities of this drug for the diagnosis of narcolepsy. Your request has been denied based on the information we have. [Short Description: Over max quantity for narcolepsy diagnosis]
25.	1=26; 2=27; 3=27; 4=28; 5=29; 6=27	N/A	
26.	Deny For the denial verbiage, only include the requested drug. Remove all the other drugs from the verbiage.	Approve, 12 Months, See Quantity Limit Chart for Narcolepsy	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to: - 120 tablets per month of Adderall 5 mg, 7.5 mg, 10 mg, 12.5 mg - 90 tablets per month of Adderall 15 mg, 20 mg - 60 tablets per month of Adderall 30mg Your request has been partially approved. You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity narcolepsy Adderall]
27.	Deny For the denial verbiage, only include the requested drug. Remove all the other drugs from the verbiage.	Approve, 12 Months, See Quantity Limit Chart for Narcolepsy	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to: - 150 capsules per month of Dexedrine Spansule 5 mg, 10 mg - 120 capsules per month of Dexedrine Spansule 15 mg - 180 tablets per month of dextroamphetamine 5 mg, 10 mg - 180 tablets per month of Zenzedi (dextroamphetamine) 2.5 mg, 5 mg, 7.5 mg, 10 mg - 120 tablets per month of Zenzedi (dextroamphetamine) 15 mg - 90 tablets per month of Zenzedi (dextroamphetamine) 20mg - 60 tablets per month of Zenzedi (dextroamphetamine) 30 mg

			Your request has been partially approved. You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity narcolepsy Dexedrine, dextroamphetamine, Zenzedi]
28.	Deny For the denial verbiage, only include the requested drug. Remove all the other drugs from the verbiage.	Approve, 12 Months, See Quantity Limit Chart for Narcolepsy	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 180 tablets per month of Evekeo 5 mg or 10 mg. Your request has been partially approved. You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity narcolepsy Evekeo]
29.	Deny For the denial verbiage, only include the requested drug. Remove all the other drugs from the verbiage.	Approve, 12 Months, See Quantity Limit Chart for Narcolepsy	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 1800 ml per month of ProCentra. Your request has been partially approved. You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity narcolepsy ProCentra]

PRIOR AUTHORIZATION CRITERIA

BRAND NAME*
(generic)

AKLIEF
(trifarotene)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization ***Ref # 3362-A***

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Aklief Cream is a retinoid indicated for the topical treatment of acne vulgaris in patients 9 years of age and older.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for the topical treatment of acne vulgaris

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Aklief Cream is a retinoid indicated for the topical treatment of acne vulgaris in patients 9 years of age and older.[1-3]

The American Academy of Dermatology (AAD) guidelines state that the topical therapy of acne vulgaris includes the usage of agents that are available over the counter or via prescription. Therapy choice may be influenced by age of the patient, site of involvement, extent and severity of disease, and patient preference. Topical therapies may be used as monotherapy, in combination with other topical agents, or in combination with oral agents in both initial control and maintenance. Topical retinoids are considered to be first-line agents for the treatment of mild, moderate, and severe acne vulgaris; these agents are important in addressing the development and maintenance of acne and are recommended as monotherapy in primarily comedonal acne, or in combination with topical or oral antimicrobials in patients with mixed or primarily inflammatory acne lesions.[4]

The safety and effectiveness of Aklief cream have not been established in pediatric subjects under the age of 9 years.[1] Per AAD guidelines, current data show that retinoids in younger patients are effective and are not associated with increased irritation or risk.[4]

REFERENCES

1. Aklief cream [package insert]. Dallas, TX: Galderma Laboratories, LP; January 2022.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2022; Accessed July 1, 2022.
3. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed July 1, 2022.
4. Zaenglein AL, Pathy AL, Schlosser BJ, et al. Guidelines of care for the management of acne vulgaris. *J Am Acad Dermatol*. 2016;74:945-73.

Written by:	UM Development (RP)
Date Written:	10/2019
Revised:	(MAC) 07/2020 (updated document name/title), 07/2021 (no changes); (RZ) 07/2022 (no clinical changes); (DRS) 08/2022 (removed age)
Reviewed:	Medical Affairs (CHART) 10/17/2019, (CHART) 07/30/2020, (CHART) 08/05/2021, 07/28/2022, 09/08/2022

CRITERIA FOR APPROVAL

1	Is the requested drug being prescribed for the topical treatment of acne vulgaris? [No further questions]	Yes	No

Mapping Instructions			
	Yes	**No**	**DENIAL REASONS**
1.	Approve, 12 Months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have acne vulgaris. Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]

QUANTITY LIMIT CRITERIA

BRAND NAME*
(generic)

AKYNZEO CAPSULES
(netupitant/palonosetron)

AKYNZEO INJECTION
(fosnetupitant/palonosetron)

Status: CVS Caremark Criteria
Type: Quantity Limit ***Ref # 1211-H***

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Akynzeo capsules are indicated in combination with dexamethasone in adults for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of cancer chemotherapy, including, but not limited to, highly emetogenic chemotherapy. Akynzeo capsules is a combination of palonosetron and netupitant: palonosetron prevents nausea and vomiting during the acute phase and netupitant prevents nausea and vomiting during both the acute and delayed phase after cancer chemotherapy.

Akynzeo for injection and Akynzeo injection are indicated in combination with dexamethasone in adults for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy. Akynzeo for injection is a combination of palonosetron and fosnetupitant, a prodrug of netupitant: palonosetron prevents nausea and vomiting during the acute phase and fosnetupitant prevents nausea and vomiting during both the acute and delayed phase after cancer chemotherapy.

Limitations of Use

Akynzeo for injection and Akynzeo injection have not been studied for the prevention of nausea and vomiting associated with anthracycline plus cyclophosphamide chemotherapy.

RATIONALE

Akynzeo capsules are indicated in combination with dexamethasone in adults for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of cancer chemotherapy, including, but not limited to, highly emetogenic chemotherapy. Akynzeo for injection and Akynzeo injection are indicated in combination with dexamethasone in adults for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy.[1-3]

The recommended oral dosage in adults for highly emetogenic chemotherapy, including cisplatin based chemotherapy, is one capsule of Akynzeo administered approximately 1 hour prior to the start of chemotherapy with dexamethasone 12 mg administered 30 minutes prior to chemotherapy on day 1; followed by dexamethasone 8 mg once daily on days 2 to 4. The recommended dosage in adults for anthracyclines and cyclophosphamide based chemotherapy and chemotherapy not considered highly emetogenic is one capsule of Akynzeo approximately 1 hour prior to the start of chemotherapy with dexamethasone 12 mg administered 30 minutes prior to chemotherapy on day 1. Administration of dexamethasone on days 2 to 4 is not necessary.[1-3]

The recommended injection dosage in adults for highly emetogenic chemotherapy, including cisplatin based chemotherapy, is one vial of Akynzeo administered approximately 30 minutes prior to the start of chemotherapy with

dexamethasone 12 mg administered 30 minutes prior to chemotherapy on day 1; followed by dexamethasone 8 mg once daily on days 2 to 4. Akynzeo for injection and Akynzeo injection have not been studied for the prevention of nausea and vomiting associated with anthracycline plus cyclophosphamide chemotherapy.[1-3]

The limit allows a quantity sufficient for two chemotherapy cycles per month (i.e., one chemotherapy cycle every 2 weeks). If the patient is requesting more than the initial quantity limit, then the claim will reject with a message indicating that a prior authorization is required.

REFERENCES

1. Akynzeo [package insert]. Iselin, NJ: Helsinn Therapeutics.; January 2021.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. http://online.lexi.com/. Accessed December 2021.
3. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. http://www.micromedexsolutions.com/. Accessed December 2021.

Written by:	UM Development (RP)
Date Written:	10/2014
Revised:	01/2015; (MS) 01/2016 (no clinical changes), 01/2017 (no clinical changes), (ME) 01/2018 (no clinical changes), 05/2018 (added injection), 01/2019 (no clinical changes), 01/2020 (no clinical changes), 01/2021 (no clinical changes), (VS) 01/2022 (added Akynzeo injection and updated QL)
Reviewed:	Medical Affairs (SES) 10/2014, 01/2015; (JG) 01/2017, (ME) 05/2018, (CHART) 01/30/20, (CHART) 1/28/01, (CHART) 02/03/2022 External Review: 11/2014, 04/2015, 04/2016, 04/2017, 04/2018, 06/2018, 04/2019, 04/2020, 04/2021, 04/2022

LIMIT CRITERIA

Limits do not accumulate together, patient is allowed the maximum limit for each drug and strength

Drug	4 Week Limit*	12 Week Limit*
Akynzeo capsules	2 capsules / 21 days	Does Not Apply*
Akynzeo for injection	2 vials / 21 days	Does Not Apply*
Akynzeo injection	40 mL / 21 days	Does Not Apply*

** The duration of 21 days is used for a 28-day fill period to allow time for refill processing.*

**** These drugs are for short-term acute use; therefore, the mail limit will be the same as the retail limit. The intent is for prescriptions of the requested drug to be filled one month at a time, even if filled at mail order; there should be no 3 month supplies filled.***

PRIOR AUTHORIZATION CRITERIA

BRAND NAME
(generic)

ALBENZA
(albendazole)

BILTRICIDE
(praziquantel)

EGATEN
(triclabendazole)

EMVERM
(mebendazole)

Status: CVS Caremark Criteria
Type: Post Limit Prior Authorization

POLICY

FDA-APPROVED INDICATIONS

Albenza

Neurocysticercosis

Albenza is indicated for the treatment of parenchymal neurocysticercosis due to active lesions caused by larval forms of the pork tapeworm, *Taenia solium.*

Hydatid Disease

Albenza is indicated for the treatment of cystic hydatid disease of the liver, lung, and peritoneum, caused by the larval form of the dog tapeworm, *Echinococcus granulosus.*

Biltricide

Biltricide is indicated in patients aged 1 year and older for the treatment of the following infections:

- Schistosomiasis due to all species of schistosoma (for example, *Schistosoma mekongi, Schistosoma japonicum, Schistosoma mansoni and Schistosoma hematobium*), and
- Clonorchiasis and Opisthorchiasis due to the liver flukes, *Clonorchis sinensis/Opisthorchis viverrini* (approval of this indication was based on studies in which the two species were not differentiated).

Compendial Uses

Treatment of intestinal infections caused by *Taenia solium, Taenia saginata, Diphyllobothrium latum and Hymenolepis nana*.[5,6]

Egaten

Egaten is indicated for the treatment of fascioliasis in patients 6 years of age and older.

Emverm

Emverm is indicated for the treatment of patients two years of age and older with gastrointestinal infections caused by *Ancylostoma duodenale* (hookworm), *Ascaris lumbricoides* (roundworm), *Enterobius vermicularis* (pinworm), *Necator americanus* (hookworm), and *Trichuris trichiura* (whipworm).

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The infection has been confirmed by a diagnostic or laboratory test (e.g., imaging scans, scotch tape test, blood, stool, or urine test)

AND

- The request is for mebendazole (Emverm) in a patient 2 years of age and older for a second course of therapy (first course of therapy administered within the past year) at a dose up to 2 tablets per day for two 3-day treatments for any of the following infections: A) Ancylostoma duodenale (hookworm), B) Ascaris lumbricoides (roundworm), C) Enterobius vermicularis (pinworm), D) Necator americanus (hookworm), E) Trichuris trichiura (whipworm).

OR

- The request is for albendazole (Albenza) for the treatment of Hydatid Disease for a second course of therapy (first course of therapy administered within the past year) at a dose up to 4 tablets per day for three 28-day cycles with 14-day free intervals.

OR

- The request is for praziquantel (Biltricide) in a patient 1 year of age and older for the treatment of schistosomiasis, clonorchiasis, or opisthorchiasis for any of the following: A) a quantity up to 36 tablets, B) a second day or course of therapy (first course of therapy administered within the past year)

OR

- The request is for triclabendazole (Egaten) in a patient 6 years of age or older for the treatment of fascioliasis for any of the following: A) a quantity up to 32 tablets, B) a second day or course of therapy (first course of therapy administered within the past year)

Quantity Limits apply.
Albenza (albendazole): 336 tablets per 365 days
Biltricide (praziquantel): 72 tablets per 365 days
Egaten (triclabendazole): 32 tablets per 365 days
Emverm (mebendazole): 12 tablets per 365 days
** This drug is indicated for short-term acute use; therefore, the mail limit will be the same as the retail limit.*

REFERENCES

1. Albenza [package insert]. Bridgewater, NJ: Amneal Pharmaceuticals LLC; September 2019.
2. Biltricide [package insert]. Whippany, NJ: Bayer HealthCare Pharmaceuticals Inc.; January 2019.
3. Egaten [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; February 2022.
4. Emverm [package insert]. Bridgewater, NJ: Amneal Pharmaceuticals LLC; August 2021.
5. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2023; Accessed January 20, 2023.
6. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed January 20, 2023.
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8. Parasites – Clonorchis. Available at: https://www.cdc.gov/parasites/clonorchis/health_professionals/index.html. Accessed January 25, 2023.
9. Parasites - Opisthorchis Infection. Available at: https://www.cdc.gov/parasites/opisthorchis/health_professionals/index.html. Accessed January 25, 2023.
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11. Parasites – Cysticercosis. Available at: https://www.cdc.gov/parasites/cysticercosis/. Accessed January 25, 2023.
12. Parasites - Fasciola. Available at: https://www.cdc.gov/parasites/fasciola/health_professionals/index.html#tx. Accessed January 25, 2023.
13. Parasites – Taeniasis. Available at: https://www.cdc.gov/parasites/taeniasis/health_professionals/index.html#tx/. Accessed January 25, 2023.
14. Parasites – Diphyllobothrium. Available at: https://www.cdc.gov/parasites/diphyllobothrium/health_professionals/index.html/. Accessed January 25, 2023.

15. Parasites – Hymenolepiasis. Available at: https://www.cdc.gov/parasites/hymenolepis/health_professionals/index.html. Accessed January 25, 2023.
16. Fryar CD, Carroll MD, Gu Q, Afful J, Ogden CL. Anthropometric reference data for children and adults: United States, 2015–2018. National Center for Health Statistics. Vital Health Stat 3(46). 2021. Available at: https://stacks.cdc.gov/view/cdc/100478. Accessed January 25, 2023.
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PRIOR AUTHORIZATION CRITERIA

BRAND NAME
(generic)

ALBENZA
(albendazole)

BILTRICIDE
(praziquantel)

EGATEN
(triclabendazole)

EMVERM
(mebendazole)

Status: CVS Caremark Criteria
Type: Post Limit Prior Authorization

POLICY

FDA-APPROVED INDICATIONS

Albenza

Neurocysticercosis

Albenza is indicated for the treatment of parenchymal neurocysticercosis due to active lesions caused by larval forms of the pork tapeworm, Taenia solium.

Hydatid Disease

Albenza is indicated for the treatment of cystic hydatid disease of the liver, lung, and peritoneum, caused by the larval form of the dog tapeworm, Echinococcus granulosus.

Biltricide

Biltricide is indicated in patients aged 1 year and older for the treatment of the following infections:
Schistosomiasis due to all species of schistosoma (for example, Schistosoma mekongi, Schistosoma japonicum, Schistosoma mansoni and Schistosoma hematobium), and Clonorchiasis and Opisthorchiasis due to the liver flukes, Clonorchis sinensis/Opisthorchis viverrini (approval of this indication was based on studies in which the two species were not differentiated).

Compendial Uses

Treatment of intestinal infections caused by Taenia solium, Taenia saginata, Diphyllobothrium latum and Hymenolepis nana.[5,6]

Egaten

Egaten is indicated for the treatment of fascioliasis in patients 6 years of age or older.

Emverm

Emverm is indicated for the treatment of patients two years of age and older with gastrointestinal infections caused by Ancylostoma duodenale (hookworm), Ascaris lumbricoides (roundworm), Enterobius vermicularis (pinworm), Necator americanus (hookworm), and Trichuris trichiura (whipworm).

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The infection has been confirmed by a diagnostic or laboratory test (e.g. imaging scans, blood, stool, or urine test)

AND

- The request is for mebendazole (Emverm) in a patient 2 years of age or older for a second course of therapy (first course of therapy administered within the past year) at a dose up to 2 tablets per day for two 3 day treatments for any of the following: A) Ancylostoma duodenale (hookworm), B) Ascaris lumbricoides (roundworm), C) Enterobius vermicularis (pinworm), D) Necator americanus (hookworm), E) Trichuris trichiura (whipworm).

  OR

- The request is for albendazole (Albenza) for the treatment of Hydatid Disease for a second course of therapy (first course of therapy administered within the past year) at a dose up to 4 tablets per day for three 28-day cycles with 14-day free intervals

  OR

- The request is for praziquantel (Biltricide) in a patient 1 year of age or older for the treatment of schistosomiasis, clonorchiasis, or opisthorchiasis for any of the following: A) a quantity up to 36 tablets, B) a second day or course of therapy (first course of therapy administered within the past year)

  OR

- The request is for triclabendazole (Egaten) in a patient 6 years of age or older for the treatment of fascioliasis for any of the following: A) a quantity up to 32 tablets, B) a second day or course of therapy (first course of therapy administered within the past year)

Quantity Limits apply.

REFERENCES

1. Albenza [package insert]. Bridgewater, NJ: Amneal Pharmaceuticals LLC; September 2019.
2. Biltricide [package insert]. Whippany, NJ: Bayer HealthCare Pharmaceuticals Inc.; January 2019.
3. Egaten [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corp.; September 2019
4. Emverm [package insert]. Bridgewater, NJ: Amneal Pharmaceuticals LLC; January 2019.
5. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2022; Accessed January 27, 2022.
6. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed January 27, 2022.
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9. Parasites - Opisthorchis Infection. Available at: https://www.cdc.gov/parasites/opisthorchis/health_professionals/index.html. Accessed February 2022.
10. Parasites - Echinococcosis. Available at: https://www.cdc.gov/parasites/echinococcosis/. Accessed February 2022.
11. Parasites – Cysticercosis. Available at: https://www.cdc.gov/parasites/cysticercosis/. Accessed February 2022.
12. Parasites - Fasciola. Available at: https://www.cdc.gov/parasites/fasciola/health_professionals/index.html#tx. Accessed February 2022.
13. Parasites – Taeniasis. Available at: https://www.cdc.gov/parasites/taeniasis/health_professionals/index.html#tx/. Accessed February 2022.
14. Parasites – Diphyllobothrium. Available at: https://www.cdc.gov/parasites/diphyllobothrium/health_professionals/index.html/. Accessed February 2022.
15. Parasites – Hymenolepiasis. Available at: https://www.cdc.gov/parasites/hymenolepis/health_professionals/index.html. Accessed February 2022.
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QUANTITY LIMIT CRITERIA

BRAND NAME
(generic)

ALDARA
(imiquimod cream 5%)

Status: CVS Caremark® Criteria
Type: Quantity Limit

POLICY

FDA-APPROVED INDICATIONS

Actinic Keratosis

Imiquimod Cream is indicated for the topical treatment of clinically typical, nonhyperkeratotic, nonhypertrophic actinic keratoses on the face or scalp in immunocompetent adults.

Superficial Basal Cell Carcinoma

Imiquimod cream 5% is indicated for the topical treatment of biopsy-confirmed, primary superficial basal cell carcinoma (sBCC) in immunocompetent adults, with a maximum tumor diameter of 2.0 cm, located on the trunk (excluding anogenital skin), neck, or extremities (excluding hands and feet), only when surgical methods are medically less appropriate and patient follow-up can be reasonably assured. The histological diagnosis of superficial basal cell carcinoma should be established prior to treatment, since safety and efficacy of imiquimod cream have not been established for other types of basal cell carcinomas, including nodular and morpheaform (fibrosing or sclerosing) types.

External Genital Warts

Imiquimod cream 5% is indicated for the treatment of external genital and perianal warts/condyloma acuminata in patients 12 years or older.

Limitations of Use

Imiquimod cream 5% has been evaluated in children ages 2 to 12 years with molluscum contagiosum and these studies failed to demonstrate efficacy.

Unevaluated Populations

The safety and efficacy of imiquimod cream 5% in immunosuppressed patients have not been established. Imiquimod cream 5% should be used with caution in patients with pre-existing autoimmune conditions. The efficacy and safety of imiquimod cream have not been established for patients with Basal Cell Nevus Syndrome or Xeroderma Pigmentosum.

INITIAL LIMIT QUANTITY

Limits should accumulate across all drugs and strengths up to highest quantity listed depending on the order the claims are processed.

Drug	4 Week Limit*	12 Week Limit*
Aldara (imiquimod cream 5 percent)	24 packets / 21 days	72 packets / 63 days

**The duration of 21 days is used for a 28-day fill period and 63 days is used for an 84-day fill period to allow time for refill processing.*

REFERENCES

1. Aldara Cream 5% [package insert]. Bridgewater, NJ: Valeant Pharmaceuticals North America LLC; June 2022.
2. Imiquimod Cream 5% [package insert]. Mahwah, NJ: Glenmark Pharmaceuticals Inc., USA; March 2021.

3. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Waltham, MA: UpToDate, Inc.; 2023. https://online.lexi.com. Accessed June 12, 2023.
4. Micromedex (electronic version). Merative, Ann Arbor, Michigan, USA. Available at: https://www.micromedexsolutions.com/ (cited: 06/12/2023).
5. NCCN Clinical Practice Guidelines in Oncology. Basal Cell Skin Cancer. Version 1.2023, March 10, 2023. https://www.nccn.org/professionals/physician_gls/pdf/nmsc.pdf

Reference number(s)
2150-A

SPECIALTY GUIDELINE MANAGEMENT

ALECENSA (alectinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication
Alecensa is indicated for the treatment of patients with anaplastic lymphoma kinase (ALK)-positive, metastatic non-small cell lung cancer (NSCLC) as detected by an FDA-approved test.

B. Compendial Uses
1. Recurrent or advanced NSCLC, ALK rearrangement-positive as a single agent
2. Brain metastases from ALK rearrangement-positive NSCLC as a single agent
3. Relapsed/refractory ALK+ anaplastic large cell lymphoma as a single agent

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: ALK mutation status

III. CRITERIA FOR INITIAL APPROVAL

A. Non-Small Cell Lung Cancer (NSCLC)
Authorization of 12 months may be granted for treatment of recurrent, advanced or metastatic ALK-positive NSCLC (including brain metastases from NSCLC) as a single agent.

B. Anaplastic Large Cell Lymphoma (ALCL)
Authorization of 12 months may be granted for treatment of relapsed/refractory ALK-positive ALCL as a single agent.

IV. CONTINUATION OF THERAPY

A. Non-Small Cell Lung Cancer (NSCLC)
Authorization of 12 months may be granted for continued treatment in members requesting reauthorization when there is no evidence of unacceptable toxicity while on the current regimen.

B. Anaplastic Large Cell Lymphoma (ALCL)
Authorization of 12 months may be granted for continued treatment in members requesting reauthorization when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

V. REFERENCES

1. Alecensa [package insert]. South San Francisco, CA: Genentech USA, Inc.; September 2021.
2. The NCCN Drugs & Biologics Compendium® © 2022 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed March 9, 2022.

QUANTITY LIMIT CRITERIA

BRAND NAME
(generic)

ALINIA
(nitazoxanide)

Status: CVS Caremark Criteria
Type: Quantity Limit with Age Edit

POLICY

FDA-APPROVED INDICATIONS
Alinia for Oral Suspension (patients 1 year of age and older) and Alinia Tablets (patients 12 years and older) are indicated for the treatment of diarrhea caused by *Giardia lamblia* or *Cryptosporidium parvum*.

Limitations of Use
Alinia for Oral Suspension and Alinia Tablets have not been shown to be effective for the treatment of diarrhea caused by *Cryptosporidium parvum* in HIV-infected or immunodeficient patients.

Compendial Uses
Human fascioliasis (Fasciola hepatica)[2,3]
Clostridium difficile colitis[2,3]

LIMIT CRITERIA
Limits do not accumulate together; patient is allowed the maximum limit for each drug and strength

Drug	1 Month Limit*	3 Month Limit*	Age Edit
Alinia 100 mg/5 mL Oral Suspension (nitazoxanide)	540 mL per 25 days	Does Not Apply*	1 year of age and older
Alinia 500 mg Tablets	20 tablets per 25 days	Does Not Apply*	12 years of age and older

** The duration of 25 days is used for a 30-day fill period to allow time for refill processing.*

**** These drugs are for short-term acute use; therefore, the mail limit will be the same as the retail limit. The intent is for prescriptions of the requested drug to be filled one month at a time, even if filled at mail order; there should be no 3 month supplies filled.***

REFERENCES

1. Alinia [package insert]. Tampa, FL: Romark Laboratories, L.C.; January 2022.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2023; Accessed February 3, 2023.
3. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed February 3, 2023.
4. Centers for Disease Control. https://www.cdc.gov/parasites/fasciola/health_professionals/index.html#tx. Accessed February 3, 2023.
5. L Clifford McDonald, Dale N Gerding, Stuart Johnson, Johan S Bakken, Karen C Carroll, Susan E Coffin, Erik R Dubberke, Kevin W Garey, Carolyn V Gould, Ciaran Kelly, Vivian Loo, Julia Shaklee Sammons, Thomas J Sandora, Mark H Wilcox, Clinical Practice Guidelines for *Clostridium difficile* Infection in Adults and Children: 2017 Update by

the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA), *Clinical Infectious Diseases*, Volume 66, Issue 7, 1 April 2018, Pages e1–e48, https://doi.org/10.1093/cid/cix1085. Accessed February 3, 2023.

Reference number(s)
1815-A

SPECIALTY GUIDELINE MANAGEMENT

ALUNBRIG (brigatinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication
Alunbrig is indicated for the treatment of adult patients with anaplastic lymphoma kinase (ALK)-positive metastatic non-small cell lung cancer (NSCLC) as detected by an FDA-approved test.

B. Compendial Uses
1. Recurrent, advanced or metastatic ALK rearrangement-positive NSCLC
2. Brain metastases from ALK rearrangement-positive NSCLC
3. Inflammatory myofibroblastic tumor (IMT) with ALK translocation
4. Erdheim-Chester Disease (ECD) with ALK-fusion

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: ALK mutation status

III. CRITERIA FOR INITIAL APPROVAL

A. Non-Small Cell Lung Cancer (NSCLC)
Authorization of 12 months may be granted for treatment of recurrent, advanced, or metastatic ALK-positive NSCLC (including brain metastases from NSCLC) as a single agent.

B. Inflammatory Myofibroblastic Tumor (IMT)
Authorization of 12 months may be granted for treatment of ALK-positive IMT as a single agent when either of the following criteria are met:
1. The member has uterine sarcoma and the disease is advanced, recurrent, metastatic, or inoperable
2. The member has a soft tissue sarcoma (not including uterine sarcoma)

C. Erdheim-Chester Disease (ECD)
Authorization of 12 months may be granted for treatment of symptomatic or relapsed/refractory ALK-positive Erdheim-Chester Disease as a single agent.

IV. CONTINUATION OF THERAPY

A. Non-Small Cell Lung Cancer (NSCLC)

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization when there is no evidence of unacceptable toxicity while on the current regimen.

B. All Other Indications

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for all other indications listed in Section III when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

V. REFERENCES

1. Alunbrig [package insert]. Lexington, MA: Takeda Pharmaceuticals America, Inc.; February 2022.
2. The NCCN Drugs & Biologics Compendium® © 2023 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed February 27, 2023.

Reference number(s)
1646-A

SPECIALTY GUIDELINE MANAGEMENT

Letairis (ambrisentan)
ambrisentan

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Indicated for the treatment of pulmonary arterial hypertension (PAH) (World Health Organization [WHO] Group 1):
A. To improve exercise ability and delay clinical worsening.
B. In combination with tadalafil to reduce the risks of disease progression and hospitalization for worsening PAH, and to improve exercise ability.

Studies establishing effectiveness included trials predominantly in patients with WHO Functional Class II-III symptoms and etiologies of idiopathic or heritable PAH or PAH associated with connective tissue diseases.

All other indications are considered experimental/investigational and not medically necessary.

II. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with a pulmonologist or cardiologist.

III. CRITERIA FOR INITIAL APPROVAL

Pulmonary Arterial Hypertension (PAH)
Authorization of 12 months may be granted for treatment of PAH when ALL of the following criteria are met:
A. Member has PAH defined as WHO Group 1 class of pulmonary hypertension (refer to Appendix).
B. PAH was confirmed by either criterion (1) or criterion (2) below:
    1. Pretreatment right heart catheterization with all of the following results:
        i. Mean pulmonary arterial pressure (mPAP) > 20 mmHg
        ii. Pulmonary capillary wedge pressure (PCWP) ≤ 15 mmHg
        iii. Pulmonary vascular resistance (PVR) ≥ 3 Wood units in adult patients or pulmonary vascular resistance index (PVRI) ≥ 3 Wood units x m^2 in pediatric patients
    2. For infants less than one year of age, PAH was confirmed by Doppler echocardiogram if right heart catheterization cannot be performed.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for members with an indication listed in Section III who are currently receiving the requested medication through a paid pharmacy or medical benefit, and who are experiencing benefit from therapy as evidenced by disease stability or disease improvement.

V. APPENDIX

WHO Classification of Pulmonary Hypertension

1 PAH

1.1 Idiopathic (PAH)
1.2 Heritable PAH
1.3 Drug- and toxin-induced PAH
1.4. PAH associated with:
- 1.4.1 Connective tissue diseases
- 1.4.2 HIV infection
- 1.4.3 Portal hypertension
- 1.4.4 Congenital heart diseases
- 1.4.5 Schistosomiasis

1.5 PAH long-term responders to calcium channel blockers
1.6 PAH with overt features of venous/capillaries (PVOD/PCH) involvement
1.7 Persistent PH of the newborn syndrome

2 PH due to left heart disease

2.1 PH due to heart failure with preserved LVEF
2.2 PH due to heart failure with reduced LVEF
2.3 Valvular heart disease
2.4 Congenital/acquired cardiovascular conditions leading to post-capillary PH

3 PH due to lung diseases and/or hypoxia

3.1 Obstructive lung disease
3.2 Restrictive lung disease
3.3 Other lung disease with mixed restrictive/obstructive pattern
3.4 Hypoxia without lung disease
3.5 Developmental lung disorders

4 PH due to pulmonary artery obstruction

4.1 Chronic thromboembolic PH
4.2 Other pulmonary artery obstructions
- 4.2.1 Sarcoma (high or intermediate grade) or angiosarcoma
- 4.2.2 Other malignant tumors
  - Renal carcinoma
  - Uterine carcinoma
  - Germ cell tumours of the testis
  - Other tumours
- 4.2.3 Non-malignant tumours
  - Uterine leiomyoma
- 4.2.4 Arteritis without connective tissue disease
- 4.2.5 Congenital pulmonary artery stenosis
- 4.2.6 Parasites
  - Hydatidosis

5 PH with unclear and/or multifactorial mechanisms

5.1 Hematologic disorders: Chronic hemolytic anemia, myeloproliferative disorders

5.2 Systemic and metabolic disorders: Pulmonary Langerhans cell histiocytosis, Gaucher disease, glycogen storage disease, neurofibromatosis, sarcoidosis
5.3 Others: chronic renal failure with or without hemodialysis, fibrosing mediastinitis
5.4 Complex congenital heart disease

VI. REFERENCES

1. Letairis [package insert]. Foster City, CA: Gilead Sciences, Inc.; August 2019.
2. Ambrisentan [package insert]. Weston, FL: Apotex Corp.; November 2020.
3. Chin KM, Rubin LJ. Pulmonary arterial hypertension. *J Am Coll Cardiol*. 2008;51(16):1527-1538.
4. McLaughlin VV, Archer SL, Badesch DB, et al. ACCF/AHA 2009 expert consensus document on pulmonary hypertension a report of the American College of Cardiology Foundation Task Force on Expert Consensus Documents and the American Heart Association developed in collaboration with the American College of Chest Physicians, American Thoracic Society, Inc., and the Pulmonary Hypertension Association. *J Am Coll Cardiol*. 2009;53(17):1573-1619.
5. Badesch DB, Champion HC, Gomez-Sanchez MA, et al. Diagnosis and assessment of pulmonary arterial hypertension. *J Am Coll Cardiol.* 2009;54:S55-S66.
6. Rubin LJ; American College of Chest Physicians. Diagnosis and management of pulmonary arterial hypertension: ACCP evidence-based clinical practice guidelines. *Chest*. 2004;126(1 Suppl):7S-10S.
7. Barst RJ, Gibbs SR, Ghofrani HA, et al. Updated evidence-based treatment algorithm in pulmonary arterial hypertension. *J Am Coll Cardiol.* 2009;54:S78-S84.
8. Taichman DB, Ornelas J, Chung L, et al. Pharmacologic therapy for pulmonary arterial hypertension in adults. CHEST guideline and expert panel report. *Chest*. 2014;46(2):449-475.
9. Abman SH, Hansmann G, Archer SL, et al. Pediatric pulmonary hypertension: guidelines from the American Heart Association and American Thoracic Society. *Circulation*. 2015;132(21):2037-99.
10. Klinger JR, Elliott CG, Levine DJ, et al. Therapy for Pulmonary Arterial Hypertension in Adults: Update of the CHEST Guidelines and Expert Panel Report. *Chest*. 2019:155(3): 565-586.
11. Galie N, McLaughlin VV, Rubin LJ, Simonneau G. An overview of the 6th World Symposium on Pulmonary Hypertension. *Eur Respir J.* 2019; 53: 1802148; DOI: 10.1183/13993003.02148-2018. Published 24 January 2019.
12. Simonneau G, Montani D, Celermajer DS, et al. Haemodynamic definitions and updated clinical classification of pulmonary hypertension. *Eur Respir J.* 2019;53:1801913; doi:10.1183/13993003.01913-2018.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME*
(generic)

ANADROL-50
(oxymetholone)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization ***Ref # 1087-A***

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Anadrol-50 Tablets are indicated in the treatment of anemias caused by deficient red cell production. Acquired aplastic anemia, congenital aplastic anemia, myelofibrosis and the hypoplastic anemias due to the administration of myelotoxic drugs often respond. Anadrol-50 Tablets should not replace other supportive measures such as transfusion, correction of iron, folic acid, vitamin B_{12} or pyridoxine deficiency, antibacterial therapy and the appropriate use of corticosteroids.

Compendial Uses
Cachexia associated with AIDS (HIV wasting)[3]

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for any of the following: A) Anemia due to deficient red cell production, (e.g., acquired aplastic anemia, congenital aplastic anemia, myelofibrosis, the hypoplastic anemias due to the administration of myelotoxic drugs, Fanconi's anemia), B) Cachexia associated with acquired immunodeficiency syndrome (AIDS) (human immunodeficiency virus [HIV] wasting)

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Anadrol-50 (oxymetholone) is indicated in the treatment of anemias caused by deficient red cell production. Acquired aplastic anemia, congenital aplastic anemia, myelofibrosis and the hypoplastic anemias due to the administration of myelotoxic drugs often respond.[1]

Fanconi's anemia is categorized under the FDA-approved indication.[3] Additionally, oxymetholone produced significant gains in lean body mass and body cell mass in HIV patients with wasting.[3]

Androgens have been misused and abused by athletes, bodybuilders, weight lifters, and others to enhance athletic performance or physique. Following review of data from published literature and case reports in October 2016, the FDA concluded that misuse and abuse of androgens are associated with serious adverse cardiovascular, hepatic, endocrine, and mental health effects.[4]

The manufacturer states that response is not often immediate, and a minimum trial of three to six months should be given.[1] Therefore, the duration of approval will be 6 months.

REFERENCES

1. Anadrol-50 [package insert]. Marietta, GA: Alaven Pharmaceuticals LLC; December 2006.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2021; Accessed December 7, 2021.

CVS caremark

3. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed December 7, 2021.
4. Food and Drug Administration. Testosterone and other anabolic androgenic steroids (AAS): FDA statement – risks associated with abuse and dependence. Silver Spring, MD; 2016 Oct 25. Available at: https://wayback.archive-it.org/7993/20170111133941/http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm526151.htm. Accessed December 2021.

Written by:	UM Development (GP)
Date Written:	8/1997
Revised:	(LS) 12/1998; (MG) 12/2002, 12/2003; (TM) 09/2004; (MC) 10/2005; (MG) 10/2006(2); (NB) 07/2007; (CT) 09/2007; (AM) 09/2008; (CT) 09/2009; (MS) 09/2010, 06/2011, 11/2011, 03/2012; (PL) 06/2012; (CT) 06/2013, 12/2013 (split Anadrol-50 and Oxandrin into separate criteria), 02/2014; (RP) 02/2015; (MS) 02/2016, 02/2017; (DS) 02/2018; (RP) 12/2018 (no clinical changes), (JK) 12/2019 (no clinical changes, removed MDC designation from title/document), 12/2020 (Updated document title); (PM) 12/2021 (no clinical changes)
Reviewed:	CRC 01/2004; CDPR/Medical Affairs 09/2004, 10/2005, 10/2006; (WF) 07/2007, 09/2007, 09/2008, 09/2009; (KP) 09/2010, 06/2011, 11/2011, 06/2012; (SES) 06/2013; (KP) 02/2014; (SES) 02/2015; (DC) 02/2016; (ME) 02/2017; (AN) 02/2018; (DNC) 12/2018; (CHART) 01/02/2020; (CHART) 12/31/2020, 12/30/2021 External Review: 04/2008, 02/2009, 12/2009, 1/2011, 10/2011, 10/2012, 08/2013, 06/2014, 06/2015, 06/2016, 04/2017, 04/2018, 02/2019, 02/2020, 04/2021, 04/2022

CRITERIA FOR APPROVAL

1	Is the requested drug being prescribed for any of the following: A) Anemia due to deficient red cell production, (e.g., acquired aplastic anemia, congenital aplastic anemia, myelofibrosis, the hypoplastic anemias due to the administration of myelotoxic drugs, Fanconi's anemia), B) Cachexia associated with acquired immunodeficiency syndrome (AIDS) (human immunodeficiency virus [HIV] wasting)?	Yes	No

Guidelines for Approval	
Duration of Approval 6 Months	
Set 1	
Yes to question(s)	**No to question(s)**
1	None

Mapping Instructions			
	Yes	**No**	**DENIAL REASONS – DO NOT USE FOR MEDICARE PART D**
1.	Approve, 6 months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have any of these conditions: - Anemia due to deficient red-cell production, (e.g., acquired aplastic anemia, congenital aplastic anemia, myelofibrosis, hypoplastic anemias due to the administration of myelotoxic drugs, Fanconi's anemia) - Cachexia associated with AIDS (HIV-wasting) Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]

QUANTITY LIMIT CRITERIA

DRUG CLASS	**ANTICHOLINERGIC, COMBINATION, AND MAST CELL STABILIZER ORAL INHALATION**
BRAND NAME (generic)	
	ATROVENT HFA (ipratropium)
	COMBIVENT RESPIMAT (ipratropium/albuterol)
	(cromolyn inhalation solution)
	INCRUSE ELLIPTA (umeclidinium)
	(ipratropium inhalation solution)
	(ipratropium/albuterol inhalation solution)
	LONHALA MAGNAIR (glycopyrrolate inhalation solution)
	SPIRIVA HANDIHALER (tiotropium)
	SPIRIVA RESPIMAT (tiotropium)
	TUDORZA PRESSAIR (aclidinium)
	YUPELRI (revefenacin inhalation solution)

Status: CVS Caremark Criteria
Type: Quantity Limit

POLICY

FDA-APPROVED INDICATIONS

Atrovent HFA

Atrovent HFA Inhalation Aerosol is indicated as a bronchodilator for maintenance treatment of bronchospasm associated with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and emphysema.

Combivent Respimat
Combivent Respimat is a combination of ipratropium bromide (an anticholinergic agent) and albuterol sulfate (a beta-adrenergic agonist) indicated for use in patients with chronic obstructive pulmonary disease (COPD) on a regular aerosol bronchodilator who continue to have evidence of bronchospasm and who require a second bronchodilator.

Cromolyn Inhalation Solution
Cromolyn sodium inhalation solution USP is a prophylactic agent indicated in the management of patients with bronchial asthma. In patients whose symptoms are sufficiently frequent to require a continuous program of medication, cromolyn sodium inhalation solution USP is given by inhalation on a regular daily basis. The effect of cromolyn sodium is usually evident after several weeks of treatment, although some patients show an almost immediate response. In patients who develop acute bronchoconstriction in response to exposure to exercise, toluene diisocyanate, environmental pollutants, etc, cromolyn sodium should be given shortly before exposure to the precipitating factor.

Incruse Ellipta
Incruse Ellipta is indicated for the maintenance treatment of patients with chronic obstructive pulmonary disease (COPD).

Ipratropium Inhalation Solution
Ipratropium Bromide Inhalation Solution administered either alone or with other bronchodilators, especially beta adrenergics, is indicated as a bronchodilator for maintenance treatment of bronchospasm associated with chronic obstructive pulmonary disease, including chronic bronchitis and emphysema.

Ipratropium Bromide / Albuterol Sulfate inhalation solution
Ipratropium Bromide and Albuterol Sulfate Inhalation Solution is indicated for the treatment of bronchospasm associated with COPD in patients requiring more than one bronchodilator.

Lonhala Magnair
Lonhala Magnair is indicated for the long-term maintenance treatment of airflow obstruction in patients with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and/or emphysema.

Spiriva HandiHaler
Spiriva HandiHaler (tiotropium bromide inhalation powder) is indicated for the long-term, once daily, maintenance treatment of bronchospasm associated with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and emphysema. Spiriva HandiHaler is indicated to reduce exacerbations in COPD patients.

Spiriva Respimat
Maintenance Treatment of Chronic Obstructive Pulmonary Disease
Spiriva Respimat (tiotropium bromide) is indicated for the long-term, once-daily, maintenance treatment of bronchospasm associated with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and emphysema. Spiriva Respimat is indicated to reduce exacerbations in COPD patients.

Important Limitation of Use:
Spiriva Respimat is NOT indicated for the relief of acute bronchospasm.

Maintenance Treatment of Asthma
Spiriva Respimat is a bronchodilator indicated for the long-term, once-daily, maintenance treatment of asthma in patients 6 years of age and older.

Important Limitation of Use:
Spiriva Respimat is NOT indicated for the relief of acute bronchospasm.

Tudorza Pressair
Tudorza Pressair (aclidinium bromide inhalation powder) is indicated for the maintenance treatment of patients with chronic obstructive pulmonary disease (COPD).

Yupelri
Yupelri is indicated for the maintenance treatment of patients with chronic obstructive pulmonary disease (COPD).

LIMIT CRITERIA
Limits do not accumulate together; patient is allowed the maximum limit for each drug and strength

Medication*	Maintenance Dose	Maximum Daily Dose	Package Size	1 Month Limit* 3 Months Limit*
Atrovent HFA (ipratropium)	2 inhalations four times daily	12 inhalations	200 inhalations per 12.9gm canister	2 packages (12.9gm each) / 25 days 6 packages (12.9gm each) / 75 days
Combivent Respimat (ipratropium / albuterol)	1 inhalation four times daily	6 inhalations	120 inhalations per 4gm cartridge	2 packages (4gm each) / 25 days 6 packages (4gm each) / 75 days
Cromolyn inhalation solution	nebulization of 1 vial (2mL) four times daily	4 vials (2mL each)	60 vials (2mL each) per carton	2 packages (120 vials x 2mL) / 25 days 6 packages (360 vials x 2mL) / 75 days
Incruse Ellipta (umeclidinium)	1 inhalation once daily	1 inhalation	30 blisters per inhaler	1 package (30 blisters) / 25 days 3 packages (90 blisters) / 75 days
Ipratropium inhalation solution, 0.02%	nebulization of 1 vial (2.5 mL) three to four times daily	4 vials (2.5mL each)	25 vials (2.5mL each) per carton)	5 packages (125 vials x 2.5mL) / 25 days 15 packages (375 vials x 2.5mL) / 75 days
			30 vials (2.5mL each) per carton)	4 packages (120 vials x 2.5mL) / 25 days 12 packages (360 vials x 2.5mL) / 75 days
			60 vials (2.5mL each) per carton	2 packages (120 vials x 2.5mL) / 25 days 6 packages (360 vials x 2.5mL) / 75 days
Ipratropium Bromide / Albuterol sulfate inhalation solution	nebulization of 1 vial (3mL) four times daily	6 vials (3mL each)	30 vials (3mL each) per carton	6 packages (180 vials x 3mL) / 25 days 18 packages (540 vials x 3mL) / 75 days
			60 vials (3mL each) per carton	3 packages (180 vials x 3mL) / 25 days 9 packages (540 vials x 3mL) / 75 days
Lonhala Magnair Starter and Refill Kit (glycopyrrolate)	1 inhalation twice daily	2 inhalations	60 vials (1mL each) (2 vials in each pouch, 30 pouches in each box) per kit	1 package (60 vials x 1mL) / 25 days 3 packages (180 vials x 1mL) / 75 days
Spiriva HandiHaler (tiotropium)	2 inhalations of the powder contents of 1 capsule once daily	1 capsule	30 capsules per carton	1 package (30 capsules) / 25 days 3 packages (90 capsules) / 75 days
			90 capsules per carton	1 package (90 capsules) / 75 days
Spiriva Respimat (tiotropium)	2 inhalations once daily	2 inhalations	60 inhalations per 4gm cartridge	1 package (4gm) / 25 days 3 packages (4gm each) / 75 days
Tudorza Pressair (aclidinium)	1 inhalation twice daily	2 inhalations	30 inhalations per inhaler	2 packages / 25 days 6 packages / 75 days
			60 inhalations per inhaler	1 package / 25 days 3 packages / 75 days
Yupelri (revefenacin)	nebulization of 1 vial (3mL) once daily	1 vial (3 mL each)	30 vials (3mL each) per carton	1 package (30 vials x 3mL) / 25 days 3 packages (90 vials x 3mL) / 75 days

**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*

REFERENCES

1. Atrovent HFA [package insert]. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc.; February 2020.
2. Combivent Respimat [package insert]. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc.; December 2021.

3. Cromolyn Sodium [package insert]. North Wales, PA: Teva Pharmaceuticals USA, Inc.; October 2015.
4. Incruse Ellipta [package insert]. Research Triangle Park, NC: GlaxoSmithKline; August 2020.
5. Ipratropium Bromide [package insert]. Columbia, SC: Ritedose Pharmaceuticals, LLC; January 2013.
6. Ipratropium Bromide and Albuterol Sulfate [package insert]. West Columbia, SC: Nephron Pharmaceuticals Corporation; August 2012.
7. Lonhala Magnair [package insert]. Marlborough, MA: Sunovion Pharmaceuticals Inc.; August 2020.
8. Spiriva Handihaler [package insert]. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc.; November 2021.
9. Spiriva Respimat [package insert]. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc.; November 2021.
10. Tudorza Pressair [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; February 2021.
11. Yupelri [package insert]. Morgantown, WV: Mylan Specialty L.P.; May 2022.

QUANTITY LIMIT CRITERIA

DRUG CLASS	**GLUCAGON-LIKE PEPTIDE 1 (GLP-1) RECEPTOR AGONISTS AND GLUCOSE-DEPENDENT INSULINOTROPIC POLYPEPTIDE (GIP)/GLUCAGON-LIKE PEPTIDE 1 (GLP-1) RECEPTOR AGONIST**
BRAND NAME* **(generic)**	**ADLYXIN** **(lixisenatide)**
	BYDUREON **(exenatide extended-release)**
	BYDUREON BCISE **(exenatide extended-release)**
	BYETTA **(exenatide)**
	MOUNJARO **(tirzepatide)**
	OZEMPIC **(semaglutide)**
	RYBELSUS **(semaglutide)**
	TRULICITY **(dulaglutide)**
	VICTOZA **(liraglutide)**

Status: CVS Caremark Criteria
Type: Quantity Limit ***Ref # 4525-H***

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Adlyxin

Adlyxin is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Limitations of Use:

- Adlyxin has not been studied in patients with chronic pancreatitis or a history of unexplained pancreatitis. Consider other antidiabetic therapies in patients with a history of pancreatitis.
- Adlyxin should not be used in patients with type 1 diabetes mellitus.
- Adlyxin has not been studied in patients with gastroparesis and is not recommended in patients with gastroparesis.

Bydureon/Bydureon BCise
Bydureon and Bydureon BCise are indicated as an adjunct to diet and exercise to improve glycemic control in adults and pediatric patients aged 10 years and older with type 2 diabetes mellitus.
Limitations of Use:
- Bydureon/Bydureon BCise is not recommended as first-line therapy for patients who have inadequate glycemic control on diet and exercise because of the uncertain relevance of the rat thyroid C-cell tumor findings to humans.
- Bydureon/Bydureon BCise is not indicated for use in patients with type 1 diabetes mellitus.
- Bydureon/Bydureon BCise is an extended-release formulation of exenatide and should not be used with other products containing the active ingredient exenatide.
- Bydureon/Bydureon BCise has not been studied in patients with a history of pancreatitis. Consider other antidiabetic therapies in patients with a history of pancreatitis.

Byetta
Byetta is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.
Limitations of Use
- Byetta is not indicated for use in patients with type 1 diabetes.
- Byetta contains exenatide and should not be used with other products containing the active ingredient exenatide.
- Byetta has not be studied in patients with a history of pancreatitis. Consider other antidiabetic therapies in patients with a history of pancreatitis.

Mounjaro
Mounjaro is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.
Limitations of Use
- Mounjaro has not been studied in patients with a history of pancreatitis.
- Mounjaro is not indicated for use in patients with type 1 diabetes mellitus.

Ozempic
Ozempic is indicated as:
- an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.
- to reduce the risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke) in adults with type 2 diabetes mellitus and established cardiovascular disease.

Limitations of Use:
- Ozempic has not been studied in patients with a history of pancreatitis. Consider other antidiabetic therapies in patients with a history of pancreatitis.
- Ozempic is not indicated for use in patients with type 1 diabetes mellitus.

Rybelsus
Rybelsus is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.
Limitations of Use
- Rybelsus is not recommended as a first-line therapy for patients who have inadequate glycemic control on diet and exercise because of the uncertain relevance of rodent C-cell tumor findings to humans.
- Rybelsus has not been studied in patients with a history of pancreatitis. Consider other antidiabetic therapies in patients with a history of pancreatitis.
- Rybelsus is not indicated for use in patients with type 1 diabetes mellitus.

Trulicity

Trulicity is indicated:

- as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.
- to reduce the risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke) in adults with type 2 diabetes mellitus who have established cardiovascular disease or multiple cardiovascular risk factors.

Limitations of Use

- Trulicity has not been studied in patients with a history of pancreatitis. Consider other antidiabetic therapies in patients with a history of pancreatitis.
- Trulicity should not be used in patients with type 1 diabetes mellitus.
- Trulicity has not been studied in patients with severe gastrointestinal disease, including severe gastroparesis and is therefore not recommended in these patients.

Victoza

Victoza is indicated:

- as an adjunct to diet and exercise to improve glycemic control in patients 10 years and older with type 2 diabetes mellitus.
- to reduce the risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke) in adults with type 2 diabetes mellitus and established cardiovascular disease.

Limitations of Use:

- Victoza should not be used in patients with type 1 diabetes mellitus.
- Victoza contains liraglutide and should not be coadministered with other liraglutide-containing products.

INITIAL LIMIT QUANTITY

Limits do not accumulate together; patient is allowed the maximum limit for each drug and strength.

PLEASE NOTE: Since manufacturer package sizes may vary, it is the discretion of the dispensing pharmacy to fill quantities per package size up to these quantity limits. In such cases the filling limit and day supply may be less than what is indicated.

Drug	Maximum Dosing	Package Size(s)	1 Month Limit* 3 Months Limit*
Adlyxin	20mcg daily	Starter pack - 2 pens (1 pen of 10mcg, 1 pen of 20mcg), 14 doses per pen, 3mL each Maintenance pack - 2 pens of 20mcg, 14 doses per pen, 3mL each	2 prefilled pens (6mL) / 21 days 6 prefilled pens (18mL) / 63 days
Bydureon	2mg once weekly	Carton of 4 single-dose pens	4 pens / 21 days 12 pens / 63 days
Bydureon BCISE	2mg once weekly	Carton of 4 single-dose autoinjectors (2mg/0.85mL each)	4 auto-injectors (3.4mL) / 21 days 12 auto-injectors (10.2mL) / 63 days
Byetta	10mcg twice daily	5mcg dose, 60 doses, 1.2mL prefilled pen	1 prefilled pen (1.2mL) / 25 days 3 prefilled pens (3.6mL) / 75 days
		10mcg dose, 60 doses, 2.4mL prefilled pen	1 prefilled pen (2.4mL) / 25 days 3 prefilled pens (7.2mL) / 75 days
Mounjaro	15mg once weekly	2.5mg/0.5mL, 5mg/0.5mL, 7.5mg/0.5mL, 10mg/0.5mL, 12.5mg/0.5mL, 15mg/0.5mL in cartons of 4 single-dose pens (0.5mL each)	4 pens (2mL) / 21 days 12 pens (6mL) / 63 days
Ozempic	2mg once weekly	Carton of 1 pen (2mg/1.5mL)	1 prefilled pen (1.5mL) / 21 days 3 prefilled pens (4.5mL) / 63 days
		Carton of 1 pen (2mg/3mL)	1 prefilled pen (3mL) / 21 days 3 prefilled pens (9mL) / 63 days

		Carton of 1 pen (4mg/3mL)	1 prefilled pen (3mL) / 21 days 3 prefilled pens (9mL) / 63 days
		Carton of 1 pen (8mg/3mL)	1 prefilled pen (3mL) / 21 days 3 prefilled pens (9mL) / 63 days
Rybelsus	14mg once daily	3mg, 7mg, 14mg in bottles of 30 tablets	30 tablets / 25 days 90 tablets / 75 days
Trulicity	4.5mg once weekly	0.75mg/0.5mL, 1.5mg/0.5mL, 3mg/0.5mL, 4.5mg/0.5mL in cartons of 4 single-dose pens (0.5mL each)	4 pens (2mL) / 21 days 12 pens (6mL) / 63 days
Victoza	1.8mg once daily	Package of 2 or 3 pens (18mg/3mL each)	3 pens (9mL) / 25 days 9 pens (27mL) / 75 days
** The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing OR the duration of 21 days is used for a 28-day fill period and 63 days is used for an 84-day fill period to allow time for refill processing.*			

RATIONALE

Quantity limits are set to allow quantities sufficient for the maximum/maintenance dosing per the package insert. If the patient is requesting more than the initial quantity limit, the claim will reject with a message indicating that quantity limits are exceeded.

Adlyxin[1]

The starting dose of Adlyxin is 10 mcg subcutaneously once daily for 14 days. Increase the dose to the maintenance dose of 20 mcg once daily starting on Day 15.

Adlyxin (lixisenatide) injection is supplied in a disposable single-patient use pen for subcutaneous administration. Each prefilled pen contains 3 mL solution. The green starter pen contains 50 mcg/mL of Adlyxin and delivers 14 doses of 10 mcg, and the burgundy maintenance pen contains 100 mcg/mL of Adlyxin and delivers 14 doses of 20 mcg.

The following packages are available:

- Starter Pack: For treatment initiation, Starter Pack contains 1 single-patient-use prefilled green pen of Adlyxin 10 mcg and 1 single-patient-use prefilled burgundy pen of Adlyxin 20 mcg
- Maintenance Pack: Contains 2 single-patient-use prefilled burgundy pens for Adlyxin 20 mcg

After first use, the pen can be stored at room temperature for 14 days.

Bydureon[2]

The recommended dose of Bydureon is 2 mg subcutaneously once every 7 days (weekly).

Bydureon (exenatide extended-release) single-dose tray is supplied in cartons that contain four single-dose trays containing one single-dose vial containing 2 mg exenatide (as a white to off-white powder), one prefilled syringe delivering 0.65 mL diluent, one vial connector and two custom needles (one spare needle). Each single-dose pen contains 2 mg of exenatide (as a white to off-white powder) and delivers 0.65 mL diluent.

Bydureon can be kept at room temperature for no more than 4 weeks, if needed. Bydureon must be administered immediately after the exenatide powder is suspended in the diluent.

Bydureon BCise[3]

The recommended dose of Bydureon BCise is 2 mg subcutaneously once every 7 days (weekly).

Bydureon BCise (exenatide extended-release) contains 2 mg of exenatide in 0.85 mL vehicle, in a pre-filled, single-dose autoinjector. It is a white to off-white, opaque, extended-release injectable suspension, available in cartons that contain four single-dose autoinjectors.

The single-dose pen can be stored at room temperature for no more than 4 weeks, if needed.

Byetta[4]

Initiate Byetta at 5 mcg administered subcutaneously twice daily. Based on clinical response, the dose of Byetta can be increased to 10 mcg twice daily after 1 month of therapy.

Byetta (exenatide) is supplied as a clear, colorless solution for subcutaneous injection containing 250 mcg/mL exenatide.

The following packages are available:

- 5 mcg per dose, 60 doses, 1.2 mL prefilled pen
- 10 mcg per dose, 60 doses, 2.4 mL prefilled pen

After first use, the pen can be stored at room temperature and should be discarded after 30 days.

Mounjaro[5]

The recommended starting dosage of Mounjaro is 2.5 mg injected subcutaneously once weekly. The 2.5 mg dosage is for treatment initiation and is not intended for glycemic control. After 4 weeks, increase the dosage to 5 mg injected subcutaneously once weekly. If additional glycemic control is needed, increase the dosage in 2.5 mg increments after at least 4 weeks on the current dose. The maximum dosage of Mounjaro is 15 mg injected subcutaneously once weekly.

Mounjaro is a clear, colorless to slightly yellow solution available in pre-filled single-dose pens as follows:
Carton of 4 single-dose pens

- 2.5 mg/0.5 mL
- 5 mg/0.5 mL
- 7.5 mg/0.5 mL
- 10 mg/0.5 mL
- 12.5 mg/0.5 mL
- 15 mg/0.5 mL

Store MOUNJARO in a refrigerator at 2°C to 8°C (36°F to 46°F). If needed, each single-dose pen can be stored unrefrigerated at temperatures not to exceed 30ºC (86ºF) for up to 21 days.

Ozempic[6]

Start Ozempic with a 0.25 mg subcutaneous injection once weekly for 4 weeks. The 0.25 mg dose is intended for treatment initiation and is not effective for glycemic control. After 4 weeks on the 0.25 mg dose, increase the dosage to 0.5 mg once weekly. If additional glycemic control is needed after at least 4 weeks on the 0.5 mg dose, the dosage may be increased to 1 mg once weekly. If additional glycemic control is needed after at least 4 weeks on the 1 mg dosage, the dosage may be increased to 2 mg once weekly. The maximum recommended dosage is 2 mg once weekly.
Ozempic (semaglutide) injection is a clear, colorless solution of 0.68 mg/mL, 1.34 mg/mL or 2.68 mg/mL of semaglutide available in pre-filled, disposable, single-patient-use pens in the following packaging configurations:
2 mg/1.5 mL, which provides:

- 4 doses of 0.25 mg (initiation) and 2 doses of 0.5 mg (maintenance)
  or
- 4 doses of 0.5 mg (maintenance)

2 mg/3 mL, which provides:

- 4 doses of 0.25 mg (initiation) and 2 doses of 0.5 mg (maintenance)
  or
- 4 doses of 0.5 mg (maintenance)

4 mg/3 mL, which provides:

- 4 doses of 1 mg (maintenance)

8 mg/3 mL, which provides:

- 4 doses of 2 mg (maintenance)

After first use, the pen can be stored at room temperature for 56 days.

Rybelsus[7]

Start Rybelsus with 3 mg once daily for 30 days. The 3 mg dose is intended for treatment initiation and is not effective for glycemic control. After 30 days on the 3 mg dose, increase the dose to 7 mg once daily. The dose may be increased to 14 mg once daily if additional glycemic control is needed after at least 30 days on the 7 mg dose.
Taking two 7 mg Rybelsus tablets to achieve a 14 mg dose is not recommended.
Patients treated with Rybelsus 14 mg daily can be transitioned to Ozempic subcutaneous injection 0.5 mg once weekly. Patients can start Ozempic the day after their last dose of Rybelsus. Patients treated with once weekly Ozempic 0.5 mg subcutaneous injection can be transitioned to Rybelsus 7 mg or 14 mg. Patients can start Rybelsus up to 7 days after their last injection of Ozempic. There is no equivalent dose of Rybelsus for Ozempic 1 mg.
Rybelsus tablets are available as follows:

- 3 mg, Bottle of 30 tablets

- 7 mg, Bottle of 30 tablets
- 14 mg, Bottle of 30 tablets

Trulicity[8]
The recommended initiating dose of Trulicity is 0.75 mg injected subcutaneously once weekly. Increase the dose to 1.5 mg once weekly for additional glycemic control. If additional glycemic control is needed, increase the dose to 3 mg once weekly after at least 4 weeks on the 1.5 mg dose. If additional glycemic control is needed, increase the dose to the maximum dose of 4.5 mg once weekly after at least 4 weeks on the 3 mg dose.
Trulicity (dulaglutide) injection is a clear and colorless solution supplied in single-dose pens. Each Trulicity single-dose pen is packaged in a cardboard outer carton.
Carton of 4 Single-Dose Pens
- 0.75 mg/0.5 mL solution in a single-dose pen
- 1.5 mg/0.5 mL solution in a single-dose pen
- 3 mg/0.5 mL solution in a single-dose pen
- 4.5 mg/0.5 mL solution in a single-dose pen

If needed, each single-dose pen can be stored at room temperature for a total of 14 days.

Victoza[9]
Adults - Initiate Victoza with a dose of 0.6 mg daily for one week. The 0.6 mg dose is a starting dose intended to reduce gastrointestinal symptoms during initial titration and is not effective for glycemic control in adults. After one week at 0.6 mg per day, increase the dose to 1.2 mg daily. If additional glycemic control is required, increase the dose to 1.8 mg daily after at least one week of treatment with the 1.2 mg daily dose.
Pediatrics- Initiate Victoza with a dose of 0.6 mg daily. After at least one week at 0.6 mg daily, the dose may be increased to 1.2 mg daily if additional glycemic control is required. If additional glycemic control is required, increase the dose to 1.8 mg daily after at least one week of treatment with the 1.2 mg daily dose.
Victoza (liraglutide) injection is a 18 mg/3 mL (6 mg/mL) clear, colorless solution in a pre-filled, single-patient-use pen that delivers doses of 0.6 mg, 1.2 mg, or 1.8 mg and is available in package sizes containing 2 or 3 Victoza pens.
After first use, the pen can be stored at room temperature for 30 days.

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Written by:	UM Development (RP)
Date Written:	02/2021
Revised:	(RZ) 07/2021 (no clinical changes), (DFW) 03/2022 (add new Ozempic 8 mg/3 mL pen), 03/2022 (updated QL for 2 mg/1.5 mL package strength based on package size availability), (VLS) 05/2022 (added new Mounjaro), (VLS) 07/2022 (no clinical changes), (VLS) 10/2022 (added Ozempic 2mg/3mL)
Reviewed:	Medical Affairs (CHART) 03/11/2021, 08/05/2021, 04/14/2022, 04/14/2022, 05/2022, (CHART) 07/28/2022, (CHART) 10/27/2022 External Review: 03/2021, 10/2021, 06/2022 (FYI), 06/2022 (FYI), 08/2022, 10/2022, 12/2022 (FYI)

PRIOR AUTHORIZATION CRITERIA

DRUG CLASS	**ANTIEMETIC AGENTS – 5HT3 ANTAGONISTS**
BRAND NAME (generic)	
	ANZEMET (dolasetron mesylate)
	(granisetron hydrochloride) (ALL PRODUCTS)
	(palonosetron hydrochloride) (ALL PRODUCTS)
	SANCUSO (granisetron transdermal system)
	SUSTOL (granisetron extended-release injection)
	ZOFRAN (ALL DOSAGE FORMS) (ondansetron, ondansetron hydrochloride)
	ZUPLENZ (ondansetron oral soluble film)

Status: CVS Caremark Criteria
Type: Post Limit Prior Authorization

POLICY

FDA-APPROVED INDICATIONS

Anzemet Tablets

Anzemet tablets are indicated for the prevention of nausea and vomiting associated with moderately emetogenic cancer chemotherapy, including initial and repeat courses in adults and children 2 years and older.

Granisetron

Granisetron Tablets

Granisetron Hydrochloride Tablets are indicated for the prevention of:

- Nausea and vomiting associated with initial and repeat courses of emetogenic cancer therapy, including high-dose cisplatin.
- Nausea and vomiting associated with radiation, including total body irradiation and fractionated abdominal radiation.

Granisetron Injection:

Granisetron Hydrochloride Injection is indicated for:

- Prevention of nausea and/or vomiting associated with initial and repeat courses of emetogenic cancer therapy, including high-dose cisplatin.
- Prevention and treatment of postoperative nausea and vomiting in adults. As with other antiemetics, routine prophylaxis is not recommended in patients in whom there is little expectation that nausea and/or vomiting will occur postoperatively. In patients where nausea and/or vomiting must be avoided during the postoperative period,

granisetron hydrochloride injection USP is recommended even where the incidence of postoperative nausea and/or vomiting is low.

Ondansetron Injection
Prevention of Nausea and Vomiting Associated with Initial and Repeat Courses of Emetogenic Cancer Chemotherapy
Ondansetron injection is indicated for the prevention of nausea and vomiting associated with initial and repeat courses of emetogenic cancer chemotherapy, including high-dose cisplatin. Ondansetron injection is approved for patients aged 6 months and older.

Prevention of Postoperative Nausea and/or Vomiting
Ondansetron injection is indicated for the prevention of postoperative nausea and/or vomiting. As with other antiemetics, routine prophylaxis is not recommended for patients in whom there is little expectation that nausea and/or vomiting will occur postoperatively. In patients in whom nausea and/or vomiting must be avoided postoperatively, ondansetron injection is recommended even when the incidence of postoperative nausea and/or vomiting is low. For patients who do not receive prophylactic ondansetron injection and experience nausea and/or vomiting postoperatively, ondansetron injection may be given to prevent further episodes. Ondansetron injection is approved for patients aged 1 month and older.

Palonosetron Hydrochloride Injection 2mL single-dose vial
Palonosetron hydrochloride (HCl) injection is indicated for:
- Moderately emetogenic cancer chemotherapy - prevention of acute and delayed nausea and vomiting associated with initial and repeat courses
- Highly emetogenic cancer chemotherapy - prevention of acute nausea and vomiting associated with initial and repeat courses

Palonosetron Hydrochloride Injection 5 mL single-dose vial
Palonosetron hydrochloride injection is indicated in adults for prevention of:
- acute and delayed nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy (MEC).
- acute nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy (HEC).
- postoperative nausea and vomiting (PONV) for up to 24 hours following surgery. Efficacy beyond 24 hours has not been demonstrated.

As with other antiemetics, routine prophylaxis is not recommended in patients in whom there is little expectation that nausea and/or vomiting will occur postoperatively. In patients where nausea and vomiting must be avoided during the postoperative period, palonosetron hydrochloride is recommended even where the incidence of postoperative nausea and/or vomiting is low.

Palonosetron hydrochloride injection is indicated in pediatric patients 1 months to less than 17 years of age for prevention of:
- acute nausea and vomiting associated with initial and repeat courses of emetogenic cancer chemotherapy, including highly emetogenic cancer chemotherapy (HEC).

Sancuso Transdermal System
Sancuso is indicated for the prevention of nausea and vomiting in adults receiving moderately and/or highly emetogenic chemotherapy regimens of up to 5 consecutive days duration.

Sustol Extended-Release Injection
Sustol is indicated in combination with other antiemetics in adults for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of moderately emetogenic chemotherapy (MEC) or anthracycline and cyclophosphamide (AC) combination chemotherapy regimens.

Zofran Tablets, Zofran ODT, and Zofran Oral Solution
Zofran is indicated for the prevention of nausea and vomiting associated with:
- highly emetogenic cancer chemotherapy, including cisplatin greater than or equal to 50 mg/m^2
- initial and repeat courses of moderately emetogenic cancer chemotherapy

- radiotherapy in patients receiving either total body irradiation, single high-dose fraction to the abdomen, or daily fractions to the abdomen

Zofran is also indicated for the prevention of postoperative nausea and/or vomiting.

Zuplenz

Zuplenz is indicated for the prevention of nausea and vomiting associated with:

- highly emetogenic cancer chemotherapy, including cisplatin greater than or equal to 50 mg/m^2, in adults
- initial and repeat courses of moderately emetogenic cancer chemotherapy in adults and pediatric patients 4 years of age and older
- radiotherapy in adult patients receiving either total body irradiation, single high-dose fraction to the abdomen, or daily fractions to the abdomen

Zuplenz is also indicated for the prevention of postoperative nausea and/or vomiting in adults.

Compendial Uses:

- Treatment and/or prophylaxis of radiation-induced nausea and vomiting[15]

Compendial Use Ondansetron Only:

- Hyperemesis Gravidarum[15,16]

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The patient is receiving radiation therapy or moderate to highly emetogenic chemotherapy.

OR

- The patient is pregnant with the diagnosis of Hyperemesis Gravidarum and has a documented risk for hospitalization
  AND
  - The request is for Zofran, Zuplenz or ondansetron

  AND
  - The patient has experienced an inadequate treatment response, intolerance, or the patient has a contraindication to TWO of the following medications: A) vitamin B6, B) vitamin B6 in combination with doxylamine, C) doxylamine/pyridoxine extended-release (Bonjesta), D) doxylamine/pyridoxine delayed-release (Diclegis), E) promethazine (Phenergan), F) trimethobenzamide (Tigan), G) metoclopramide (Reglan), H) diphenhydramine (Benadryl), I) dimenhydrinate (Dramamine)

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QUANTITY LIMIT PRIOR AUTHORIZATION CRITERIA

DRUG CLASS	**DERMATOLOGICAL TOPICAL ANTIFUNGAL COMBINATIONS BRAND AND GENERIC ALL DOSAGE FORMS**
BRAND NAME* (generic)	**(clotrimazole and betamethasone dipropionate) LOTRISONE (clotrimazole and betamethasone dipropionate) (nystatin and triamcinolone acetonide)**
Status: CVS Caremark Criteria	
Type: Quantity Limit; Post Limit Prior Authorization	***Ref # 2912-HJ***

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Clotrimazole and Betamethasone Dipropionate Lotion

Clotrimazole and betamethasone dipropionate lotion is indicated in patients 17 years and older for the topical treatment of symptomatic inflammatory tinea pedis, tinea cruris, and tinea corporis due to Epidermophyton floccosum, Trichophyton mentagrophytes, and Trichophyton rubrum. Effective treatment without the risks associated with topical corticosteroid use may be obtained using a topical antifungal agent that does not contain a corticosteroid, especially for noninflammatory tinea infections. The efficacy of clotrimazole and betamethasone dipropionate lotion for the treatment of infections caused by zoophilic dermatophytes (e.g., Microsporum canis) has not been established.

Lotrisone Cream

Lotrisone cream is a combination of an azole antifungal and corticosteroid and is indicated for the topical treatment of symptomatic inflammatory tinea pedis, tinea cruris, and tinea corporis due to Epidermophyton floccosum, Trichophyton mentagrophytes, and Trichophyton rubrum in patients 17 years and older.

Nystatin and Triamcinolone Cream and Ointment

Nystatin and triamcinolone acetonide cream and ointment are indicated for the treatment of cutaneous candidiasis; it has been demonstrated that the nystatin-steroid combination provides greater benefit than the nystatin component alone during the first few days of treatment.

INITIAL QUANTITY LIMIT**

LIMIT CRITERIA
Limits should accumulate across same chemical entity up to highest quantity listed depending on the order the claims are processed. Accumulation does not apply if limit is coded for daily dose.

PLEASE NOTE: Since manufacturer package sizes may vary, it is the discretion of the dispensing pharmacy to fill quantities per package size up to these quantity limits. In such cases the filling limit and day supply may be less than what is indicated.

Drug	1 Month Limit*	3 Month Limit*
clotrimazole and betamethasone dipropionate lotion	60mL / 25 days	Does Not Apply*
Lotrisone cream (clotrimazole and betamethasone dipropionate cream)	60gm / 25 days	Does Not Apply*
nystatin and triamcinolone acetonide cream and ointment	60gm / 25 days	Does Not Apply*

** The duration of 25 days is used for a 30-day fill period to allow time for refill processing.*
**** These drugs are for short-term acute use; therefore, the mail limit will be the same as the retail limit. The intent is for prescriptions of the requested drug to be filled one month at a time, even if filled at mail order; there should be no 3 month supplies filled.***

**If the patient is requesting more than the initial quantity limit, the claim will reject with a message indicating that a prior authorization is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

COVERAGE CRITERIA
The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is not being used in a footbath

AND

- The request is for clotrimazole/betamethasone (Lotrisone) for the treatment of any of the following: tinea pedis, tinea corporis, tinea cruris
  OR
- The request is for nystatin/triamcinolone for the treatment of cutaneous candidiasis

Quantity Limits apply.

RATIONALE
The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Clotrimazole and betamethasone dipropionate lotion is indicated in patients 17 years and older for the topical treatment of symptomatic inflammatory tinea pedis, tinea cruris, and tinea corporis due to Epidermophyton floccosum, Lotrisone cream is a combination of an azole antifungal and corticosteroid and is indicated for the topical treatment of symptomatic inflammatory tinea pedis, tinea cruris, and tinea corporis due to Epidermophyton floccosum, Trichophyton mentagrophytes, and Trichophyton rubrum in patients 17 years and older. Nystatin and triamcinolone acetonide cream and ointment are indicated for the treatment of cutaneous candidiasis; it has been demonstrated that the nystatin-steroid combination provides greater benefit than the nystatin component alone during the first few days of treatment.

Initial Limit
The initial quantity limits take into consideration available packages sizes, including at least the smallest package size, and quantity sufficient for FDA-approved dosage for approximate body surface area (BSA) treated. The quantity for an application and the percent BSA were chosen based on estimations of the areas that may be affected following the fingertip method and Rule of 9s. Creams, lotions, and ointments will follow this approximation for determining the quantity

limits. The dosing and duration of use for the target drugs varies. Since manufacturer package sizes may also vary, it is the discretion of the dispensing pharmacy to fill quantities per package size up to these quantity limits. In such cases the filling limit and day supply may be less than what is indicated.

The initial quantity limit is set at 60 gm or mL per month taking into consideration available packages sizes, and quantity sufficient for short-term acute use.

If the patient is requesting more than the initial quantity limit, the claim will reject with a message indicating that a prior authorization is required.

Post Limit
The Post Limit prior authorization criteria do not approve topical antifungals for use in a footbath, as this is not an FDA-approved use.

The post limit approval quantity will be set at 90gm or 90mL per month of clotrimazole and betamethasone dipropionate (Lotrisone) or 120gm per month of nystatin and triamcinolone acetonide taking into consideration available package sizes, typical percent body surface area (%BSA) affected, and dosage.

The Post Limit quantity for approval per month is set at the maximum recommended dosage for clotrimazole-betamethasone (Lotrisone) and twice the initial quantity limit for nystatin-triamcinolone.

These drugs are for short-term acute use; therefore, the intent is for prescriptions of the requested drug to be filled one month at a time; there should be no 3 month supplies filled. The Post Limit duration of approval will be 3 months to accommodate a re-infection.

Clotrimazole and Betamethasone Dipropionate Lotion
Treatment of tinea corporis or tinea cruris:
Massage sufficient clotrimazole and betamethasone dipropionate lotion into the affected skin areas twice a day, in the morning and evening.
Clotrimazole and betamethasone dipropionate lotion should not be used longer than 2 weeks in the treatment of tinea corporis or tinea cruris and amounts greater than 45mL per week of clotrimazole and betamethasone dipropionate lotion should not be used. If a patient with tinea corporis or tinea cruris shows no clinical improvement after one week of treatment with clotrimazole and betamethasone dipropionate lotion, the diagnosis should be reviewed.
Treatment of tinea pedis:
Massage sufficient clotrimazole and betamethasone dipropionate lotion into the affected skin areas twice a day, in the morning and evening.
Clotrimazole and betamethasone dipropionate lotion should not be used longer than 4 weeks in the treatment of tinea pedis, and amounts greater than 45mL per week of clotrimazole and betamethasone dipropionate lotion should not be used. If a patient with tinea pedis shows no clinical improvement after 2 weeks of treatment with clotrimazole and betamethasone dipropionate lotion, the diagnosis should be reviewed.

Clotrimazole and betamethasone dipropionate lotion, 1%/0.05% (base) is available as a 30 mL bottle.

Lotrisone Cream
Treatment of tinea corporis or tinea cruris:
Apply a thin film of Lotrisone cream into the affected skin areas twice a day for one week. Do not use more than 45 grams per week. If a patient shows no clinical improvement after 1 week of treatment with Lotrisone cream, the diagnosis should be reviewed. Do not use longer than 2 weeks.
Treatment of tinea pedis:
Massage a sufficient amount of Lotrisone cream into the affected skin areas twice a day for two weeks. Do not use more than 45 grams per week. If a patient shows no clinical improvement after 2 weeks of treatment with Lotrisone cream, the diagnosis should be reviewed. Do not use longer than 4 weeks.

Lotrisone, clotrimazole and betamethasone dipropionate cream, brand, is available as 15gm and 45gm packages.

Nystatin and Triamcinolone Cream and Ointment

Treatment of cutaneous candidiasis:
Nystatin and Triamcinolone Acetonide Cream and Ointment are usually applied to the affected areas twice daily, in the morning and evening by massaging the preparation into the skin. The preparation should be discontinued if symptoms persist after 25 days of therapy.

Nystatin and Triamcinolone Acetonide Cream and Ointment are available in 15gm, 30gm, and 60gm packages.

Cutaneous candidiasis can involve almost any skin on the body, but most often occurs in warm, moist, creased areas such as the armpits and groin. Possible symptoms include intense itching; a red, growing skin rash; rash on the skin folds, genitals, middle of the body, buttocks, under the breasts, and other areas of skin; and infection of the hair follicles that may look like pimples.[7]

No universal standard exists for quantity of application, although suggested methods include use of the adult fingertip unit (the amount from the distal interphalangeal joint to the fingertip, or approximately 0.5 grams (gm), being applied over an area equal to 2 adult palms), following the rule of 9's that measures the percent affected area, and use of charts that propose amounts based on patient age and body site.[8]

The Rule of Nines estimation of body surface area is based on assigning percentages to different body areas.[9] Palmar hand surface is approximately 1% BSA.[10]

Anatomic Surface	**% of Body Surface**
head and neck	9%
anterior trunk	18%
posterior trunk	18%
arms, including hands	9% each
legs, including feet	18% each
genitalia	1%

Quantity for 1% BSA, suggested AAD estimation
- Grams per application:
  0.5gm per application over 2 palms (1% BSA per palm) = 0.25gm per application over 1% BSA

Clotrimazole/Betamethasone
Initial Limit
- Tinea Cruris
  1% BSA x 0.25gm per 1% BSA x 2 applications per day x 14 days = 7gm per 2 weeks
- Tinea Pedis
  3% BSA (~foot) x 0.25gm per 1% BSA x 2 applications per day x 14 days = 21gm per 2 weeks
- Tinea Corporis
  60gm / 0.25gm per 1% BSA / 2 applications per day / 14 days = 8.5% BSA

Post Limit
- Tinea Pedis
  6% BSA (~both feet) x 0.25gm per 1% BSA x 2 applications per day x 28 days= 84gm per 4 weeks
- Tina Corporis, Tinea Cruris
  90gm / 0.25gm per 1% BSA / 2 applications per day / 14 days = 12.8% BSA

Nystatin/Triamcinolone
Initial Limit
- Cutaneous candidiasis
  60gm / 0.25 per 1% BSA / 2 applications per day / 25 days = 4.8% BSA

Post Limit
- Cutaneous candidiasis
  120gm / 0.25gm per 1% BSA / 2 applications per day / 25 days = 9.6% BSA

Drug	Initial Limit	Post Limit	Indication	Dosage	Package Size
Clotrimazole-Betamethasone Lotion	60mL	90mL	tinea corporis, tinea cruris, tinea pedis	twice a day, no longer than 2 weeks, max 45mL/week; pedis: no longer than 4 weeks	30mL
Clotrimazole-Betamethasone (Lotrisone) Cream	60gm	90gm	tinea corporis, tinea cruris, tinea pedis	twice a day, for 1 week, no longer than 2 weeks, max 45gm/week; pedis: for 2 weeks, no longer than 4 weeks	15gm, 45gm
Nystatin-Triamcinolone Cream	60gm	120gm	cutaneous candidiasis	twice daily, discontinue if symptoms persist after 25 days	15gm, 30gm, 60gm
Nystatin-Triamcinolone Ointment	60gm	120gm	cutaneous candidiasis	twice daily, discontinue if symptoms persist after 25 days	15gm, 30gm, 60gm

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Written by: UM Development (TM)
Date Written: 04/2019 (Aetna Integration net new request)
Revised: (TM) 03/2020, (ME) 03/2021 (no clinical changes); (DRS) 03/2022 (no clinical changes)
Reviewed: Medical Affairs (GD) 04/2019, (CHART) 03/26/20, (CHART) 03/25/21, (CHART) 03/31/22
External Review: 06/2019, 04/2020 , 06/2021, 06/2022

CRITERIA FOR APPROVAL

1	Is the requested drug being used in a footbath? [If yes, then no further questions.]	Yes	No
2	Is this request for clotrimazole/betamethasone (Lotrisone) for the treatment of any of the following: A) tinea pedis, B) tinea corporis, C) tinea cruris? [If no, then skip to question 4.]	Yes	No
3	Is this request for more than 90gm or 90mL per month? [No further questions.]	Yes	No

[RPh Note: If yes, then deny and partial approve 90gm or 90mL / 25 days*, (*3 month limit does not apply).]

4	Is this request for nystatin/triamcinolone for the treatment of cutaneous candidiasis? [If no, then no further questions.]	Yes	No
5	Is this request for more than 120gm per month?	Yes	No

[RPh Note: If yes, then deny and partial approve 120gm / 25 days*, (*3 month limit does not apply).]

Mapping Instructions			
	Yes	**No**	**DENIAL REASONS – DO NOT USE FOR MEDICARE PART D**
1.	Deny	Go to 2	You do not meet the requirements of your plan. Your plan covers additional quantities of this drug when the requested drug is not being used in a footbath. Your request has been denied based on the information we have. [Short Description: No approvable use]
2.	Go to 3	Go to 4	
3.	Deny	Approve, 3 months, 90gm or 90mL / 25 days*, *3 month limit does not apply	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 90 grams or 90 milliliters per month of clotrimazole/betamethasone (Lotrisone). Your request has been partially approved. You have been approved for the maximum quantity that your plan covers for a duration of 3 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity- clotrimazole/betamethasone]
4.	Go to 5	Deny	You do not meet the requirements of your plan. Your plan covers additional quantities of this drug when you meet one of the following conditions: -You are using clotrimazole/betamethasone (Lotrisone) for tinea pedis, tinea corporis, or tinea cruris -You are using nystatin/triamcinolone for cutaneous candidiasis Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]
5.	Deny	Approve, 3 months, 120gm / 25 days*, *3 month limit does not apply	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 120 grams per month of nystatin/triamcinolone. Your request has been partially approved. You have been approved for the maximum quantity that your plan covers for a duration of 3 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity- nystatin/triamcinolone]

** The duration of 25 days is used for a 30-day fill period to allow time for refill processing.*

**** These drugs are for short-term acute use; therefore, the mail limit will be the same as the retail limit. The intent is for prescriptions of the requested drug to be filled one month at a time, even if filled at mail order; there should be no 3 month supplies filled.***

STEP THERAPY CRITERIA

DRUG CLASS	**TOPICAL ANTIFUNGAL AGENTS BRAND PRODUCTS ONLY**
BRAND NAME (generic)	
	ECOZA (econazole)
	ERTACZO (sertaconazole)
	EXELDERM (sulconazole nitrate)
	EXTINA (ketoconazole)
	LOPROX (ciclopirox)
	LUZU (luliconazole)
	MENTAX (butenafine)
	NAFTIN (naftifine)
	OXISTAT (oxiconazole)
	VUSION (miconazole/zinc oxide/white petrolatum)
	XOLEGEL (ketoconazole)

Status: CVS Caremark® Criteria
Type: Initial Step Therapy; Post Step Therapy Prior Authorization

POLICY

FDA-APPROVED INDICATIONS

Ecoza
Ecoza (econazole nitrate) topical foam, 1% is indicated for the treatment of interdigital tinea pedis caused by Trichophyton rubrum, Trichophyton mentagrophytes, and Epidermophyton floccosum in patients 12 years of age and older.

Ertaczo
Ertaczo (sertaconazole nitrate) cream, 2%, is indicated for the topical treatment of interdigital tinea pedis in immunocompetent adult and pediatric patients 12 years of age and older caused by Trichophyton rubrum, Trichophyton mentagrophytes, and Epidermophyton floccosum**.**

Exelderm
Exelderm (sulconazole nitrate, USP) Cream, 1.0% is an antifungal agent indicated for the treatment of tinea pedis (athlete's foot), tinea cruris, and tinea corporis caused by Trichophyton rubrum, Trichophyton mentagro-phytes, Epidermophyton floccosum, and Microsporum canis, and for the treatment of tinea versicolor.

Exelderm (sulconazole nitrate, USP) Solution, 1.0% is a broad-spectrum antifungal agent indicated for the treatment of tinea cruris and tinea corporis caused by Trichophyton rubrum, Trichophyton mentagrophytes, Epidermophyton floccosum, and Microsporum canis; and for the treatment of tinea versicolor. Effectiveness has not been proven in tinea pedis (athlete's foot).
Symptomatic relief usually occurs within a few days after starting Exelderm Solution and clinical improvement usually occurs within one week.

Extina
Extina (ketoconazole) Foam, 2% is indicated for the topical treatment of seborrheic dermatitis in immunocompetent patients 12 years of age and older.
Limitations of Use
Safety and efficacy of Extina Foam for treatment of fungal infections have not been established.

Loprox
Loprox Cream is indicated for the topical treatment of the following dermal infections: tinea pedis, tinea cruris, and tinea corporis due to Trichophyton rubrum, Trichophyton mentagrophytes, Epidermophyton floccosum, and Microsporum canis; candidiasis (moniliasis) due to Candida albicans; and tinea (pityriasis) versicolor due to Malassezia furfur.

Loprox (ciclopirox) Shampoo, 1% is indicated for the topical treatment of seborrheic dermatitis of the scalp in adults.

Loprox Topical Suspension is indicated for the topical treatment of the following dermal infections: tinea pedis, tinea cruris, and tinea corporis due to Trichophyton rubrum, Trichophyton mentagrophytes, Epidermophyton floccosum, and Microsporum canis; cutaneous candidiasis (moniliasis) due to Candida albicans; and tinea (pityriasis) versicolor due to Malassezia furfur.

Luzu
Luzu (luliconazole) Cream, 1% is indicated for the topical treatment of interdigital tinea pedis, tinea cruris, and tinea corporis caused by the organisms Trichophyton rubrum and Epidermophyton floccosum.

Mentax
Mentax (butenafine HCl) Cream, 1% is indicated for the topical treatment of the dermatologic infection, tinea (pityriasis) versicolor due to M. furfur (formerly P. orbiculare). Butenafine HCl cream was not studied in immunocompromised patients.

Naftin
Naftin Hydrochloride Cream USP, 2% is indicated for the treatment of interdigital tinea pedis, tinea cruris, and tinea corporis caused by the organism Trichophyton rubrum.

Naftin Gel 1% is indicated for the topical treatment of tinea pedis, tinea cruris, and tinea corporis caused by the organisms Trichophyton rubrum, Trichophyton mentagrophytes, Trichophyton tonsurans, Epidermophyton floccosum.

Naftin Gel 2% is an allylamine antifungal indicated for the treatment of interdigital tinea pedis caused by the organisms Trichophyton rubrum, Trichophyton mentagrophytes, and Epidermophyton floccosum.

Oxistat
Oxistat Cream and Lotion are indicated for the topical treatment of the following dermal infections: tinea pedis, tinea cruris, and tinea corporis due to Trichophyton rubrum, Trichophyton mentagrophytes, or Epidermophyton floccosum.
Oxistat Cream is indicated for the topical treatment of tinea (pityriasis) versicolor due to Malassezia furfur.
Oxistat Cream may be used in pediatric patients for tinea corporis, tinea cruris, tinea pedis, and tinea (pityriasis) versicolor; however, these indications for which Oxistat Cream has been shown to be effective rarely occur in children below the age of 12.

Vusion
Vusion Ointment is indicated for the adjunctive treatment of diaper dermatitis only when complicated by documented candidiasis (microscopic evidence of pseudohyphae and/or budding yeast), in immunocompetent pediatric patients 4 weeks and older. A positive fungal culture for Candida albicans is not adequate evidence of candidal infection since colonization with C. albicans can result in a positive culture. The presence of candidal infection should be established by microscopic evaluation prior to initiating treatment.
Vusion should be used as part of a treatment regimen that includes measures directed at the underlying diaper dermatitis, including gentle cleansing of the diaper area and frequent diaper changes. Vusion should not be used as a substitute for frequent diaper changes.
Limitations of Use
The safety and efficacy of Vusion have not been demonstrated in immunocompromised patients, or in infants less than 4 weeks of age (premature or term).
The safety and efficacy of Vusion have not been evaluated in incontinent adult patients. Vusion should not be used to prevent the occurrence of diaper dermatitis, such as in an adult institutional setting, since preventative use may result in the development of drug resistance.

Xolegel
Xolegel is indicated for the topical treatment of seborrheic dermatitis in immunocompetent adults and children 12 years of age and older.
Safety and efficacy of Xolegel for treatment of fungal infections have not been established.

INITIAL STEP THERAPY*

**Include Rx and OTC products unless otherwise stated.*

If the patient has filled a prescription for at least a 7 day supply of a generic topical antifungal agent within the past 120 days under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit. If the patient does not meet the initial step therapy criteria, then the claim will reject with a message indicating that a prior authorization (PA) is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is not being used in a footbath

AND

- The patient experienced an inadequate treatment response to a generic topical antifungal agent

OR

- The patient experienced an intolerance to a generic topical antifungal agent

OR

- The patient has a contraindication that would prohibit a trial of a generic topical antifungal agent

Duration of Approval (DOA):

- 1380-D: DOA: 3 months

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QUANTITY LIMIT PRIOR AUTHORIZATION CRITERIA

DRUG CLASS	**DERMATOLOGICAL TOPICAL ANTIFUNGAL COMBINATIONS BRAND AND GENERIC ALL DOSAGE FORMS**
BRAND NAME (generic)	**(clotrimazole and betamethasone dipropionate)**
	(nystatin and triamcinolone acetonide)

Status: CVS Caremark® Criteria
Type: Quantity Limit; Post Limit Prior Authorization

POLICY

FDA-APPROVED INDICATIONS

Clotrimazole and Betamethasone Dipropionate Lotion
Clotrimazole and betamethasone dipropionate lotion is indicated in patients 17 years and older for the topical treatment of symptomatic inflammatory tinea pedis, tinea cruris, and tinea corporis due to Epidermophyton floccosum, Trichophyton mentagrophytes, and Trichophyton rubrum. Effective treatment without the risks associated with topical corticosteroid use may be obtained using a topical antifungal agent that does not contain a corticosteroid, especially for noninflammatory tinea infections. The efficacy of clotrimazole and betamethasone dipropionate lotion for the treatment of infections caused by zoophilic dermatophytes (e.g., Microsporum canis) has not been established.

Clotrimazole and Betamethasone Dipropionate Cream
Clotrimazole and betamethasone dipropionate cream is a combination of an azole antifungal and corticosteroid and is indicated for the topical treatment of symptomatic inflammatory tinea pedis, tinea cruris, and tinea corporis due to Epidermophyton floccosum, Trichophyton mentagrophytes, and Trichophyton rubrum in patients 17 years and older.

Nystatin and Triamcinolone Cream and Ointment
Nystatin and triamcinolone acetonide cream and ointment are indicated for the treatment of cutaneous candidiasis; it has been demonstrated that the nystatin-steroid combination provides greater benefit than the nystatin component alone during the first few days of treatment.

INITIAL QUANTITY LIMIT**

LIMIT CRITERIA
Limits should accumulate across same chemical entity up to highest quantity listed depending on the order the claims are processed. Accumulation does not apply if limit is coded for daily dose.

PLEASE NOTE: Since manufacturer package sizes may vary, it is the discretion of the dispensing pharmacy to fill quantities per package size up to these quantity limits. In such cases the filling limit and day supply may be less than what is indicated.

Drug	1 Month Limit*	3 Month Limit*
clotrimazole and betamethasone dipropionate lotion	60mL / 25 days	Does Not Apply*
clotrimazole and betamethasone dipropionate cream	60gm / 25 days	Does Not Apply*
nystatin and triamcinolone acetonide cream and ointment	60gm / 25 days	Does Not Apply*

** The duration of 25 days is used for a 30-day fill period to allow time for refill processing.*
** These drugs are for short-term acute use; therefore, the mail limit will be the same as the retail limit. The intent is for prescriptions of the requested drug to be filled one month at a time, even if filled at mail order; there should be no 3 month supplies filled.*

**If the patient is requesting more than the initial quantity limit, the claim will reject with a message indicating that a prior authorization is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

COVERAGE CRITERIA
The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is not being used in a footbath
  AND
  - The request is for clotrimazole/betamethasone for the treatment of any of the following: tinea pedis, tinea corporis, tinea cruris

  OR
  - The request is for nystatin/triamcinolone for the treatment of cutaneous candidiasis

Quantity Limits apply.
90gm or 90mL per 25 days* for clotrimazole/betamethasone, 120gm per 25 days* for nystatin/triamcinolone, 3 month limit does not apply
** The duration of 25 days is used for a 30-day fill period to allow time for refill processing. These drugs are for short-term acute use; therefore, the mail limit will be the same as the retail limit. The intent is for prescriptions of the requested drug to be filled one month at a time, even if filled at mail order; there should be no 3 month supplies filled.*

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QUANTITY LIMIT PRIOR AUTHORIZATION CRITERIA

DRUG CLASS	**TOPICAL ANTIFUNGALS**
BRAND NAME (generic)	
	(ciclopirox gel)
	(clotrimazole cream, solution)
	(econazole)
	ECOZA (econazole)
	ERTACZO (sertaconazole)
	EXELDERM (sulconazole)
	EXTINA (ketoconazole)
	(ketoconazole)
	LOPROX (ciclopirox)
	LUZU (luliconazole)
	MENTAX (butenafine HCl)
	(naftifine)
	NAFTIN (naftifine)
	(nystatin cream, ointment, topical powder)
	OXISTAT (oxiconazole)
	VUSION (miconazole-zinc oxide-white petrolatum)

XOLEGEL
(ketoconazole)

Status: CVS Caremark® Criteria
Type: Quantity Limit; Post Limit Prior Authorization

POLICY

FDA-APPROVED INDICATIONS

Butenafine

Mentax (butenafine cream)

Mentax (butenafine HCl) Cream, 1% is indicated for the topical treatment of the dermatologic infection, tinea (pityriasis) versicolor due to M. furfur (formerly P. orbiculare). Butenafine HCl cream was not studied in immunocompromised patients.

Ciclopirox

Loprox (ciclopirox cream)

Ciclopirox olamine cream USP, 0.77% is indicated for the topical treatment of the following dermal infections: tinea pedis, tinea cruris, and tinea corporis due to Trichophyton rubrum, Trichophyton mentagrophytes, Epidermophyton floccosum, and Microsporum canis; candidiasis (moniliasis) due to Candida albicans; and tinea (pityriasis) versicolor due to Malassezia furfur.

Ciclopirox gel

Superficial Dermatophyte Infections

Ciclopirox gel is indicated for the topical treatment of interdigital tinea pedis and tinea corporis due to Trichophyton rubrum, Trichophyton mentagrophytes, or Epidermophyton floccosum.

Seborrheic Dermatitis

Ciclopirox gel is indicated for the topical treatment of seborrheic dermatitis of the scalp.

Loprox (ciclopirox shampoo)

Ciclopirox shampoo 1% is indicated for the topical treatment of seborrheic dermatitis of the scalp in adults.

Loprox (ciclopirox suspension/lotion)

Ciclopirox Topical Suspension USP, 0.77% (Lotion) is indicated for the topical treatment of the following dermal infections: tinea pedis, tinea cruris, and tinea corporis due to Trichophyton rubrum, Trichophyton mentagrophytes, Epidermophyton floccosum, and Microsporum canis; cutaneous candidiasis (moniliasis) due to Candida albicans; and tinea (pityriasis) versicolor due to Malassezia furfur.

Clotrimazole

Clotrimazole cream

Clotrimazole cream USP is indicated for the topical treatment of candidiasis due to Candida albicans and tinea versicolor due to Malassezia furfur.

Clotrimazole is also available as a nonprescription item which is indicated for the topical treatment of the following dermal infections: tinea pedis, tinea cruris, and tinea corporis due to Trichophyton rubrum, Trichophyton mentagrophytes, Epidermophyton floccosum, and Microsporum canis.

Clotrimazole solution

Prescription Clotrimazole Topical Solution product is indicated for the topical treatment of candidiasis due to Candida albicans and tinea versicolor due to Malassezia furfur.

This formulation is also available as a nonprescription product which is indicated for the topical treatment of the following dermal infections: tinea pedis, tinea cruris, and tinea corporis due to Trichophyton rubrum, Trichophyton mentagrophytes, Epidermophyton floccosum, and Microsporum canis.

Econazole

Econazole cream

Econazole nitrate cream 1% is indicated for topical application in the treatment of tinea pedis, tinea cruris, and tinea corporis caused by Trichophyton rubrum, Trichophyton mentagrophytes, Trichophyton tonsurans, Microsporum canis, Microsporum audouinii, Microsporum gypseum, and Epidermophyton floccosum, in the treatment of cutaneous candidiasis, and in the treatment of tinea versicolor.

Ecoza (econazole foam)

Ecoza is indicated for the treatment of interdigital tinea pedis caused by Trichophyton rubrum, Trichophyton mentagrophytes, and Epidermophyton floccosum in patients 12 years of age and older.

Ketoconazole

Ketoconazole cream

Ketoconazole Cream 2% is indicated for the topical treatment of tinea corporis, tinea cruris and tinea pedis caused by Trichophyton rubrum, T. mentagrophytes and Epidermophyton floccosum; in the treatment of tinea (pityriasis) versicolor caused by Malassezia furfur (Pityrosporum orbiculare); in the treatment of cutaneous candidiasis caused by Candida spp. and in the treatment of seborrheic dermatitis.

Extina (ketoconazole foam)

Extina (ketoconazole) foam, 2% is indicated for the topical treatment of seborrheic dermatitis in immunocompetent patients 12 years of age and older.

Limitations of Use

Safety and efficacy of Extina Foam for treatment of fungal infections have not been established.

Xolegel (ketoconazole gel)

Xolegel is indicated for the topical treatment of seborrheic dermatitis in immunocompetent adults and children 12 years of age and older.

Safety and efficacy of Xolegel for treatment of fungal infections have not been established

ketoconazole shampoo

Ketoconazole shampoo, 2%, is indicated for the treatment of tinea (pityriasis) versicolor caused by or presumed to be caused by Pityrosporum orbiculare (also known as Malassezia furfur or M. orbiculare). Note: Tinea (pityriasis) versicolor may give rise to hyperpigmented or hypopigmented patches on the trunk which may extend to the neck, arms and upper thighs. Treatment of the infection may not immediately result in normalization of pigment to the affected sites. Normalization of pigment following successful therapy is variable and may take months, depending on individual skin type and incidental sun exposure. Although tinea versicolor is not contagious, it may recur because the organism that causes the disease is part of the normal skin flora.

Luliconazole

Luzu (luliconazole cream)

Luliconazole Cream, 1% is indicated for the topical treatment of interdigital tinea pedis, tinea cruris, and tinea corporis caused by the organisms Trichophyton rubrum and Epidermophyton floccosum.

Miconazole

Vusion (miconazole-zinc oxide-white petrolatum ointment)

Miconazole nitrate, zinc oxide and white petrolatum ointment is indicated for the adjunctive treatment of diaper dermatitis only when complicated by documented candidiasis (microscopic evidence of pseudohyphae and/or budding yeast), in immunocompetent pediatric patients 4 weeks and older. A positive fungal culture for Candida albicans is not adequate evidence of candidal infection since colonization with C. albicans can result in a positive culture. The presence of candidal infection should be established by microscopic evaluation prior to initiating treatment.

Miconazole nitrate, zinc oxide and white petrolatum ointment should be used as part of a treatment regimen that includes measures directed at the underlying diaper dermatitis, including gentle cleansing of the diaper area and frequent diaper changes. Miconazole nitrate, zinc oxide and white petrolatum ointment should not be used as a substitute for frequent diaper changes.

Naftifine

naftifine cream

Naftifine Hydrochloride Cream USP, 1% is indicated for the topical treatment of tinea pedis, tinea cruris and tinea corporis caused by the organisms Trichophyton rubrum, Trichophyton mentagrophytes, and Epidermophyton floccosum.
Naftifine Hydrochloride Cream, 2% is indicated for the treatment of interdigital tinea pedis, tinea cruris, and tinea corporis caused by the organism Trichophyton rubrum.

Naftin (naftifine gel)

Naftifine Hydrochloride Gel USP, 1% is indicated for the topical treatment of tinea pedis, tinea cruris and tinea corporis caused by the organisms Trichophyton rubrum, Trichophyton mentagrophytes, Trichophyton tonsurans and Epidermophyton floccosum.
Naftin 2% gel is an allylamine antifungal indicated for the treatment of interdigital tinea pedis caused by the organisms Trichophyton rubrum, Trichophyton mentagrophytes, and Epidermophyton floccosum.

Nystatin

Nystatin cream

Nystatin Cream, USP is indicated in the treatment of cutaneous or mucocutaneous mycotic infections caused by Candida albicans and other susceptible Candida species.

Nystatin ointment

Nystatin Ointment, USP is indicated in the treatment of cutaneous or mucocutaneous mycotic infections caused by Candida albicans and other susceptible Candida species.

Nystatin topical powder

Nystatin topical powder is indicated in the treatment of cutaneous or mucocutaneous mycotic infections caused by Candida albicans and other susceptible Candida species.

Oxiconazole

Oxistat (oxiconazole)

Oxistat Cream and Lotion are indicated for the topical treatment of the following dermal infections: tinea pedis, tinea cruris, and tinea corporis due to Trichophyton rubrum, Trichophyton mentagrophytes, or Epidermophyton floccosum.
Oxistat Cream is indicated for the topical treatment of tinea (pityriasis) versicolor due to Malassezia furfur Oxistat Cream may be used in pediatric patients for tinea corporis, tinea cruris, tinea pedis, and tinea (pityriasis) versicolor; however, these indications for which Oxistat Cream has been shown to be effective rarely occur in children below the age of 12.

Sertaconazole

Ertaczo (sertaconazole cream)

Ertaczo cream, 2%, is indicated for the topical treatment of interdigital tinea pedis in immunocompetent patients 12 years of age and older, caused by Trichophyton rubrum, Trichophyton mentagrophytes, and Epidermophyton floccosum.

Sulconazole

Exelderm Cream (sulconazole cream)

Exelderm (sulconazole nitrate, USP) Cream, 1.0% is an antifungal agent indicated for the treatment of tinea pedis (athlete's foot), tinea cruris, and tinea corporis caused by Trichophyton rubrum, Trichophyton mentagrophytes, Epidermophyton floccosum, and Microsporum canis, and for the treatment of tinea versicolor**.**

Exelderm Solution (sulconazole solution)

Exelderm (sulconazole nitrate, USP) Solution, 1.0% is a broad-spectrum antifungal agent indicated for the treatment of tinea cruris and tinea corporis caused by Trichophyton rubrum, Trichophyton mentagrophytes, Epidermophyton floccosum, and Microsporum canis; and for the treatment of tinea versicolor. Effectiveness has not been proven in tinea pedis (athlete's foot). Symptomatic relief usually occurs within a few days after starting Exelderm Solution and clinical improvement usually occurs within one week.

Compendial Uses

Seborrheic Dermatitis – Ketoconazole 2% Shampoo[27,28]

INITIAL QUANTITY LIMIT**

LIMIT CRITERIA
Limits should accumulate across same chemical entity up to highest quantity listed depending on the order the claims are processed. Accumulation does not apply if limit is coded for daily dose.

PLEASE NOTE: Since manufacturer package sizes may vary, it is the discretion of the dispensing pharmacy to fill quantities per package size up to these quantity limits. In such cases the filling limit and day supply may be less than what is indicated.

Medication	1 Month Limit*	3 Month Limit*
BUTENAFINE		
Mentax (butenafine cream)	60 gm / 25 days	Does not apply
CICLOPIROX		
Loprox Cream (ciclopirox cream)	120 gm / 25 days	Does not apply
ciclopirox gel	120 gm / 25 days	Does not apply
Loprox Shampoo (ciclopirox shampoo)	120 mL / 25 days	Does not apply
Loprox Suspension/Lotion (ciclopirox suspension/lotion)	120 mL / 25 days	Does not apply
CLOTRIMAZOLE		
clotrimazole cream	120 gm / 25 days	Does not apply
clotrimazole solution	120 mL / 25 days	Does not apply
ECONAZOLE		
econazole cream	60 gm / 25 days	Does not apply
Ecoza (econazole foam)	70 gm / 25 days	Does not apply
KETOCONAZOLE		
ketoconazole cream	120 gm / 25 days	Does not apply
Extina (ketoconazole foam)	100 gm / 25 days	Does not apply
Xolegel (ketoconazole gel)	45 gm / 25 days	Does not apply
ketoconazole shampoo	120 mL / 25 days	Does not apply
LULICONAZOLE		
Luzu (luliconazole cream)	60 gm / 25 days	Does not apply
MICONAZOLE		
Vusion (miconazole-zinc oxide-white petrolatum ointment)	100 gm / 25 days	Does not apply
NAFTIFINE		
naftifine cream	60 gm / 25 days	Does not apply
Naftin 1% Gel (naftifine 1% gel)	120 gm / 25 days	Does not apply
Naftin 2% Gel (naftifine 2% gel)	60 gm / 25 days	Does not apply
NYSTATIN		
nystatin cream	120 gm / 25 days	Does not apply
nystatin ointment	120 gm / 25 days	Does not apply
nystatin topical powder	120 gm / 25 days	Does not apply

OXICONAZOLE		
Oxistat Cream (oxiconazole cream)	60 gm / 25 days	Does not apply
Oxistat Lotion (oxiconazole lotion)	60 mL / 25 days	Does not apply
SERTACONAZOLE		
Ertaczo (sertaconazole cream)	60 gm / 25 days	Does not apply
SULCONAZOLE		
Exelderm Cream (sulconazole cream)	60 gm / 25 days	Does not apply
Exelderm Solution (sulconazole solution)	60 mL / 25 days	Does not apply
** The duration of 25 days is used for a 30-day fill period to allow time for refill processing.* ** These drugs are for short-term acute use; therefore, the mail limit will be the same as the retail limit. The intent is for prescriptions of the requested drug to be filled one month at a time, even if filled at mail order; there should be no 3 month supplies filled.*		

**If the patient is requesting more than the initial quantity limit, the claim will reject with a message indicating that a prior authorization is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is not being used in a footbath

AND

- The requested drug is being prescribed for the treatment of Candidiasis/Candida

  AND

  - The requested drug is any of the following:
    ciclopirox cream, suspension/lotion (Loprox cream, suspension/lotion)
    clotrimazole cream, solution
    econazole cream
    ketoconazole cream
    miconazole-zinc oxide-white petrolatum ointment (Vusion)
    nystatin cream, ointment, powder

OR

- The requested drug is being prescribed for the treatment Seborrheic Dermatitis

  AND

  - The requested drug is any of the following:
    ciclopirox gel, ciclopirox shampoo (Loprox shampoo)
    ketoconazole cream, ketoconazole foam (Extina), ketoconazole gel (Xolegel), ketoconazole shampoo

OR

- The requested drug is being prescribed for the treatment Tinea (Pityriasis) Versicolor

  AND

  - The requested drug is any of the following:
    butenafine cream (Mentax)
    ciclopirox cream, suspension/lotion, (Loprox cream, suspension/lotion)
    clotrimazole cream, solution
    econazole cream
    ketoconazole cream, ketoconazole shampoo
    oxiconazole cream (Oxistat cream)
    sulconazole cream, solution (Exelderm)

OR

- The requested drug is being prescribed for the treatment of Tinea Corporis

  AND

- The requested drug is any of the following:
  ciclopirox gel, ciclopirox cream, suspension/lotion (Loprox cream, suspension/lotion)
  clotrimazole cream, solution
  econazole cream
  ketoconazole cream
  luliconazole cream (Luzu)
  naftifine cream, 1% gel (Naftin 1% gel)
  oxiconazole cream, lotion (Oxistat)
  sulconazole cream, solution (Exelderm)

OR

- The requested drug is being prescribed for the treatment of Tinea Pedis
  AND
  - The requested drug is any of the following:
    ciclopirox gel, ciclopirox cream, suspension/lotion (Loprox cream, suspension/lotion)
    clotrimazole cream, solution
    econazole cream, econazole foam (Ecoza)
    ketoconazole cream
    luliconazole cream (Luzu)
    naftifine cream, gel (Naftin)
    oxiconazole cream, lotion (Oxistat)
    sertaconazole cream (Ertaczo)
    sulconazole cream (Exelderm cream)

OR

- The requested drug is being prescribed for the treatment of Tinea Cruris
  AND
  - The requested drug is any of the following:
    ciclopirox cream, suspension/lotion (Loprox cream, suspension/lotion)
    clotrimazole cream, solution
    econazole cream
    ketoconazole cream
    luliconazole cream (Luzu)
    naftifine cream, 1% gel (Naftin 1% gel)
    oxiconazole cream, lotion (Oxistat)
    sulconazole cream, solution (Exelderm)

Quantity Limits apply.

POST LIMIT QUANTITY		
Drug	**1 Month Limit***	**3 Month Limit***
ketoconazole gel (Xolegel)	90gm / 25 days	Does not apply
luliconazole cream (Luzu) butenafine cream (Mentax) naftifine gel 2% (Naftin 2% gel) naftifine cream sertaconazole cream (Ertaczo) oxiconazole lotion/cream (Oxistat) econazole cream sulconazole solution/cream (Exelderm)	120gm or mL / 25 days	Does not apply
econazole foam (Ecoza)	140gm / 25 days	Does not apply
ketoconazole foam (Extina) miconazole-zinc-petrolatum ointment (Vusion)	200gm / 25 days	Does not apply
Naftifine gel 1% (Naftin 1% gel) ciclopirox gel/cream/suspension/lotion/shampoo (Loprox) clotrimazole cream/solution ketoconazole cream nystatin cream/ointment/topical powder 100000	240gm / 25 days	Does not apply

ketoconazole shampoo		

** The duration of 25 days is used for a 30-day fill period to allow time for refill processing.*
** These drugs are for short-term acute use; therefore, the mail limit will be the same as the retail limit. The intent is for prescriptions of the requested drug to be filled one month at a time, even if filled at mail order; there should be no 3 month supplies filled.*

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QUANTITY LIMIT CRITERIA

DRUG CLASS **ANTIHISTAMINES, STEROIDS, COMBINATIONS NASAL SPRAYS**

BRAND NAME (GENERIC)

ANTIHISTAMINES:

(azelastine nasal solution)

PATANASE
(olopatadine)

STEROIDS:

BECONASE AQ
(beclomethasone)

(flunisolide nasal solution)

(fluticasone propionate nasal spray)

NASONEX
(mometasone)

OMNARIS
(ciclesonide)

QNASL
(beclomethasone)

XHANCE
(fluticasone propionate nasal spray)

ZETONNA
(ciclesonide)

COMBINATIONS:

DYMISTA
(azelastine / fluticasone)

RYALTRIS
(olopatadine hydrochloride/mometasone furoate monohydrate)

Status: CVS Caremark Criteria
Type: Quantity Limit

POLICY

FDA-APPROVED INDICATIONS

Antihistamines:

Azelastine 0.15% nasal solution (nasal spray)

Azelastine hydrochloride nasal spray is indicated for the relief of the symptoms of seasonal allergic rhinitis in patients 6 years of age and older and perennial allergic rhinitis in patients 6 years of age and older.

Azelastine 0.1% nasal solution (nasal spray)

Azelastine hydrochloride nasal spray is indicated for the treatment of the symptoms of seasonal allergic rhinitis in adults and pediatric patients 5 years and older, and for the treatment of the symptoms of vasomotor rhinitis in adults and adolescent patients 12 years and older.

Patanase

Patanase Nasal Spray is indicated for the relief of the symptoms of seasonal allergic rhinitis (SAR) in adults and pediatric patients 6 years of age and older.

Steroids:

Beconase AQ

Beconase AQ Nasal Spray is indicated for the relief of the symptoms of seasonal or perennial allergic and nonallergic (vasomotor) rhinitis.

Results from 2 clinical trials have shown that significant symptomatic relief was obtained within 3 days. However, symptomatic relief may not occur in some patients for as long as 2 weeks. Beconase AQ Nasal Spray should not be continued beyond 3 weeks in the absence of significant symptomatic improvement. Beconase AQ Nasal Spray should not be used in the presence of untreated localized infection involving the nasal mucosa.

Beconase AQ Nasal Spray is also indicated for the prevention of recurrence of nasal polyps following surgical removal. Clinical studies have shown that treatment of the symptoms associated with nasal polyps may have to be continued for several weeks or more before a therapeutic result can be fully assessed. Recurrence of symptoms due to polyps can occur after stopping treatment, depending on the severity of the disease.

Flunisolide Nasal Solution

Flunisolide Nasal Solution is indicated for the treatment of the nasal symptoms of seasonal or perennial rhinitis. Flunisolide Nasal Solution should not be used in the presence of untreated localized infection involving nasal mucosa.

Fluticasone Propionate Nasal Spray

Fluticasone propionate nasal spray is indicated for the management of the nasal symptoms of perennial nonallergic rhinitis in adults and pediatric patients aged 4 years and older.

Nasonex

Treatment of Allergic Rhinitis

Nasonex is indicated for the treatment of the nasal symptoms of seasonal allergic and perennial allergic rhinitis, in adults and pediatric patients 2 years of age and older.

Treatment of Nasal Congestion Associated with Seasonal Allergic Rhinitis

Nasonex is indicated for the relief of nasal congestion associated with seasonal allergic rhinitis, in adults and pediatric patients 2 years of age and older.

Prophylaxis of Seasonal Allergic Rhinitis

Nasonex is indicated for the prophylaxis of the nasal symptoms of seasonal allergic rhinitis in adult and adolescent patients 12 years and older.

Treatment of Nasal Polyps

Nasonex is indicated for the treatment of nasal polyps in patients 18 years of age and older.

Omnaris

Treatment of Seasonal Allergic Rhinitis

Omnaris Nasal Spray is indicated for the treatment of nasal symptoms associated with seasonal allergic rhinitis in adults and children 6 years of age and older.

Treatment of Perennial Allergic Rhinitis
Omnaris Nasal Spray is indicated for the treatment of nasal symptoms associated with perennial allergic rhinitis in adults and adolescents 12 years of age and older.

QNASL
QNASL Nasal Aerosol is indicated for the treatment of the nasal symptoms associated with seasonal and perennial allergic rhinitis in patients 4 years of age and older.

Xhance
Xhance is indicated for the treatment of chronic rhinosinusitis with nasal polyps (CRSwNP) in adult patients 18 years of age or older.

Zetonna
Zetonna Nasal Aerosol is indicated for the treatment of symptoms associated with seasonal and perennial allergic rhinitis in adults and adolescents 12 years of age and older.

Combinations:
Dymista
Dymista is indicated for the relief of symptoms of seasonal allergic rhinitis in adult and pediatric patients 6 years of age and older.

Ryaltris
Ryaltris is indicated for the treatment of symptoms of seasonal allergic rhinitis in adult and pediatric patients 12 years of age and older.

LIMIT CRITERIA
Limits do not accumulate together; patient is allowed the maximum limit for each drug and strength.

Medication	Maintenance Dose	Maximum Daily Dose	Package Size	1 Month Limit* 3 Months Limit*
Azelastine 0.15% nasal solution	1-2 sprays per nostril once to twice daily	8 sprays	200 sprays per 30mL bottle	2 packages (30mL each) / 25 days 6 packages (30mL each) / 75 days
Azelastine 0.1% nasal solution	1-2 sprays per nostril twice daily	8 sprays	200 sprays per 30mL bottle	2 packages (30mL each) / 25 days 6 packages (30mL each) / 75 days
Beconase AQ (beclomethasone)	1-2 sprays per nostril twice daily	8 sprays	180 sprays per 25gm bottle	2 packages (25gm each) / 25 days 6 packages (25gm each) / 75 days
Dymista (azelastine/fluticasone)	1 spray per nostril twice daily	4 sprays	120 sprays per 23gm bottle	1 package (23gm) / 25 days 3 packages (23gm each) / 75 days
Flunisolide nasal solution	1-2 sprays per nostril one to three times daily	16 sprays	200 sprays per 25mL bottle	3 packages (25mL each) / 25 days 9 packages (25mL each) / 75 days
Fluticasone Propionate nasal spray	1-2 sprays per nostril once to twice daily	4 sprays	120 sprays per 16gm bottle	1 package (16gm) / 25 days 3 packages (16gm each) /75 days
Nasonex (mometasone)	1-2 sprays per nostril once to twice daily	8 sprays	120 sprays per 17gm bottle	2 packages (17gm each) / 25 days 6 packages (17gm each) / 75 days
Omnaris (ciclesonide)	2 sprays per nostril once daily	4 sprays	120 sprays per 12.5gm bottle	1 package (12.5gm) / 25 days 3 packages (12.5gm each) / 75 days
Patanase (olopatadine)	1-2 sprays per nostril twice daily	8 sprays	240 sprays per 30.5gm bottle	1 package (30.5gm) / 25 days 3 packages (30.5gm each) / 75 days
QNASL 40mcg	1 spray per nostril	2 sprays	60 sprays	1 package (6.8gm) / 25 days

(beclomethasone)	once daily		per 6.8gm canister	3 packages (6.8gm each) / 75 days
QNASL 80mcg (beclomethasone)	2 sprays per nostril once daily	4 sprays	120 sprays per 10.6gm canister	1 package (10.6gm) / 25 days 3 packages (10.6gm each) / 75 days
Ryaltris (olopatadine/mometasone)	2 sprays per nostril twice daily	8 sprays	240 sprays per 29gm bottle	1 package (29gm) / 25 days 3 packages (29gm each) / 75 days
Xhance (fluticasone propionate)	1-2 sprays per nostril twice daily	8 sprays	120 sprays per 16mL bottle	2 packages (16mL each) / 25 days 6 packages (16mL each) / 75 days
Zetonna (ciclesonide)	1 spray per nostril once daily	2 sprays	60 sprays per 6.1gm canister	1 package (6.1gm) / 25 days 3 packages (6.1gm each) / 75 days
**The duration of 25 days is used for a 30-day fill period, and 75 days is used for a 90-day fill period to allow time for refill processing.*				

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12. Xhance [package insert]. Yardley, PA: OptiNose US, Inc; January 2023.
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QUANTITY LIMIT PRIOR AUTHORIZATION CRITERIA

DRUG CLASS	**SELECT INJECTABLE, INTRAVENOUS ANTIMICROBIALS**
BRAND NAME (generic)	
	ABELCET (amphotericin B lipid complex)
	AMBISOME (amphotericin B liposome)
	(amphotericin B)
	CANCIDAS (caspofungin)
	(ceftriaxone vials)
	COLY-MYCIN M (colistimethate)
	CUBICIN (daptomycin)
	CUBICIN RF (daptomycin)
	DALVANCE (dalbavancin)
	(daptomycin)
	DAPZURA RT (daptomycin)
	INVANZ (ertapenem)
	KIMYRSA (oritavancin)
	(levofloxacin injection)
	MERREM (meropenem)
	MYCAMINE (micafungin)

ORBACTIV
(oritavancin)

(streptomycin)

(tobramycin injection)

TYGACIL
(tigecycline)

(vancomycin injection vials, bottles)

VFEND IV
(voriconazole injection)

Status: CVS Caremark Criteria
Type: Quantity Limit; Post Limit Prior Authorization

POLICY

FDA-APPROVED INDICATIONS

Abelcet
Abelcet is indicated for the treatment of invasive fungal infections in patients who are refractory to or intolerant of conventional amphotericin B therapy. This is based on open-label treatment of patients judged by their physicians to be intolerant to or failing conventional amphotericin B therapy.

AmBisome
AmBisome is indicated for the following:
- Empirical therapy for presumed fungal infection in febrile, neutropenic patients.
- Treatment of Cryptococcal Meningitis in HIV-infected patients.
- Treatment of patients with Aspergillus species, Candida species and/or Cryptococcus species infections (see above for the treatment of Cryptococcal Meningitis) refractory to amphotericin B deoxycholate, or in patients where renal impairment or unacceptable toxicity precludes the use of amphotericin B deoxycholate.
- Treatment of visceral leishmaniasis. In immunocompromised patients with visceral leishmaniasis treated with AmBisome, relapse rates were high following initial clearance of parasites.

Amphotericin B
Amphotericin B for Injection USP should be administered primarily to patients with progressive, potentially life-threatening fungal infections. This potent drug should not be used to treat noninvasive fungal infections, such as oral thrush, vaginal candidiasis and esophageal candidiasis in patients with normal neutrophil counts.
Amphotericin B for Injection USP is specifically intended to treat potentially life threatening fungal infections: aspergillosis, cryptococcosis (torulosis), North American blastomycosis, systemic candidiasis, coccidioido-mycosis, histoplasmosis, zygomycosis including mucormycosis due to susceptible species of the genera Absidia, Mucor and Rhizopus, and infections due to related susceptible species of Conidiobolus and Basidiobolus, and sporotrichosis.
Amphotericin B may be useful in the treatment of American mucocutaneous leishmaniasis, but it is not the drug of choice as primary therapy.

Cancidas
Empirical Therapy for Presumed Fungal Infections in Febrile, Neutropenic Patients
Cancidas is indicated as empirical therapy for presumed fungal infections in febrile, neutropenic adult and pediatric patients (3 months of age and older).

Treatment of Candidemia and Other Candida Infections
Cancidas is indicated for the treatment of candidemia and the following candida infections: intraabdominal abscesses, peritonitis, and pleural space infections in adult and pediatric patients (3 months of age and older).
Limitations of Use: Cancidas has not been studied in endocarditis, osteomyelitis, and meningitis due to Candida.
Treatment of Esophageal Candidiasis
Cancidas is indicated for the treatment of esophageal candidiasis in adult and pediatric patients (3 months of age and older).
Limitations of Use: Cancidas has not been approved for the treatment of oropharyngeal candidiasis (OPC). In the study that evaluated the efficacy of caspofungin in the treatment of esophageal candidiasis, patients with concomitant OPC had higher relapse rate of the OPC.
Treatment of Invasive Aspergillosis in Patients Who Are Refractory to or Intolerant of Other Therapies
Cancidas is indicated for the treatment of invasive aspergillosis in adult and pediatric patients (3 months of age and older) who are refractory to or intolerant of other therapies.
Limitations of Use: Cancidas has not been studied as initial therapy for invasive aspergillosis.

Ceftriaxone
Before instituting treatment with Ceftriaxone appropriate specimens should be obtained for isolation of the causative organism and for determination of its susceptibility to the drug. Therapy may be instituted prior to obtaining results of susceptibility testing.
To reduce the development of drug-resistant bacteria and maintain the effectiveness of Ceftriaxone for injection, USP and other antibacterial drugs, Ceftriaxone for injection, USP should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.
Ceftriaxone for injection, USP is indicated for the treatment of the following infections when caused by susceptible organisms:
Lower Respiratory Tract Infections caused by Streptococcus pneumoniae, Staphylococcus aureus, Haemophilus influenzae, Haemophilus parainfluenzae, Klebsiella pneumoniae, Escherichia coli, Enterobacter aerogenes, Proteus mirabilis or Serratia marcescens.
Acute Bacterial Otitis Media caused by Streptococcus pneumoniae, Haemophilus influenzae (including beta-lactamase producing strains) or Moraxella catarrhalis (including beta-lactamase producing strains).
Note: In one study lower clinical cure rates were observed with a single dose of Ceftriaxone compared to 10 days of oral therapy. In a second study comparable cure rates were observed between single dose Ceftriaxone and the comparator. The potentially lower clinical cure rate of Ceftriaxone should be balanced against the potential advantages of parenteral therapy.
Skin and Skin Structure Infections caused by Staphylococcus aureus, Staphylococcus epidermidis, Streptococcus pyogenes, Viridans group streptococci, Escherichia coli, Enterobacter cloacae, Klebsiella oxytoca, Klebsiella pneumoniae, Proteus mirabilis, Morganella morganii,* Pseudomonas aeruginosa, Serratia marcescens, Acinetobacter calcoaceticus, Bacteroides fragilis* or Peptostreptococcus species.
Urinary Tract Infections (complicated and uncomplicated) caused by Escherichia coli, Proteus mirabilis, Proteus vulgaris, Morganella morganii or Klebsiella pneumoniae.
Uncomplicated Gonorrhea (cervical/urethral and rectal) caused by Neisseria gonorrhoeae, including both penicillinase- and nonpenicillinase-producing strains, and pharyngeal gonorrhea caused by nonpenicillinase-producing strains of Neisseria gonorrhoeae.
Pelvic Inflammatory Disease caused by Neisseria gonorrhoeae. Ceftriaxone sodium, like other cephalosporins, has no activity against Chlamydia trachomatis. Therefore, when cephalosporins are used in the treatment of patients with pelvic inflammatory disease and Chlamydia trachomatis is one of the suspected pathogens, appropriate antichlamydial coverage should be added.
Bacterial Septicemia caused by Staphylococcus aureus, Streptococcus pneumoniae, Escherichia coli, Haemophilus influenzae or Klebsiella pneumoniae.
Bone and Joint Infections caused by Staphylococcus aureus, Streptococcus pneumoniae, Escherichia coli, Proteus mirabilis, Klebsiella pneumoniae or Enterobacter species.
Intra-Abdominal Infections caused by Escherichia coli, Klebsiella pneumoniae, Bacteroides fragilis, Clostridium species (Note: most strains of Clostridium difficile are resistant) or Peptostreptococcus species.
Meningitis caused by Haemophilus influenzae, Neisseria meningitidis or Streptococcus pneumoniae. Ceftriaxone has also been used successfully in a limited number of cases of meningitis and shunt infection caused by Staphylococcus epidermidis* and Escherichia coli.*
* Efficacy for this organism in this organ system was studied in fewer than ten infections.

Surgical Prophylaxis: The preoperative administration of a single 1g dose of Ceftriaxone may reduce the incidence of postoperative infections in patients undergoing surgical procedures classified as contaminated or potentially contaminated (e.g., vaginal or abdominal hysterectomy or cholecystectomy for chronic calculous cholecystitis in high-risk patients, such as those over 70 years of age, with acute cholecystitis not requiring therapeutic antimicrobials, obstructive jaundice or common duct bile stones) and in surgical patients for whom infection at the operative site would present serious risk (e.g., during coronary artery bypass surgery). Although Ceftriaxone has been shown to have been as effective as cefazolin in the prevention of infection following coronary artery bypass surgery, no placebo-controlled trials have been conducted to evaluate any cephalosporin antibiotic in the prevention of infection following coronary artery bypass surgery.
When administered prior to surgical procedures for which it is indicated, a single 1g dose of Ceftriaxone provides protection from most infections due to susceptible organisms throughout the course of the procedure.

Coly-Mycin M
Coly-Mycin M Parenteral is indicated for the treatment of acute or chronic infections due to sensitive strains of certain gram-negative bacilli. It is particularly indicated when the infection is caused by sensitive strains of Pseudomonas aeruginosa. This antibiotic is not indicated for infections due to Proteus or Neisseria. Coly-Mycin M Parenteral has proven clinically effective in treatment of infections due to the following gram-negative organisms: Enterobacter aerogenes, Escherichia coli, Klebsiella pneumoniae and Pseudomonas aeruginosa.
Coly-Mycin M Parenteral may be used to initiate therapy in serious infections that are suspected to be due to gram-negative organisms and in the treatment of infections due to susceptible gram-negative pathogenic bacilli.
To reduce the development of drug-resistant bacteria and maintain the effectiveness of Coly-Mycin M and other antibacterial drugs, Coly-Mycin M should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

Cubicin[8], Cubicin RF[9], Daptomycin 350mg[10,11,12], Daptomycin 500mg[11], Dapzura RT[13]
Complicated Skin and Skin Structure Infections (cSSSI) [8,9,10,11,12,13]
Cubicin, Cubicin RF, Daptomycin for Injection, and Dapzura RT are indicated for the treatment of adult[11] and pediatric patients (1 to 17 years of age) with complicated skin and skin structure infections (cSSSI) caused by susceptible isolates of the following Gram-positive bacteria: Staphylococcus aureus (including methicillin-resistant isolates), Streptococcus pyogenes, Streptococcus agalactiae, Streptococcus dysgalactiae subsp. equisimilis, and Enterococcus faecalis (vancomycin-susceptible isolates only).
Staphylococcus aureus Bloodstream Infections (Bacteremia) in Adult Patients, Including Those with Right-Sided Infective Endocarditis, Caused by Methicillin-Susceptible and Methicillin-Resistant Isolates [8,9,10,11,12,13]
Cubicin, Cubicin RF, Daptomycin for Injection, and Dapzura RT are indicated for the treatment of adult patients with Staphylococcus aureus bloodstream infections (bacteremia), including adult patients with right-sided infective endocarditis, caused by methicillin-susceptible and methicillin-resistant isolates.
Staphylococcus aureus Bloodstream Infections (Bacteremia) in Pediatric Patients (1 to 17 Years of Age)[8,9,10,12,13]
Cubicin, Cubicin RF, Daptomycin for Injection, and Dapzura RT are indicated for the treatment of pediatric patients (1 to 17 years of age) with Staphylococcus aureus bloodstream infections (bacteremia).
Limitations of Use [8,9,10,11,12,13]
Cubicin, Cubicin RF, Daptomycin for Injection, and Dapzura RT are not indicated for the treatment of pneumonia.
Cubicin, Cubicin RF, Daptomycin for Injection, and Dapzura RT are not indicated for the treatment of left-sided infective endocarditis due to S. aureus. The clinical trial of Cubicin, Cubicin RF, Daptomycin for Injection, and Dapzura RT in adult patients with S. aureus bloodstream infections included limited data from patients with left-sided infective endocarditis; outcomes in these patients were poor. Cubicin, Cubicin RF, Daptomycin for Injection, and Dapzura RT have not been studied in patients with prosthetic valve endocarditis.
Cubicin, Cubicin RF, Daptomycin for Injection, and Dapzura RT are not recommended in pediatric patients younger than 1 year of age due to the risk of potential effects on muscular, neuromuscular, and/or nervous systems (either peripheral and/or central) observed in neonatal dogs.[8,9,10,13]
Usage [8,9,10,11,12,13]
Appropriate specimens for microbiological examination should be obtained in order to isolate and identify the causative pathogens and to determine their susceptibility to daptomycin.
To reduce the development of drug-resistant bacteria and maintain the effectiveness of Cubicin, Cubicin RF, Daptomycin for Injection, Dapzura RT and other antibacterial drugs, Cubicin, Cubicin RF, Daptomycin for Injection, and Dapzura RT should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria.

When culture and susceptibility information is available, it should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy. Empiric therapy may be initiated while awaiting test results.

Dalvance
Dalvance is indicated for the treatment of adult and pediatric patients with acute bacterial skin and skin structure infections (ABSSSI), caused by designated susceptible strains of the following Gram-positive microorganisms: Staphylococcus aureus (including methicillin-susceptible and methicillin-resistant isolates), Streptococcus pyogenes, Streptococcus agalactiae, Streptococcus dysgalactiae, Streptococcus anginosus group (including S. anginosus, S. intermedius, S. constellatus) and Enterococcus faecalis (vancomycin susceptible strains).
Usage
To reduce the development of drug-resistant bacteria and maintain the effectiveness of Dalvance and other antibacterial agents, Dalvance should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

Invanz
Complicated Intra-Abdominal Infections
Invanz is indicated for the treatment of adult patients and pediatric patients (3 months of age and older) with complicated intra-abdominal infections due to Escherichia coli, Clostridium clostridiiforme, Eubacterium lentum, Peptostreptococcus species, Bacteroides fragilis, Bacteroides distasonis, Bacteroides ovatus, Bacteroides thetaiotaomicron, or Bacteroides uniformis.
Complicated Skin and Skin Structure Infections, Including Diabetic Foot Infections without Osteomyelitis
Invanz is indicated for the treatment of adult patients and pediatric patients (3 months of age and older) with complicated skin and skin structure infections, including diabetic foot infections without osteomyelitis due to Staphylococcus aureus (methicillin susceptible isolates only), Streptococcus agalactiae, Streptococcus pyogenes, Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis, Bacteroides fragilis, Peptostreptococcus species, Porphyromonas asaccharolytica, or Prevotella bivia. Invanz has not been studied in diabetic foot infections with concomitant osteomyelitis.
Community Acquired Pneumonia
Invanz is indicated for the treatment of adult patients and pediatric patients (3 months of age and older) with community acquired pneumonia due to Streptococcus pneumoniae (penicillin susceptible isolates only) including cases with concurrent bacteremia, Haemophilus influenzae (beta-lactamase negative isolates only), or Moraxella catarrhalis.
Complicated Urinary Tract Infections Including Pyelonephritis
Invanz is indicated for the treatment of adult patients and pediatric patients (3 months of age and older) with complicated urinary tract infections including pyelonephritis due to Escherichia coli, including cases with concurrent bacteremia, or Klebsiella pneumoniae.
Acute Pelvic Infections Including Postpartum Endomyometritis, Septic Abortion and Post Surgical Gynecologic Infections
Invanz is indicated for the treatment of adult patients and pediatric patients (3 months of age and older) with acute pelvic infections including postpartum endomyometritis, septic abortion and post surgical gynecological infections due to Streptococcus agalactiae, Escherichia coli, Bacteroides fragilis, Porphyromonas asaccharolytica, Peptostreptococcus species, or Prevotella bivia.
Prophylaxis of Surgical Site Infection Following Elective Colorectal Surgery
Invanz is indicated in adults for the prevention of surgical site infection following elective colorectal surgery.
Usage
To reduce the development of drug-resistant bacteria and maintain the effectiveness of Invanz and other antibacterial drugs, Invanz should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

Kimyrsa
Kimyrsa is indicated for the treatment of adult patients with acute bacterial skin and skin structure infections (ABSSSI) caused by susceptible isolates of the following Gram positive microorganisms:
Staphylococcus aureus (including methicillin-susceptible and methicillin-resistant isolates), Streptococcus pyogenes, Streptococcus agalactiae, Streptococcus dysgalactiae, Streptococcus anginosus group (includes S. anginosus, S. intermedius, and S. constellatus), and Enterococcus faecalis (vancomycin-susceptible isolates only).
Usage

To reduce the development of drug-resistant bacteria and maintain the effectiveness of Kimyrsa and other antibacterial drugs, Kimyrsa should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

Levofloxacin injection

Levofloxacin injection is indicated for the treatment of adults (≥18 years of age) with mild, moderate, and severe infections caused by susceptible isolates of the designated microorganisms in the conditions listed in this section. Levofloxacin injection is indicated when intravenous administration offers a route of administration advantageous to the patient (e.g., patient cannot tolerate an oral dosage form).

Nosocomial Pneumonia

Levofloxacin injection is indicated for the treatment of nosocomial pneumonia due to methicillin-susceptible Staphylococcus aureus, Pseudomonas aeruginosa, Serratia marcescens, Escherichia coli, Klebsiella pneumoniae, Haemophilus influenzae, or Streptococcus pneumoniae. Adjunctive therapy should be used as clinically indicated. Where Pseudomonas aeruginosa is a documented or presumptive pathogen, combination therapy with an anti-pseudomonal β-lactam is recommended.

Community-Acquired Pneumonia: 7- to 14-day Treatment Regimen

Levofloxacin injection is indicated for the treatment of community-acquired pneumonia due to methicillin-susceptible Staphylococcus aureus, Streptococcus pneumoniae (including multi-drug-resistant Streptococcus pneumoniae [MDRSP]), Haemophilus influenzae, Haemophilus parainfluenzae, Klebsiella pneumoniae, Moraxella catarrhalis, Chlamydophila pneumoniae, Legionella pneumophila, or Mycoplasma pneumoniae.

MDRSP isolates are isolates resistant to two or more of the following antibacterials: penicillin (MIC ≥2 mcg/mL), second generation cephalosporins, e.g., cefuroxime, macrolides, tetracyclines and trimethoprim/sulfamethoxazole.

Community-Acquired Pneumonia: 5-day Treatment Regimen

Levofloxacin injection is indicated for the treatment of community-acquired pneumonia due to Streptococcus pneumoniae (excluding multi-drug-resistant isolates [MDRSP]), Haemophilus influenzae, Haemophilus parainfluenzae, Mycoplasma pneumoniae, or Chlamydophila pneumoniae.

Complicated Skin and Skin Structure Infections

Levofloxacin injection is indicated for the treatment of complicated skin and skin structure infections due to methicillin-susceptible Staphylococcus aureus, Enterococcus faecalis, Streptococcus pyogenes, or Proteus mirabilis.

Uncomplicated Skin and Skin Structure Infections

Levofloxacin injection is indicated for the treatment of uncomplicated skin and skin structure infections (mild to moderate) including abscesses, cellulitis, furuncles, impetigo, pyoderma, wound infections, due to methicillin-susceptible Staphylococcus aureus, or Streptococcus pyogenes.

Chronic Bacterial Prostatitis

Levofloxacin injection is indicated for the treatment of chronic bacterial prostatitis due to Escherichia coli, Enterococcus faecalis, or methicillin-susceptible Staphylococcus epidermidis.

Inhalational Anthrax (Post-Exposure)

Levofloxacin injection is indicated for inhalational anthrax (post-exposure) to reduce the incidence or progression of disease following exposure to aerosolized Bacillus anthracis. The effectiveness of levofloxacin is based on plasma concentrations achieved in humans, a surrogate endpoint reasonably likely to predict clinical benefit. Levofloxacin injection has not been tested in humans for the post-exposure prevention of inhalation anthrax. The safety of levofloxacin injection in adults for durations of therapy beyond 28 days or in pediatric patients for durations of therapy beyond 14 days has not been studied. Prolonged levofloxacin injection therapy should only be used when the benefit outweighs the risk.

Plague

Levofloxacin injection is indicated for treatment of plague, including pneumonic and septicemic plague, due to Yersinia pestis (Y. pestis) and prophylaxis for plague in adults and pediatric patients, 6 months of age and older. Efficacy studies of levofloxacin injection could not be conducted in humans with plague for ethical and feasibility reasons. Therefore, approval of this indication was based on an efficacy study conducted in animals.

Complicated Urinary Tract Infections: 5-day Treatment Regimen

Levofloxacin injection is indicated for the treatment of complicated urinary tract infections due to Escherichia coli, Klebsiella pneumoniae, or Proteus mirabilis.

Complicated Urinary Tract Infections: 10-day Treatment Regimen

Levofloxacin injection is indicated for the treatment of complicated urinary tract infections (mild to moderate) due to Enterococcus faecalis, Enterobacter cloacae, Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis, or Pseudomonas aeruginosa.

Acute Pyelonephritis: 5- or 10-day Treatment Regimen

Levofloxacin injection is indicated for the treatment of acute pyelonephritis caused by Escherichia coli, including cases with concurrent bacteremia.

Uncomplicated Urinary Tract Infections

Levofloxacin injection is indicated for the treatment of uncomplicated urinary tract infections (mild to moderate) due to Escherichia coli, Klebsiella pneumoniae, or Staphylococcus saprophyticus.

Because fluoroquinolones, including levofloxacin injection, have been associated with serious adverse reactions and for some patients uncomplicated urinary tract infection is self-limiting, reserve levofloxacin injection for treatment of uncomplicated urinary tract infections in patients who have no alternative treatment options.

Acute Bacterial Exacerbation of Chronic Bronchitis

Levofloxacin injection is indicated for the treatment of acute bacterial exacerbation of chronic bronchitis (ABECB) due to methicillin-susceptible Staphylococcus aureus, Streptococcus pneumoniae, Haemophilus influenzae, Haemophilus parainfluenzae, or Moraxella catarrhalis.

Because fluoroquinolones, including levofloxacin injection, have been associated with serious adverse reactions [see Warnings and Precautions (5.1 to 5.15)] and for some patients ABECB is self-limiting, reserve levofloxacin for treatment of ABECB in patients who have no alternative treatment options.

Acute Bacterial Sinusitis: 5-day and 10–14 day Treatment Regimens

Levofloxacin injection is indicated for the treatment of acute bacterial sinusitis (ABS) due to Streptococcus pneumoniae, Haemophilus influenzae, or Moraxella catarrhalis.

Because fluoroquinolones, including levofloxacin injection, have been associated with serious adverse reactions and for some patients ABS is self-limiting, reserve levofloxacin for treatment of ABS in patients who have no alternative treatment options.

Usage

To reduce the development of drug-resistant bacteria and maintain the effectiveness of levofloxacin and other antibacterial drugs, levofloxacin should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

Culture and susceptibility testing

Appropriate culture and susceptibility tests should be performed before treatment in order to isolate and identify organisms causing the infection and to determine their susceptibility to levofloxacin. Therapy with levofloxacin injection may be initiated before results of these tests are known; once results become available, appropriate therapy should be selected.

As with other drugs in this class, some isolates of Pseudomonas aeruginosa may develop resistance fairly rapidly during treatment with levofloxacin injection. Culture and susceptibility testing performed periodically during therapy will provide information about the continued susceptibility of the pathogens to the antimicrobial agent and also the possible emergence of bacterial resistance.

Merrem

Complicated Skin and Skin Structure Infections (Adult Patients and Pediatric Patients 3 Months of Age and Older Only)

Merrem IV is indicated for the treatment of complicated skin and skin structure infections (cSSSI) due to Staphylococcus aureus (methicillin-susceptible isolates only), Streptococcus pyogenes, Streptococcus agalactiae, viridans group streptococci, Enterococcus faecalis (vancomycin-susceptible isolates only), Pseudomonas aeruginosa, Escherichia coli, Proteus mirabilis, Bacteroides fragilis, and Peptostreptococcus species.

Complicated Intra-abdominal Infections (Adult and Pediatric Patients)

Merrem IV is indicated for the treatment of complicated appendicitis and peritonitis caused by viridans group streptococci, Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, Bacteroides fragilis, B. thetaiotaomicron, and Peptostreptococcus species.

Bacterial Meningitis (Pediatric Patients 3 Months of Age and Older Only)

Merrem IV is indicated for the treatment of bacterial meningitis caused by Haemophilus influenzae, Neisseria meningitidis and penicillin-susceptible isolates of Streptococcus pneumoniae.

Merrem IV has been found to be effective in eliminating concurrent bacteremia in association with bacterial meningitis.

Usage

To reduce the development of drug-resistant bacteria and maintain the effectiveness of Merrem IV and other antibacterial drugs, Merrem IV should only be used to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

Mycamine

Mycamine is indicated for:

- Treatment of Candidemia, Acute Disseminated Candidiasis, Candida Peritonitis and Abscesses in adult and pediatric patients 4 months of age and older.
- Treatment of Candidemia, Acute Disseminated Candidiasis, Candida Peritonitis and Abscesses without meningoencephalitis and/or ocular dissemination in pediatric patients younger than 4 months of age.
- Treatment of Esophageal Candidiasis in adult and pediatric patients 4 months of age and older.
- Prophylaxis of Candida Infections in adult and pediatric patients 4 months of age and older undergoing hematopoietic stem cell transplantation.

Limitations of Use

- The safety and effectiveness of Mycamine have not been established for the treatment of candidemia with meningoencephalitis and/or ocular dissemination in pediatric patients younger than 4 months of age as a higher dose may be needed.
- Mycamine has not been adequately studied in patients with endocarditis, osteomyelitis and meningoencephalitis due to Candida.
- The efficacy of Mycamine against infections caused by fungi other than Candida has not been established.

Orbactiv

Orbactiv (oritavancin) is indicated for the treatment of adult patients with acute bacterial skin and skin structure infections (ABSSSI) caused by susceptible isolates of the following Gram-positive microorganisms:
Staphylococcus aureus (including methicillin-susceptible and methicillin–resistant isolates), Streptococcus pyogenes, Streptococcus agalactiae, Streptococcus dysgalactiae, Streptococcus anginosus group (includes S. anginosus, S. intermedius, and S. constellatus), and Enterococcus faecalis (vancomycin susceptible isolates only).

Usage

To reduce the development of drug-resistant bacteria and maintain the effectiveness of Orbactiv and other antibacterial drugs, Orbactiv should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

Streptomycin

Streptomycin is indicated for the treatment of individuals with moderate to severe infections caused by susceptible strains of microorganisms in the specific conditions listed below:

1. Mycobacterium tuberculosis: The Advisory Council for the Elimination of Tuberculosis, the American Thoracic Society, and the Center for Disease Control recommend that either streptomycin or ethambutol be added as a fourth drug in a regimen containing isoniazid (INH), rifampin and pyrazinamide for initial treatment of tuberculosis unless the likelihood of INH or rifampin resistance is very low. The need for a fourth drug should be reassessed when the results of susceptibility testing are known. In the past when the national rate of primary drug resistance to isoniazid was known to be less than 4% and was either stable or declining, therapy with two and three drug regimens was considered adequate. If community rates of INH resistance are currently less than 4%, an initial treatment regimen with less than four drugs may be considered. Streptomycin is also indicated for therapy of tuberculosis when one or more of the above drugs is contraindicated because of toxicity or intolerance. The management of tuberculosis has become more complex as a consequence of increasing rates of drug resistance and concomitant HIV infection. Additional consultation from experts in the treatment of tuberculosis may be desirable in those settings.
2. Non-tuberculosis infections: The use of streptomycin should be limited to the treatment of infections caused by bacteria which have been shown to be susceptible to the antibacterial effects of streptomycin and which are not amenable to therapy with less potentially toxic agents.
    a. Pasteurella pestis (plague),
    b. Francisella tularensis (tularemia),
    c. Brucella,
    d. Calymmatobacterium granulomatis (donovanosis, granuloma inguinale),
    e. H. ducreyi (chancroid),
    f. H. influenzae (in respiratory, endocardial, and meningeal infections-concomitantly with another antibacterial agent),
    g. K. pneumoniae pneumonia (concomitantly with another antibacterial agent),
    h. E.coli, Proteus, A. aerogenes, K. pneumoniae, and Enterococcus faecalis in urinary tract infections,
    i. Streptococcus viridans, Enterococcus faecalis (in endocardial infections -concomitantly with penicillin),
    j. Gram-negative bacillary bacteremia (concomitantly with another antibacterial agent).

Tobramycin injection
Tobramycin is indicated for the treatment of serious bacterial infections caused by susceptible strains of the designated microorganisms in the diseases listed below:

Septicemia in the pediatric patient and adult caused by P. aeruginosa, E. coli, and Klebsiella sp.

Lower respiratory tract infections caused by P. aeruginosa, Klebsiella sp, Enterobacter sp, Serratia sp, E. coli, and S. aureus (penicillinase- and non-penicillinase-producing strains).

Serious central-nervous-system infections (meningitis) caused by susceptible organisms.

Intra-abdominal infections, including peritonitis, caused by E. coli, Klebsiella sp, and Enterobacter sp.

Skin, bone, and skin-structure infections caused by P. aeruginosa, Proteus sp, E. coli, Klebsiella sp, Enterobacter sp, and S. aureus.

Complicated and recurrent urinary tract infections caused by P. aeruginosa, Proteus sp (indole-positive and indole-negative), E. coli, Klebsiella sp, Enterobacter sp, Serratia sp, S. aureus, Providencia sp, and Citrobacter sp.

Aminoglycosides, including tobramycin sulfate, are not indicated in uncomplicated initial episodes of urinary tract infections unless the causative organisms are not susceptible to antibiotics having less potential toxicity. Tobramycin may be considered in serious staphylococcal infections when penicillin or other potentially less toxic drugs are contraindicated and when bacterial susceptibility testing and clinical judgment indicate its use.
Bacterial cultures should be obtained prior to and during treatment to isolate and identify etiologic organisms and to test their susceptibility to tobramycin. If susceptibility tests show that the causative organisms are resistant to tobramycin, other appropriate therapy should be instituted. In patients in whom a serious life-threatening gram-negative infection is suspected, including those in whom concurrent therapy with a penicillin or cephalosporin and an aminoglycoside may be indicated, treatment with tobramycin sulfate may be initiated before the results of susceptibility studies are obtained. The decision to continue therapy with tobramycin should be based on the results of susceptibility studies, the severity of the infection, and the important additional concepts discussed in the warnings box.
To reduce the development of drug-resistant bacteria and maintain the effectiveness of tobramycin and other antibacterial drugs, tobramycin should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antimicrobial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

Tygacil
Complicated Skin and Skin Structure Infections
Tygacil is indicated in patients 18 years of age and older for the treatment of complicated skin and skin structure infections caused by susceptible isolates of Escherichia coli, Enterococcus faecalis (vancomycin-susceptible isolates), Staphylococcus aureus (methicillin-susceptible and -resistant isolates), Streptococcus agalactiae, Streptococcus anginosus grp. (includes S. anginosus, S. intermedius, and S. constellatus), Streptococcus pyogenes, Enterobacter cloacae, Klebsiella pneumoniae, and Bacteroides fragilis.
Complicated Intra-abdominal Infections
Tygacil is indicated in patients 18 years of age and older for the treatment of complicated intra-abdominal infections caused by susceptible isolates of Citrobacter freundii, Enterobacter cloacae, Escherichia coli, Klebsiella oxytoca, Klebsiella pneumoniae, Enterococcus faecalis (vancomycin-susceptible isolates), Staphylococcus aureus (methicillin-susceptible and -resistant isolates), Streptococcus anginosus grp. (includes S. anginosus, S. intermedius, and S. constellatus), Bacteroides fragilis, Bacteroides thetaiotaomicron, Bacteroides uniformis, Bacteroides vulgatus, Clostridium perfringens, and Peptostreptococcus micros.
Community-Acquired Bacterial Pneumonia
Tygacil is indicated in patients 18 years of age and older for the treatment of community-acquired bacterial pneumonia caused by susceptible isolates of Streptococcus pneumoniae (penicillin-susceptible isolates), including cases with concurrent bacteremia, Haemophilus influenzae, and Legionella pneumophila.
Limitations of Use
Tygacil is not indicated for the treatment of diabetic foot infections. A clinical trial failed to demonstrate non-inferiority of Tygacil for treatment of diabetic foot infections.
Tygacil is not indicated for the treatment of hospital-acquired or ventilator-associated pneumonia. In a comparative clinical trial, greater mortality and decreased efficacy were reported in Tygacil treated patients.
Usage
To reduce the development of drug-resistant bacteria and maintain the effectiveness of Tygacil and other antibacterial drugs, Tygacil should be used only to treat infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

Appropriate specimens for bacteriological examination should be obtained in order to isolate and identify the causative organisms and to determine their susceptibility to tigecycline. Tygacil may be initiated as empiric monotherapy before results of these tests are known.

Vancomycin injection

Septicemia

Vancomycin Hydrochloride for Injection is indicated in adults and pediatric patients (neonates and older) for the treatment of septicemia due to:

- Susceptible isolates of methicillin-resistant Staphylococcus aureus (MRSA) and coagulase negative staphylococci.
- Methicillin-susceptible staphylococci in penicillin-allergic patients, or those patients who cannot receive or who have failed to respond to other drugs, including penicillins or cephalosporins

Infective Endocarditis

Vancomycin Hydrochloride for Injection is indicated in adults and pediatric patients (neonates and older) for the treatment of infective endocarditis due to:

- Susceptible isolates of MRSA.
- Viridans group streptococci Streptococcus gallolyticus (previously known as Streptococcus bovis), Enterococcus species and Corynebacterium species. For enterococcal endocarditis, use Vancomycin Hydrochloride for Injection in combination with an aminoglycoside.
- Methicillin-susceptible staphylococci in penicillin-allergic patients, or those patients who cannot receive or who have failed to respond to other drugs, including penicillins or cephalosporins.

Vancomycin Hydrochloride for Injection is indicated in adults and pediatric patients (neonates and older) for the treatment of early-onset prosthetic valve endocarditis caused by Staphylococcus epidermidis in combination with rifampin and an aminoglycoside.

Skin and Skin Structure Infections

Vancomycin Hydrochloride for Injection is indicated in adults and pediatric patients (neonates and older) for the treatment of skin and skin structure infections due to:

- Susceptible isolates of MRSA and coagulase negative staphylococci.
- Methicillin-susceptible staphylococci in penicillin-allergic patients, or those patients who cannot receive or who have failed to respond to other drugs, including penicillins or cephalosporins.

Bone Infections

Vancomycin Hydrochloride for Injection is indicated in adults and pediatric patients (neonates and older) for the treatment of bone infections due to:

- Susceptible isolates of MRSA and coagulase negative staphylococci.
- Methicillin-susceptible staphylococci in penicillin-allergic patients, or those patients who cannot receive or who have failed to respond to other drugs, including penicillins or cephalosporins.

Lower Respiratory Tract Infections

Vancomycin Hydrochloride for Injection is indicated in adults and pediatric patients (neonates and older) for the treatment of lower respiratory tract infections due to:

- Susceptible isolates of MRSA
- Methicillin-susceptible staphylococci in penicillin-allergic patients, or those patients who cannot receive or who have failed to respond to other drugs, including penicillins or cephalosporins.

Usage

To reduce the development of drug-resistant bacteria and maintain the effectiveness of Vancomycin Hydrochloride for Injection and other antibacterial drugs, Vancomycin Hydrochloride for Injection should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

The parenteral form of vancomycin hydrochloride for injection, USP may be administered orally for treatment of antibiotic-associated pseudomembranous colitis produced by C. difficile and for staphylococcal enterocolitis. Parenteral administration of vancomycin hydrochloride alone is of unproven benefit for these indications. Vancomycin is not effective by the oral route for other types of infections.

Vfend IV

Invasive Aspergillosis

Vfend is indicated in adults and pediatric patients (2 years of age and older) for the treatment of invasive aspergillosis (IA). In clinical trials, the majority of isolates recovered were Aspergillus fumigatus. There was a small number of cases of culture-proven disease due to species of Aspergillus other than A. fumigatus.

Candidemia in Non-neutropenic Patients and Other Deep Tissue Candida Infections

Vfend is indicated in adults and pediatric patients (2 years of age and older) for the treatment of candidemia in non-neutropenic patients and the following Candida infections: disseminated infections in skin and infections in abdomen, kidney, bladder wall, and wounds.

Esophageal Candidiasis

Vfend is indicated in adults and pediatric patients (2 years of age and older) for the treatment of esophageal candidiasis (EC) in adults and pediatric patients 2 years of age and older.

Scedosporiosis and Fusariosis

Vfend is indicated for the treatment of serious fungal infections caused by Scedosporium apiospermum (asexual form of Pseudallescheria boydii) and Fusarium spp. including Fusarium solani, in adults and pediatric patients (2 years of age and older) intolerant of, or refractory to, other therapy.

Usage

Specimens for fungal culture and other relevant laboratory studies (including histopathology) should be obtained prior to therapy to isolate and identify causative organism(s). Therapy may be instituted before the results of the cultures and other laboratory studies are known. However, once these results become available, antifungal therapy should be adjusted accordingly.

INITIAL QUANTITY LIMIT*

Duration limits (Column A) and Daily dose limits (Column B) apply for each drug.

LIMIT CRITERIA

Limits do not accumulate together; patient is allowed the maximum limit for each drug and strength

PLEASE NOTE: Since manufacturer package sizes may vary, it is the discretion of the dispensing pharmacy to fill quantities per package size up to these quantity limits. In such cases the filling limit and day supply may be less than what is indicated.

		Column A	**Column B**	
Medication	usual/maximum recommended dose (139.9kg allows for 95th percentile dosing)[32]	**Duration per 365 days**	**Daily dose**	**package size**
Abelcet (amphotericin B lipid complex)	5mg/kg/day *5mgx139.9kg = 699.5mg/day* *699.5mg/day/100mg/vial = 7vials/day* *7vialsx20mL/vial = 140mL*	14 days	140mL	5mg/mL 20mL per vial (100mg per vial)
AmBisome (amphotericin B liposome)	6mg/kg/day, *6mgx139.9kg = 839.4mg/day* *839.4mg/day/50mg/vial = 16.8vials/day*	14 days	17 vials	50mg per vial
Amphotericin B	1 mg/kg/day *1mgx139.9kg/day = 139.9mg/day* *139.9mg/day/50mg/vial = 2.8vials/day*	14 days	3 vials	50mg per vial
Cancidas (caspofungin)	50mg/day or 70mg/day *= 1vial/day*	14 days	1 vial	50mg per vial 70mg per vial
Ceftriaxone vials, bottles	1 to 2 gm once a day (or divided doses twice a day) The total daily dose should not exceed 4gm *1vial/dosex2doses/day = 2vials/day*	14 days	2 vials	250mg per vial 500mg per vial 1gm per vial 2gm per vial
			0.5 bottle	10gm per bottle
Coly-Mycin M (colistimethate)	5mg/kg/day in 2 to 4 divided doses *5mgx139.9kg = 699.5mg/day,* *699.5mg/4doses/day = 174.9mg/dose* *174.9mg/dose/150mg/vial = 1.2vials/dose* *2vials/dosex4doses/day = 8vials/day*	14 days	8 vials	150mg per vial
Cubicin, Cubicin RF (daptomycin)	6mg/kg once every 24 hours *6mgx139.9kg = 839.4/day* *839.4mg/day/500mg/vial = 1.7vials/day*	14 days	2 vials	500mg per vial
Dapzura RT (daptomycin)				
Daptomycin 500mg				
Daptomycin 350mg	6mg/kg once every 24 hours *6mgx139.9kg = 839.4mg/day* *839.4mg/day/350mg/vial = 2.4vials/day*	14 days	3 vials	350mg per vial

Dalvance (dalbavancin)	1500mg as single dose or divided *1500mg/dose/500mg/vialx1dose = 3 vials*	1 day	3 vials	500mg per vial
Invanz (ertapenem)	Adult: 1g given once a day *1vial/dosex1dose/day = 1vial/day* Pediatric: 15mg/kg twice daily (not to exceed 1g/day), *1vial/dosex2doses/day = 2vials/day*	14 days	2 vials	1gm per vial
Kimyrsa (oritavancin)	1200mg (one dose) *1200mg/dose/1200mg/vialx1dose = 1 vial*	1 day	1 vial	1200mg per vial
Levofloxacin inj	Adult: 750mg every 24 hours *750mg/day/25mg/mL = 30mL/day* *30mL/day/30mL/vial = 1 vial/day* Pediatric: 250mg every 12 hours *250mg/dose/25mg/mL = 10mL/dose* *10mL/dose/20mL/vial = 0.5vials/dose* *1vial/dosex2doses/day = 2vials/day* *2vials/dayx20mL/vial = 40mL/day*	14 days	40mL	25mg/mL 20mL per vial =500mg / 20mL vial
				25mg/mL 30mL per vial =750mg / 30mL vial
Merrem (meropenem)	2gm every 8 hours *2gm/dose/500mg/vial = 4vials/dose* *4vials/dosex3doses/day = 12vials/day* *2gm/dose/1gm/vial = 2vials/dose* *2vials/dosex3doses/day = 6vials/day*	14 days	12 vials	500mg per vial
			6 vials	1gm per vial
Mycamine (micafungin)	150mg once daily *150mg/day/50mg/vial = 3vials/day* *150mg/day/100mg/vial = 2vials/day*	14 days	3 vials	50mg per vial
			2 vials	100mg per vial
Orbactiv (oritavancin)	1200mg (one dose) *1200mg/dose/400mg/vialx1dose = 3 vials*	1 day	3 vials	400mg per vial
Streptomycin	1 to 2 gm in divided doses *1gm/vialx2doses/day = 2 vials/day*	14 days	2 vials	1gm per vial
Tobramycin inj	10mg/kg/day in 3 equal doses or in 4 equal doses. *10mgx139.9kg = 1399kg/day* *1399mg/day/4doses/day = 349.8mg/dose* *349.8mg/dose/40mg/mL = 8.7mL/dose* *9mL/dosex4doses/day = 36mL/day*	10 days	36mL	10mg/mL 2mL per vial (20mg / 2mL vial)
				80mg/2mL 2mL per vial (40mg / mL vial)
				40mg/mL 30mL per vial (1200mg / 30mL vial)
				40mg/mL 50mL per vial (2000mg / 50mL vial)
			2 vials	1.2gm powd per vial
Tygacil (tigecycline)	Initial dose of 100mg *100mg/dose/50mg/vialx1dose = 2 vials* Followed by 50mg every 12 hours *50mg/dose/50mg/vial = 1vial/dose* *1vial/dosex2doses/day = 2vials/day* **2vials initial dose + followed by 1vial = 3vials 1st day*	14 days	3 vials* **Daily limit allows for maximum quantity needed for first day of treatment*	50mg per vial
Vancomycin inj vials, bottles	2 grams divided either as 500mg every 6 hours *4doses/dayx1vial/dose = 4vials/day* or 1 g every 12 hours *2doses/dayx1vial/dose = 2vials/day* [oral: 125mg to 2gm in four divided doses for ten days]	14 days	4 vials	250mg per vial 500mg per vial 750mg per vial
			2 vials	1gm per vial 1.25gm per vial 1.5gm per vial
			0.3 bottles	5gm per bottle 10gm per bottle
Vfend IV (voriconazole inj)	Loading dose 6mg/kg every 12 hours for the first 24 hours *6mgx139.9kg/dose = 839.4mg/dose* *839.4mg/dose/200mg/vial = 4.2vials/dose* *5vials/dosex2doses = 10 vials 1st day* Maintenance dose 4mg/kg every 12 hours	14 days	10 vials* **Daily limit allows for maximum quantity needed for first day of treatment*	200mg per vial

	4mgx139.9kg/dose = 559.6mg/dose *559.6mg/dose/200mg/vial = 2.8vials/dose* *3vials/dosex2doses/day = 6vials/day*			

**If the patient is requesting more than the initial quantity limit, the claim will reject with a message indicating that a prior authorization is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug will not be used intranasally or in a footbath

AND

- The requested drug is being prescribed for an FDA-approved indication or an indication supported in the compendia of current literature (examples: AHFS, Micromedex, current accepted guidelines)

AND

- The infection is proven or strongly suspected to be caused by susceptible microorganisms

AND

  - The patient is unable to switch to oral therapy

  OR

  - The request is for vancomycin to be taken orally for the treatment of C. difficile associated diarrhea or for staphylococcal enterocolitis

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PRIOR AUTHORIZATION CRITERIA

DRUG CLASS	**ANTIOBESITY AGENTS**
BRAND NAME (generic)	
	benzphetamine products
	diethylpropion products
	phendimetrazine products
	phentermine products

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

POLICY

FDA-APPROVED INDICATIONS

Benzphetamine

Benzphetamine is indicated in the management of exogenous obesity as a short term (a few weeks) adjunct in a regimen of weight reduction based on caloric restriction in patients with an initial body mass index (BMI) of 30 kg/m^2 or higher who have not responded to appropriate weight reducing regimen (diet and/or exercise) alone. The limited usefulness of agents of this class should be weighed against possible risks inherent in their use. Benzphetamine is indicated for use as monotherapy only.

Diethylpropion

Diethylpropion is indicated in the management of exogenous obesity as a short-term adjunct (a few weeks) in a regimen of weight reduction based on caloric restriction in patients with an initial body mass index of 30 kg/m^2 or higher and who have not responded to an appropriate weight reducing regimen (diet and/or exercise) alone. The usefulness of agents of this class should be measured against possible risk factors inherent in their use. Diethylpropion is indicated for use as monotherapy only.

Phendimetrazine

Phendimetrazine tartrate extended-release capsules are indicated in the management of exogenous obesity as a short term adjunct (a few weeks) in a regimen of weight reduction based on caloric restriction in patients with an initial body mass index (BMI) of greater than or equal to 30 kg/m^2 or greater than or equal to 27 kg/m^2 in the presence of other risk factors (e.g., controlled hypertension, diabetes, hyperlipidemia) who have not responded to appropriate weight reducing regimen (diet and/or exercise) alone. The usefulness of agents of this class should be measured against possible risk factors inherent in their use. Phendimetrazine tartrate is indicated for use as monotherapy only.

Phendimetrazine tartrate is indicated in the management of exogenous obesity as a short term adjunct (a few weeks) in a regimen of weight reduction based on caloric restriction in patients with an initial body mass index (BMI) of 30 kg/m^2 or higher who have not responded to appropriate weight reducing regimen (diet and/or exercise) alone. The limited usefulness of agents of this class should be weighed against possible risks inherent in their use. Phendimetrazine tartrate is indicated for use as monotherapy only.

Phentermine

Phentermine is indicated as a short-term (a few weeks) adjunct in a regimen of weight reduction based on exercise, behavioral modification, and caloric restriction, in the management of exogenous obesity for patients with an initial body mass index greater than or equal to 30 kg/m^2, or greater than or equal to 27 kg/m^2 in the presence of other risk factors

(e.g., controlled hypertension, diabetes, hyperlipidemia). The limited usefulness of agents of this class should be measured against possible risk factors inherent in their use.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has not received 3 months of therapy with the requested drug within the past 365 days
  AND
- The requested drug will be used with a reduced calorie diet and increased physical activity in the management of exogenous obesity
  AND
- The patient has participated in a comprehensive weight management program that encourages behavioral modification, reduced calorie diet and increased physical activity with continuing follow-up for at least 6 months prior to using drug therapy
  AND
  - The patient has a body mass index (BMI) greater than or equal to 30 kg per square meter
    OR
  - The patient has a body mass index (BMI) greater than or equal to 27 kg per square meter AND has at least one weight related comorbid condition (e.g., hypertension, type 2 diabetes mellitus or dyslipidemia)

  AND
- If the request is for phentermine it will not be used in a patient who is also using Fintepla (fenfluramine)

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QUANTITY LIMIT CRITERIA

DRUG CLASS	**ANTIEMETICS**
BRAND NAME* (generic)	**ANZEMET (dolasetron mesylate)**
Status: CVS Caremark Criteria	
Type: Quantity Limit	***Ref # 19-H***

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Anzemet tablets are indicated for the prevention of nausea and vomiting associated with moderately emetogenic cancer chemotherapy, including initial and repeat courses in adults and children 2 years and older.

INITIAL LIMIT QUANTITY

Limits do not accumulate together; patient is allowed the maximum limit for each drug and strength

Drug	4 Week Limit*	12 Week Limit*
Anzemet 50mg Tablets (dolasetron mesylate)	12 tablets / 21 days	Does Not Apply*
Anzemet 100mg Tablets (dolasetron mesylate)	6 tablets / 21 days	Does Not Apply*

** The duration of 21 days is used for a 28-day fill period to allow time for refill processing.*

** These drugs are for short-term acute use; therefore, the mail limit will be the same as the retail limit. The intent is for prescriptions of the requested drug to be filled one month at a time, even if filled at mail order; there should be no 3 month supplies filled.*

RATIONALE

Anzemet tablets are indicated for the prevention of nausea and vomiting associated with moderately emetogenic cancer chemotherapy, including initial and repeat courses in adults and children 2 years and older.

For adults, the recommended oral dosage of Anzemet (dolasetron mesylate) is 100 mg given within one hour before chemotherapy. The recommended oral dosage in pediatric patients 2 to 16 years of age is 1.8 mg/kg given within one hour before chemotherapy, up to a maximum of 100 mg. Safety and effectiveness in pediatric patients under 2 years of age have not been established. [1,3]

Patients need to be protected throughout the entire period of risk, which lasts for at least 3 days for high emetic risk and 2 days for moderate emetic risk agents after the last dose of chemotherapy. According to the National Comprehensive Cancer Network (NCCN) Antiemesis Guidelines for moderately emetogenic chemotherapy, repeated doses may be given on days 2 and 3 for dolasetron, granisetron and ondansetron.[4]

These limits are designed to allow for treatment at the recommended doses on the day of chemotherapy plus an additional one to two days post-chemotherapy for Anzemet tablets. The limit allows a quantity sufficient for two chemotherapy cycles per 28 days (i.e., one chemotherapy cycle every 2 weeks).

If the patient is requesting more than the initial quantity limit the claim will reject with a message indicating that a prior authorization is required.

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Written by:	UM Development (LS)
Date Written:	01/2000
Revised:	(JG) 08/2002, (MG) 07/2003, 10/2004, 09/2005, (AK) 04/2006, (CT) 04/2007, 04/2008, (SE) 03/2009, (KD) 03/2010, (SE) 01/2011(FDA warning/CI 03-2010 (2)); (CY) 04/2011, 02/2012; (PL) 01/2013, (PL) 01/2014; (CF) 01/2015, 01/2016; (KM) 01/2017 (no clinical changes); (DS) 01/2018 (no clinical changes), 01/2019, (ME) 01/2020 (no clinical changes), 01/2021 (no clinical changes), (MRS) 01/2022 (no clinical changes), (TM) 12/2022 (off cycle update increased QL for 50mg),(TM/KJ) 12/2022 (no clinical changes)
Reviewed:	Medical Affairs 01/2000, 08/2002, 10/2004, 09/2005; (MM) 04/2006; (WLF) 04/2007, 04/2008, 3/2009, 03/2010; (KP) 01/2011, 04/2011, 02/2012; (LMS) 01/2013, (KP) 01/2014; (SES) 01/2015; (GAD) 01/2016; (CHART) 01/30/20, 01/28/21, 02/03/22, 12/29/2022
External Review:	10/2002, 08/2006, 08/2007, 08/2008, 08/2009, 08/2010, 08/2011, 04/2012, 06/2013, 04/2014, 04/2015, 04/2016, 04/2017, 04/2018, 04/2019, 04/2020, 04/2021, 04/2022, 04/2023

Reference number(s)
2258-A

SPECIALTY GUIDELINE MANAGEMENT

APOKYN (apomorphine hydrochloride injection)
KYNMOBI (apomorphine hydrochloride)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Apokyn is indicated for the acute, intermittent treatment of hypomobility, "off" episodes ("end-of-dose wearing off" and unpredictable "on/off" episodes) in patients with advanced Parkinson's disease.

Kynmobi is indicated for the acute, intermittent treatment of "off" episodes in patients with Parkinson's disease (PD).

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Parkinson's disease
Authorization of 6 months may be granted for the treatment of acute, intermittent treatment of "off" episodes for members with Parkinson's disease when all of the following criteria are met:
A. The member experiences at least 1 hour per day of off time
B. The member is currently being treated with carbidopa/levodopa
C. Attempts to manage off episodes by adjusting the dosing or formulation of carbidopa/levodopa were ineffective
D. Treatment with carbidopa/levodopa plus one of the following therapies was ineffective at managing off episodes:
    1. Dopamine agonist (e.g., pramipexole, ropinirole)
    2. Monoamine oxidase B (MAO-B) inhibitor (e.g., selegiline, rasagiline)
    3. Catechol-O-methyl transferase (COMT) inhibitor (e.g., entacapone, tolcapone)

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment of acute, intermittent treatment of "off" episodes for members with Parkinson's disease when both of the following criteria are met:
A. The member is currently being treated with carbidopa/levodopa
B. The member is experiencing improvement with the requested medication (e.g. reduction in daily off time, improvement in motor function post-administration)

IV. REFERENCES

1. Apokyn [package insert]. Louisville, KY: US WorldMeds, LLC; April 2020.
2. Kynmobi [package insert]. Marlborough, MA: Sunovion Pharmaceuticals Inc.; May 2020.
3. Miyasaki JM, Martin W, Suchowersky O, et al. Practice parameter: Initiation of treatment for Parkinson's disease: An evidence-based review. *Neurology* Jan 2002, 58 (1) 11-17.
4. National Institute for Clinical Excellence: Parkinson's disease in adults. July 2017. https://www.nice.org.uk/guidance/ng71/resources/parkinsons-disease-in-adults-pdf-1837629189061. Accessed August 1, 2021.
5. Fox SH, Katzenschlager R, Lim SY, et al. International Parkinson and movement disorder society evidence-based medicine review: update on treatments for the motor symptoms of Parkinson's disease. *Mov Disord*. 2018; 33(8):1248-1266.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME*
(generic)

APTIOM
(eslicarbazepine)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization ***Ref # 1083-A***

** Drugs that are listed in the target drug box include both brand and generic and all dosages forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Aptiom is indicated for the treatment of partial-onset seizures in patients 4 years of age and older.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for the treatment of partial-onset seizures (i.e., focal-onset seizures) in a patient 4 years of age or older

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Aptiom is indicated for the treatment of partial-onset seizures in patients 4 years of age and older.[1-3]

In 2017, the International League Against Epilepsy (ILAE) presented a revised operational classification of seizure types, changing the term “partial” to “focal”. The new classification does not represent a fundamental change but allows greater flexibility and transparency in naming seizure types.[4]

REFERENCES

1. Aptiom [package insert]. Marlborough, MA: Sunovion Pharmaceuticals, Inc.; March 2019.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2022; Accessed March 17, 2022.
3. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed March 17, 2022.
4. Fisher RS, Cross JH, French JA, et al. Operational Classification of seizure types by the International League Against Epilepsy: Position Paper of the ILAE Commission for Classification and Terminology. *Epilepsia.* 2017 Apr;58(4):522-530.

Written by:	UM Development (SE)
Date Written:	11/2013
Revised:	(CT) 05/2014; (CF) 05/2015, 09/2015 (updated indication); (KM) 05/2016 (no clinical changes); (SF) 05/2017 (no clinical changes); (KC) 05/2018, 05/2019 (no clinical changes), 05/2020 (no clinical changes); (CJH) 05/2021 (no clinical changes), (DFW) 05/2022 (no clinical changes)
Reviewed:	Medical Affairs (SES) 12/2013; (LMS) 05/2014; (DNC) 05/2015, 09/2015; (ME) 05/2018; (CHART) 05/28/2020, 05/27/2021, 05/26/2022
External Review:	02/2014, 10/2014, 10/2015, 10/2016, 10/2017, 10/2018, 10/2019, 10/2020, 08/2021, 08/2022

CVS caremark®

CRITERIA FOR APPROVAL

1	Is the requested drug being prescribed for the treatment of partial-onset seizures (i.e., focal-onset seizures) in a patient 4 years of age or older? [No further questions]	Yes	No

Mapping Instructions			
	Yes	**No**	**DENIAL REASONS**
1.	Approve, 36 Months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you meet all of these conditions: - You have partial-onset seizures (i.e., focal onset seizures) - You are 4 years of age or older Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]

Reference number
1616-A

SPECIALTY GUIDELINE MANAGEMENT

ARANESP (darbepoetin alfa)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
1. Anemia Due to Chronic Kidney Disease
   Treatment of anemia due to chronic kidney disease (CKD), including patients on dialysis and patients not on dialysis.
2. Anemia Due to Chemotherapy in Patients with Cancer
   Treatment of anemia in patients with non-myeloid malignancies where anemia is due to the effect of concomitant myelosuppressive chemotherapy, and upon initiation, there is a minimum of two additional months of planned chemotherapy.

B. Compendial Uses
1. Symptomatic anemia in patients with myelodysplastic syndromes (MDS)
2. Anemia in patients whose religious beliefs forbid blood transfusions
3. Symptomatic anemia in patients with primary myelofibrosis, post-polycythemia vera myelofibrosis, or post-essential thrombocythemia myelofibrosis
4. Cancer patients who are undergoing palliative treatment

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Note: Requirements regarding pretreatment hemoglobin level exclude values due to a recent transfusion. All members must be assessed for iron deficiency anemia and have adequate iron stores (defined as a serum transferrin saturation [TSAT] level greater than or equal to 20% within the prior 3 months) or are receiving iron therapy before starting Aranesp. Members may not use Aranesp concomitantly with other erythropoiesis stimulating agents.

A. Anemia Due to Chronic Kidney Disease (CKD)
Authorization of 12 weeks may be granted for treatment of anemia due to chronic kidney disease in members with pretreatment hemoglobin < 10 g/dL.

B. Anemia Due to Myelosuppressive Chemotherapy
Authorization of 12 weeks may be granted for treatment of anemia due to myelosuppressive chemotherapy in members with nonmyeloid malignancy and pretreatment hemoglobin < 10 g/dL.

C. Anemia in Myelodysplastic Syndrome (MDS)

Authorization of 12 weeks may be granted for treatment of anemia in myelodysplastic syndrome in members with pretreatment hemoglobin < 10 g/dL whose pretreatment serum erythropoietin (EPO) level is < 500 mU/mL.

D. Anemia in Members Whose Religious Beliefs Forbid Blood Transfusions
Authorization of 12 weeks may be granted for treatment of anemia in members whose religious beliefs forbid blood transfusions with pretreatment hemoglobin < 10 g/dL.

E. Anemia in Primary Myelofibrosis (MF), Post-polycythemia Vera MF, or Post-Essential Thrombocythemia MF
Authorization of 12 weeks may be granted for treatment of anemia in primary myelofibrosis, post-polycythemia vera myelofibrosis, or post-essential thrombocythemia myelofibrosis in members who meet ALL of the following criteria:
1. Pretreatment hemoglobin < 10 g/dL
2. Pretreatment serum EPO level < 500 mU/mL

F. Anemia Due to Cancer
Authorization of 12 weeks may be granted for treatment of anemia due to cancer in members who have cancer and are undergoing palliative treatment.

III. CONTINUATION OF THERAPY

Note: Requirements regarding pretreatment hemoglobin level exclude values due to a recent transfusion. All members must be assessed for iron deficiency anemia and have adequate iron stores (defined as a serum transferrin saturation [TSAT] level greater than or equal to 20% within the prior 3 months) or are receiving iron therapy before continuation of treatment with Aranesp. Members may not use Aranesp concomitantly with other erythropoiesis stimulating agents.

For all indications below: All members (including new members) requesting authorization for continuation of therapy after at least 12 weeks of ESA treatment must show a response with a rise in hemoglobin of $\geq$ 1 g/dL. Members who completed less than 12 weeks of ESA treatment and have not yet responded with a rise in hemoglobin of $\geq$ 1 g/dL may be granted authorization of up to 12 weeks to allow for sufficient time to demonstrate a response.

A. Anemia due to Chronic Kidney Disease (CKD)
Authorization of 12 weeks may be granted for continued treatment of anemia due to chronic kidney disease in members with current hemoglobin < 12 g/dL.

B. Anemia Due to Myelosuppressive Chemotherapy
Authorization of 12 weeks may be granted for continued treatment of anemia due to myelosuppressive chemotherapy in members with nonmyeloid malignancy and current hemoglobin < 12 g/dL.

C. Anemia in Myelodysplastic Syndrome (MDS)
Authorization of 12 weeks may be granted for continued treatment of anemia in myelodysplastic syndrome in members with current hemoglobin < 12 g/dL.

D. Anemia in members whose religious beliefs forbid blood transfusions
Authorization of 12 weeks may be granted for continued treatment of anemia in members whose religious beliefs forbid blood transfusions with current hemoglobin < 12 g/dL.

E. Anemia in Primary Myelofibrosis (MF), Post-polycythemia Vera MF, or Post-Essential Thrombocythemia MF

Authorization of 12 weeks may be granted for continued treatment of anemia in primary myelofibrosis, post-polycythemia vera myelofibrosis, or post-essential thrombocythemia myelofibrosis in members with current hemoglobin < 12 g/dL.

F. Anemia Due to Cancer

Authorization of 12 weeks may be granted for continued treatment of anemia due to cancer in members who have cancer and are undergoing palliative treatment.

IV. REFERENCES

1. Aranesp [package insert]. Thousand Oaks, CA: Amgen Inc.; January 2019.
2. National Comprehensive Cancer Network. The NCCN Drugs & Biologics Compendium. http://www.nccn.org. Accessed September 10, 2021.
3. Micromedex Solutions [database online]. Ann Arbor, MI: Truven Health Analytics Inc. Updated periodically. www.micromedexsolutions.com [available with subscription]. Accessed September 10, 2021.
4. Kidney Disease: Improving Global Outcomes (KDIGO) Anemia Work Group. KDIGO Clinical Practice Guideline for Anemia in Chronic Kidney Disease. Kidney Int. 2012; Suppl 2:279-335.
5. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Myeloproliferative Neoplasms. Version 2.2021. http://www.nccn.org/professionals/physician_gls/pdf/mpn.pdf. Accessed September 10, 2021.
6. Gabrilove J, Paquette R, Lyons R, Mushtaq C, Sekeres M, et al. Phase 2, single-arm trial to evaluate the effectiveness of darbepoetin alfa for correcting anemia in patients with myelodysplastic syndromes. Br J Haematol. 2008 Aug; 142(3): 379–393.

Reference number
1800-A

SPECIALTY GUIDELINE MANAGEMENT

ARCALYST (rilonacept)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

A. Treatment of Cryopyrin-Associated Periodic Syndromes (CAPS), including Familial Cold Autoinflammatory Syndrome (FCAS) and Muckle-Wells Syndrome (MWS) in adults and children 12 years of age and older.
B. Maintenance of remission of Deficiency of Interleukin-1 Receptor Antagonist (DIRA) in adults and pediatric patients weighing at least 10 kilograms (kg).
C. Treatment of recurrent pericarditis (RP) and reduction in risk of recurrence in adults and children 12 years and older.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

A. Deficiency of interleukin-1 receptor antagonist (DIRA) initial requests: *IL1RN* mutation status

B. Recurrent pericarditis (RP):
   1. Initial requests: Chart notes, medical record documentation, or claims history supporting previous medications tried, including response to therapy.
   2. Continuation requests: Chart notes or medical record documentation supporting positive clinical response.

III. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with one of the following:
A. Cryopyrin associated periodic syndromes (CAPS) and deficiency of interleukin-1 receptor antagonist (DIRA): rheumatologist or immunologist
B. Recurrent pericarditis (RP): cardiologist, rheumatologist, or immunologist

IV. CRITERIA FOR INITIAL APPROVAL

A. Cryopyrin-associated periodic syndromes (CAPS)
Authorization of 12 months may be granted for members 12 years of age or older for treatment of CAPS when both of the following criteria are met:

1. Member has a diagnosis of familial cold autoinflammatory syndrome (FCAS) with classic signs and symptoms (i.e., recurrent, intermittent fever and rash that were often exacerbated by exposure to generalized cool ambient temperature) or Muckle-Wells syndrome (MWS) with classic signs and symptoms (i.e., chronic fever and rash of waxing and waning intensity, sometimes exacerbated by exposure to generalized cool ambient temperature).
2. Member has functional impairment limiting the activities of daily living.

B. Deficiency of interleukin-1 receptor antagonist (DIRA)
Authorization of 12 months may be granted for members weighing at least 10 kg for treatment of DIRA when both of the following criteria are met:
1. Member has *IL1RN* mutations.
2. Arcalyst will be used for maintenance of remission following treatment with Kineret (anakinra).

C. Recurrent pericarditis (RP)
Authorization of 12 months may be granted for members 12 years of age or older for treatment of recurrent pericarditis when both of the following criteria are met:
1. Member has had at least two episodes of pericarditis.
2. Member has failed at least 2 agents of standard therapy (e.g., colchicine, non-steroidal anti-inflammatory drugs [NSAIDs], corticosteroids).

V. CONTINUATION OF THERAPY

A. Cryopyrin-associated periodic syndromes (CAPS)
Authorization of 12 months may be granted for all members 12 years of age or older (including new members) who are using the requested medication for CAPS and who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition.

B. Deficiency of interleukin-1 receptor antagonist (DIRA)
Authorization of 12 months may be granted for all members weighing at least 10 kg (including new members) who are using the requested medication for DIRA and who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition.

C. Recurrent pericarditis (RP)
Authorization of 12 months may be granted for all members 12 years of age or older (including new members) who are using the requested medication for recurrent pericarditis and who achieve or maintain a positive clinical response as evidenced by decreased recurrence of pericarditis or improvement in signs and symptoms of the condition when there is improvement in any of the following:
1. Pericarditic chest pain
2. Pericardial rubs
3. Electrocardiogram (ECG)
4. Pericardial effusion
5. C-reactive protein (CRP)

VI. OTHER

For all indications: Member has had a documented negative tuberculosis (TB) test (which can include a tuberculosis skin test [PPD], an interferon-release assay [IGRA], or a chest x-ray)* within 6 months of initiating therapy for persons who are naïve to biologic drugs or targeted synthetic drugs associated with an increased risk of TB.

* If the screening testing for TB is positive, there must be further testing to confirm there is no active disease. Do not administer the requested medication to members with active TB infection. If there is latent disease, TB treatment must be started before initiation of the requested medication.

For all indications: Member cannot use the requested medication concomitantly with any other biologic drug or targeted synthetic drug.

VII. REFERENCES

1. Arcalyst [package insert]. London, UK: Kiniksa Pharmaceuticals (UK), Ltd.; May 2021.
2. Hoffman HM, Throne ML, Amar NJ, et al. Efficacy and safety of rilonacept (interleukin-1 trap) in patients with cryopyrin-associated periodic syndromes. Results from two sequential placebo-controlled studies. *Arthritis Rheum.* 2008;58(8):2443-52.
3. Testing for TB Infection. Centers for Disease Control and Prevention. Retrieved on April 10, 2023 from: https://www.cdc.gov/tb/topic/testing/tbtesttypes.htm.
4. Adler Y, Charron P, Imazio M, et al. 2015 ESC Guidelines for the diagnosis and management of pericardial diseases: The Task Force for the Diagnosis and Management of Pericardial Diseases of the European Society of Cardiology (ESC) Endorsed by: The European Association for Cardio-Thoracic Surgery (EACTS). *Eur Heart J*. 2015;36(42):2921-64.
5. Chiabrando JG, Bonaventura A, Vecchié, et al. Management of acute and recurrent pericarditis: *JACC* State-of-the-art review. *J Am Coll Cardiol.* 2020;75(1):76-92.
6. Klein AL, Imazio M, Cremer P, et al. Phase 3 trial of interleukin-1 trap rilonacept in recurrent pericarditis. *N Engl J Med.* 2021:384(1):31-41.
7. Lachmann HJ, Kone-Paut I, Kuemmerle-Deschner JB, et al; Canakinumab in CAPS Study Group. Use of canakinumab in the cryopyrin-associated periodic syndrome. *N Engl J Med*. 2009;360(23):2416-2425.
8. Garg M, de Jesus A, Chapelle D, et al. Rilonacept maintains long-term inflammatory remission in patients with deficiency of the IL-1 receptor antagonist. *JCI Insight*. 2017;2(16):e94838. https://doi.org/10.1172/jci.insight.94838.

Reference number(s)
3150-A

SPECIALTY GUIDELINE MANAGEMENT

ARIKAYCE (amikacin liposome inhalation suspension)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Arikayce is indicated in adults who have limited or no alternative treatment options, for the treatment of Mycobacterium avium complex (MAC) lung disease as part of a combination antibacterial drug regimen in patients who do not achieve negative sputum cultures after a minimum of 6 consecutive months of a multidrug background regimen therapy.

Limitation of Use: Arikayce has only been studied in patients with refractory MAC lung disease defined as patients who did not achieve negative sputum cultures after a minimum of 6 consecutive months of a multidrug background regimen therapy. The use of Arikayce is not recommended for patients with non-refractory MAC lung disease.

All other indications are considered experimental/investigational and are not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Mycobacterium avium complex (MAC) lung disease
Authorization of 12 months may be granted for members with mycobacterium avium complex (MAC) lung disease when the following criteria is met:
A. The patient has refractory disease with limited or no other treatment options.
B. The requested medication will be used as part of a combination antibacterial drug regimen.
C. The patient has not achieved negative sputum cultures after being treated with a multidrug background regimen therapy for a minimum of 6 consecutive months.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II who are experiencing benefit from therapy as evidenced by disease stability or disease improvement (e.g., achievement and maintenance of negative sputum cultures).

IV. REFERENCES

1. Arikayce [package insert]. Bridgewater, NJ: Insmed Incorporated; October 2020.
2. Griffith, DE, Aksamit, T, Brown-Elliott, BA, et al. An Official ATS/IDSA Statement: Diagnosis, Treatment, and Prevention of Nontuberculous Mycobacterial Disease. *Am J Respir Crit Care Med. 2007;175):367-416*
3. Daley, CL, Iaccarino, JM, Lange, C, et al. Treatment of Nontuberculous Mycobacterial Pulmonary Disease: An Official ATS/ERS/ESCMID/IDSA Clinical Practice Guideline. *Clin Infect Dis. 2020 Aug 14;71(4):e1-e36*

STEP THERAPY CRITERIA

DRUG CLASS	**ATYPICAL ANTIPSYCHOTICS – ORAL/TRANSDERMAL (BRAND PRODUCTS ONLY)**
BRAND NAME (generic)	
	ABILIFY (ORAL TABLET & ORAL SOLUTION ONLY) (BRAND ONLY) (aripiprazole)
	ABILIFY MYCITE (BRAND ONLY) (aripiprazole)
	CAPLYTA (BRAND ONLY) (lumateperone)
	FANAPT (BRAND ONLY) (iloperidone)
	GEODON (ORAL CAPSULE) (BRAND ONLY) (ziprasidone)
	INVEGA (ORAL TABLET) (BRAND ONLY) (paliperidone)
	LATUDA (BRAND ONLY) (lurasidone hydrochloride)
	LYBALVI (BRAND ONLY) (olanzapine and samidorphan)
	REXULTI (BRAND ONLY) (brexpiprazole)
	RISPERDAL (ORAL TABLET & ORAL SOLUTION ONLY) (BRAND ONLY) (risperidone)
	SAPHRIS (BRAND ONLY) (asenapine)
	SECUADO (BRAND ONLY) (asenapine transdermal)
	SEROQUEL, SEROQUEL XR (BRAND ONLY) (quetiapine)

VRAYLAR (BRAND ONLY)
(cariprazine)

ZYPREXA (ORAL TABLET & ODT ONLY) (BRAND ONLY)
(olanzapine)

Status: CVS Caremark Criteria
Type: Initial Step Therapy; Post Step Therapy Prior Authorization

POLICY

FDA-APPROVED INDICATIONS

Abilify
Abilify (aripiprazole) Oral Tablets and Oral Solution are indicated for the treatment of:

- Schizophrenia
- Acute Treatment of Manic and Mixed Episodes associated with Bipolar I Disorder
- Adjunctive Treatment of Major Depressive Disorder
- Irritability Associated with Autistic Disorder
- Treatment of Tourette's Disorder

Abilify Mycite
Abilify Mycite, a drug-device combination product comprised of aripiprazole tablets embedded with an Ingestible Event Marker (IEM) sensor intended to track drug ingestion, is indicated for the:

- Treatment of adults with schizophrenia
- Treatment of bipolar I disorder
    - Acute treatment of adults with manic and mixed episodes as monotherapy and as adjunct to lithium or valproate
    - Maintenance treatment of adults as monotherapy and as adjunct to lithium or valproate
- Adjunctive treatment of adults with Major Depressive Disorder

Limitations of Use

- The ability of the Abilify Mycite to improve patient compliance or modify aripiprazole dosage has not been established.
- The use of Abilify Mycite to track drug ingestion in "real-time" or during an emergency is not recommended because detection may be delayed or not occur.

Caplyta
Caplyta is indicated for the treatment of:

- Schizophrenia in adults.
- Depressive episodes associated with bipolar I or II disorder (bipolar depression) in adults, as monotherapy and as adjunctive therapy with lithium or valproate.

Fanapt
Fanapt is indicated for the treatment of schizophrenia in adults.

When deciding among the alternative treatments available for this condition, the prescriber should consider the finding that Fanapt is associated with prolongation of the QTc interval. Prolongation of the QTc interval is associated in some other drugs with the ability to cause torsade de pointes-type arrhythmia, a potentially fatal polymorphic ventricular tachycardia which can result in sudden death. In many cases this would lead to the conclusion that other drugs should be tried first. Whether Fanapt will cause torsade de pointes or increase the rate of sudden death is not yet known.

Patients must be titrated to an effective dose of Fanapt. Thus, control of symptoms may be delayed during the first 1 to 2 weeks of treatment compared to some other antipsychotic drugs that do not require a similar titration. Prescribers should be mindful of this delay when selecting an antipsychotic drug for the treatment of schizophrenia.

Geodon
Geodon is indicated for the treatment of schizophrenia, as monotherapy for the acute treatment of bipolar manic or mixed episodes, and as an adjunct to lithium or valproate for the maintenance treatment of bipolar disorder. Geodon intramuscular is indicated for acute agitation in schizophrenic patients. When deciding among the alternative treatments available for the condition needing treatment, the prescriber should consider the finding of ziprasidone's greater capacity to prolong the QT/QTc interval compared to several other antipsychotic drugs. Prolongation of the QTc interval is associated in some other drugs with the ability to cause torsade de pointes-type arrhythmia, a potentially fatal polymorphic ventricular tachycardia, and sudden death. In many cases this would lead to the conclusion that other drugs should be tried first. Whether ziprasidone will cause torsade de pointes or increase the rate of sudden death is not yet known.

Schizophrenia
Geodon is indicated for the treatment of schizophrenia in adults.

Bipolar I Disorder (Acute Mixed or Manic Episodes and Maintenance Treatment as an Adjunct to Lithium or Valproate)
- Geodon is indicated as monotherapy for the acute treatment of adults with manic or mixed episodes associated with bipolar I disorder.
- Geodon is indicated as an adjunct to lithium or valproate for the maintenance treatment of bipolar I disorder in adults.

Acute Treatment of Agitation in Schizophrenia
- Geodon intramuscular is indicated for the treatment of acute agitation in schizophrenic adult patients for whom treatment with ziprasidone is appropriate and who need intramuscular antipsychotic medication for rapid control of agitation.

Since there is no experience regarding the safety of administering ziprasidone intramuscular to schizophrenic patients already taking oral ziprasidone, the practice of co-administration is not recommended.

Invega
Schizophrenia
Invega (paliperidone) Extended-Release Tablets are indicated for the treatment of schizophrenia.

The efficacy of Invega in schizophrenia was established in three 6-week trials in adults and one 6-week trial in adolescents, as well as one maintenance trial in adults.

Schizoaffective Disorder
Invega (paliperidone) Extended-Release Tablets are indicated for the treatment of schizoaffective disorder as monotherapy and as an adjunct to mood stabilizers and/or antidepressant therapy.

The efficacy of Invega in schizoaffective disorder was established in two 6-week trials in adults.

Latuda
Latuda is indicated for:
- Treatment of adult and adolescent patients (13 to 17 years) with schizophrenia.
- Monotherapy treatment of adult and pediatric patients (10 to 17 years) with major depressive episode associated with bipolar I disorder (bipolar depression).
- Adjunctive treatment with lithium or valproate in adult patients with major depressive episode associated with bipolar I disorder (bipolar depression).

Lybalvi
Lybalvi is indicated for the treatment of:
- Schizophrenia in adults
- Bipolar I disorder in adults

- Acute treatment of manic or mixed episodes as monotherapy and as adjunct treatment to lithium or valproate
- Maintenance monotherapy treatment

Rexulti
Rexulti is indicated for:
- Adjunctive treatment of major depressive disorder (MDD) in adults.
- Treatment of schizophrenia in adults and pediatric patients ages 13 years and older
- Treatment of agitation associated with dementia due to Alzheimer's disease

Limitations of Use:
Rexulti is not indicated as an as needed ("prn") treatment for agitation associated with dementia due to Alzheimer's disease.

Risperdal
Schizophrenia
Risperdal (risperidone) is indicated for the treatment of schizophrenia. Efficacy was established in 4 short-term trials in adults, 2 short-term trials in adolescents (ages 13 to 17 years), and one long-term maintenance trial in adults.

Bipolar Mania
Monotherapy
Risperdal is indicated for the treatment of acute manic or mixed episodes associated with Bipolar I Disorder. Efficacy was established in 2 short-term trials in adults and one short-term trial in children. and adolescents (ages 10 to 17 years).

Adjunctive Therapy
Risperdal adjunctive therapy with lithium or valproate is indicated for the treatment of acute manic or mixed episodes associated with Bipolar I Disorder. Efficacy was established in one short-term trial in adults.

Irritability Associated with Autistic Disorder
Risperdal is indicated for the treatment of irritability associated with autistic disorder, including symptoms of aggression towards others, deliberate self-injuriousness, temper tantrums, and quickly changing moods. Efficacy was established in 3 short-term trials in children and adolescents (ages 5 to 17 years)

Saphris
Saphris is indicated for:
- Schizophrenia in adults
- Bipolar I disorder
  - Acute monotherapy of manic or mixed episodes, in adults and pediatric patients 10 to 17 years of age
  - Adjunctive treatment to lithium or valproate in adults
  - Maintenance monotherapy treatment in adults

Secuado
Secuado is indicated for the treatment of adults with schizophrenia.

Seroquel
Schizophrenia
Seroquel is indicated for the treatment of schizophrenia. The efficacy of Seroquel in schizophrenia was established in three 6-week trials in adults and one 6–week trial in adolescents (13–17 years). The effectiveness of Seroquel for the maintenance treatment of schizophrenia has not been systematically evaluated in controlled clinical trials.

Bipolar Disorder
Seroquel is indicated for the acute treatment of manic episodes associated with bipolar I disorder, both as monotherapy and as an adjunct to lithium or divalproex. Efficacy was established in two 12-week monotherapy trials in adults, in one 3-week adjunctive trial in adults, and in one 3-week monotherapy trial in pediatric patients (10-17 years).

Seroquel is indicated as monotherapy for the acute treatment of depressive episodes associated with bipolar disorder. Efficacy was established in two 8-week monotherapy trials in adult patients with bipolar I and bipolar II disorder.

Seroquel is indicated for the maintenance treatment of bipolar I disorder, as an adjunct to lithium or divalproex. Efficacy was established in two maintenance trials in adults. The effectiveness of Seroquel as monotherapy for the maintenance treatment of bipolar disorder has not been systematically evaluated in controlled clinical trials.

Special Considerations in Treating Pediatric Schizophrenia and Bipolar I Disorder
Pediatric schizophrenia and bipolar I disorder are serious mental disorders, however, diagnosis can be challenging. For pediatric schizophrenia, symptom profiles can be variable, and for bipolar I disorder, patients may have variable patterns of periodicity of manic or mixed symptoms. It is recommended that medication therapy for pediatric schizophrenia and bipolar I disorder be initiated only after a thorough diagnostic evaluation has been performed and careful consideration given to the risks associated with medication treatment. Medication treatment for both pediatric schizophrenia and bipolar I disorder is indicated as part of a total treatment program that often includes psychological, educational and social interventions.

Seroquel XR
Schizophrenia
Seroquel XR is indicated for the treatment of schizophrenia. The efficacy of Seroquel XR in schizophrenia was established in one 6- week and one maintenance trial in adults with schizophrenia. Efficacy was supported by three 6-week trials in adults with schizophrenia and one 6-week trial in adolescents with schizophrenia (13-17 years) treated with Seroquel.

Bipolar Disorder
Seroquel XR is indicated for the acute treatment of manic or mixed episodes associated with bipolar I disorder, both as monotherapy and as an adjunct to lithium or divalproex. The efficacy of Seroquel XR in manic or mixed episodes of bipolar I disorder was established in one 3-week trial in adults with manic or mixed episodes associated with bipolar I disorder. Efficacy was supported by two 12-week monotherapy trials and one 3-week adjunctive trial in adults with manic episodes associated with bipolar I disorder as well as one 3-week monotherapy trial in children and adolescents (10-17 years) with manic episodes associated with bipolar I disorder treated with Seroquel.

Seroquel XR is indicated for the acute treatment of depressive episodes associated with bipolar disorder. The efficacy of Seroquel XR was established in one 8-week trial in adults with bipolar I or II disorder and supported by two 8-week trials in adults with bipolar I or II disorder treated with Seroquel.

Seroquel XR is indicated for the maintenance treatment of bipolar I disorder, as an adjunct to lithium or divalproex. Efficacy was extrapolated from two maintenance trials in adults with bipolar I disorder treated with Seroquel. The effectiveness of monotherapy for the maintenance treatment of bipolar I disorder has not been systematically evaluated in controlled clinical trials.

Adjunctive Treatment of Major Depressive Disorder (MDD)
Seroquel XR is indicated for use as adjunctive therapy to antidepressants for the treatment of MDD. The efficacy of Seroquel XR as adjunctive therapy to antidepressants in MDD was established in two 6-week trials in adults with MDD who had an inadequate response to antidepressant treatment.

Special Considerations in Treating Pediatric Schizophrenia and Bipolar I Disorder
Pediatric schizophrenia and bipolar I disorder are serious mental disorders, however, diagnosis can be challenging. For pediatric schizophrenia, symptom profiles can be variable, and for bipolar I disorder, patients may have variable patterns of periodicity of manic or mixed symptoms. It is recommended that medication therapy for pediatric schizophrenia and bipolar I disorder be initiated only after a thorough diagnostic evaluation has been performed and careful consideration given to the risks associated with medication treatment. Medication treatment for both pediatric schizophrenia and bipolar I disorder is indicated as part of a total treatment program that often includes psychological, educational and social interventions.

Vraylar
Vraylar is indicated for:
- Treatment of schizophrenia in adults
- Acute treatment of manic or mixed episodes associated with bipolar I disorder in adults

- Treatment of depressive episodes associated with bipolar I disorder (bipolar depression) in adults
- Adjunctive therapy to antidepressants for the treatment of major depressive disorder (MDD) in adults

Zyprexa

Schizophrenia

Oral Zyprexa is indicated for the treatment of schizophrenia. Efficacy was established in three clinical trials in adult patients with schizophrenia: two 6-week trials and one maintenance trial. In adolescent patients with schizophrenia (ages 13-17), efficacy was established in one 6-week trial.

When deciding among the alternative treatments available for adolescents, clinicians should consider the increased potential (in adolescents as compared with adults) for weight gain and dyslipidemia. Clinicians should consider the potential long-term risks when prescribing to adolescents, and in many cases this may lead them to consider prescribing other drugs first in adolescents.

Bipolar I Disorder (Manic or Mixed Episodes)

Monotherapy

Oral Zyprexa is indicated for the acute treatment of manic or mixed episodes associated with bipolar I disorder and maintenance treatment of bipolar I disorder. Efficacy was established in three clinical trials in adult patients with manic or mixed episodes of bipolar I disorder: two 3- to 4-week trials and one monotherapy maintenance trial. In adolescent patients with manic or mixed episodes associated with bipolar I disorder (ages 13-17), efficacy was established in one 3-week trial.

When deciding among the alternative treatments available for adolescents, clinicians should consider the increased potential (in adolescents as compared with adults) for weight gain and dyslipidemia. Clinicians should consider the potential long-term risks when prescribing to adolescents, and in many cases this may lead them to consider prescribing other drugs first in adolescents.

Adjunctive Therapy to Lithium or Valproate

Oral Zyprexa is indicated for the treatment of manic or mixed episodes associated with bipolar I disorder as an adjunct to lithium or valproate. Efficacy was established in two 6-week clinical trials in adults. The effectiveness of adjunctive therapy for longer-term use has not been systematically evaluated in controlled trials.

Special Considerations in Treating Pediatric Schizophrenia and Bipolar I Disorder

Pediatric schizophrenia and bipolar I disorder are serious mental disorders; however, diagnosis can be challenging. For pediatric schizophrenia, symptom profiles can be variable, and for bipolar I disorder, pediatric patients may have variable patterns of periodicity of manic or mixed symptoms. It is recommended that medication therapy for pediatric schizophrenia and bipolar I disorder be initiated only after a thorough diagnostic evaluation has been performed and careful consideration given to the risks associated with medication treatment. Medication treatment for both pediatric schizophrenia and bipolar I disorder should be part of a total treatment program that often includes psychological, educational and social interventions.

Zyprexa and Fluoxetine in Combination: Depressive Episodes Associated with Bipolar I Disorder

Oral Zyprexa and fluoxetine in combination is indicated for the treatment of depressive episodes associated with bipolar I disorder, based on clinical studies. When using Zyprexa and fluoxetine in combination, refer to the Clinical Studies section of the package insert for Symbyax.

Zyprexa monotherapy is not indicated for the treatment of depressive episodes associated with bipolar I disorder.

Zyprexa and Fluoxetine in Combination: Treatment Resistant Depression

Oral Zyprexa and fluoxetine in combination is indicated for the treatment of treatment resistant depression (major depressive disorder in patients who do not respond to 2 separate trials of different antidepressants of adequate dose and duration in the current episode), based on clinical studies in adult patients. When using ZYPREXA and fluoxetine in combination, refer to the Clinical Studies section of the package insert for Symbyax.

Zyprexa monotherapy is not indicated for the treatment of treatment resistant depression.

INITIAL STEP THERAPY

If the patient has filled a prescription for at least a 30-day supply of generic aripiprazole, asenapine, lurasidone, olanzapine, paliperidone, quetiapine, quetiapine extended release, risperidone, or ziprasidone within the past 180 days under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit. If the patient does not meet the initial step therapy criteria, then the claim will reject with a message indicating that a prior authorization (PA) is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The patient is currently taking the requested drug with evidence of improvement

OR

- The patient has experienced an inadequate treatment response, after a trial of at least 30 days, to ONE of the following generic products: A) aripiprazole, B) asenapine, C) lurasidone, D) olanzapine, E) paliperidone, F) quetiapine, G) quetiapine extended-release, H) risperidone, I) ziprasidone

OR

- The patient has an intolerance or a contraindication that would prohibit a 30-day trial of ONE of the following generic products: A) aripiprazole, B) asenapine, C) lurasidone, D) olanzapine, E) paliperidone, F) quetiapine, G) quetiapine extended-release, H) risperidone, I) ziprasidone

OR

- The patient has a clinical condition for which there is no generic alternative or the generic alternatives are not recommended based on published guidelines or clinical literature

REFERENCES

1. Abilify [package insert]. Rockville, MD: Otsuka America Pharmaceutical, Inc.; November 2022.
2. Abilify Mycite [package insert]. Rockville, MD: Otsuka America Pharmaceutical, Inc.; November 2022.
3. Caplyta [package insert]. New York, NY: Intra-Cellular Therapies, Inc.; April 2022.
4. Fanapt [package insert]. Washington, D.C.: Vanda Pharmaceuticals Inc.; February 2017.
5. Geodon [package insert]. New York, NY: Roerig; February 2022.
6. Invega [package insert]. Titusville, NJ: Janssen Pharmaceuticals, Inc.; March 2022.
7. Latuda [package insert]. Marlborough, MA: Sunovion Pharmaceuticals Inc.; May 2022.
8. Lybalvi [package insert]. Waltham, MA: Alkermes, Inc.; May 2021.
9. Rexulti [package insert]. Rockville, MD: Otsuka America Pharmaceutical, Inc.; May 2023.
10. Risperdal [package insert]. Titusville, NJ: Janssen Pharmaceutical, Inc.; August 2022.
11. Saphris [package insert]. Madison, NJ: Allergan USA, Inc.; October 2021.
12. Secuado [package insert]. Miami, Florida: Noven Therapeutics, LLC; November 2022.
13. Seroquel [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; January 2022.
14. Seroquel XR [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; January 2022.
15. Vraylar [package insert]. Madison, NJ: Allergan USA, Inc.; December 2022.
16. Zyprexa [package insert]. Indianapolis, IN: Lilly USA, LLC.; February 2021.
17. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: UpToDate, Inc.; 2023; Accessed January 23, 2023.
18. Lexicomp Online, Lexi-Drugs Online. Hudson, OH: UpToDate, Inc.; 2023; Accessed January 23, 2023.
19. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed January 23, 2023.
20. Keepers GA, Fochtmann LJ, Anzia JM, et al. The American Psychiatric Association Practice Guideline for the Treatment of Patients with Schizophrenia. Third Edition. Washington, DC: American Psychiatric Association; 2021. Available at: https://psychiatryonline.org/doi/pdf/10.1176/appi.books.9780890424841. Accessed January 23, 2023.
21. Gelenberg AJ, Freeman MP, Markowitz JC, et al. American Psychiatric Association (APA) Practice Guideline for the Treatment of Patients with Major Depressive Disorder, Third Edition. October 2010. Available at: https://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/mdd.pdf. Accessed January 23, 2023.

22. Hirschfeld RM, Bowden CL, Gitlin MJ, et al. American Psychiatric Association (APA) Practice Guideline for the Treatment of Patients with Bipolar Disorder. Second Edition. Washington DC: American Psychiatric Association; 2002. Available at: https://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/bipolar.pdf. Accessed January 23, 2023.

Reference number(s)
1808-A

SPECIALTY GUIDELINE MANAGEMENT

AUBAGIO (teriflunomide)
teriflunomide

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Indicated for the treatment of patients with relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.

All other indications are considered experimental/investigational and not medically necessary.

II. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with a neurologist.

III. CRITERIA FOR INITIAL APPROVAL

A. Relapsing forms of multiple sclerosis
Authorization of 12 months may be granted to members who have been diagnosed with a relapsing form of multiple sclerosis (including relapsing-remitting and secondary progressive disease for those who continue to experience relapse).

B. Clinically isolated syndrome
Authorization of 12 months may be granted to members for the treatment of clinically isolated syndrome of multiple sclerosis.

IV. CONTINUATION OF THERAPY

For all indications: Authorization of 12 months may be granted to members who are experiencing disease stability or improvement while receiving the requested medication.

V. OTHER

A. Members will not use the requested medication concomitantly with other disease modifying multiple sclerosis agents (Note: Ampyra and Nuedexta are not disease modifying).

B. Authorization may be granted for pediatric members less than 18 years of age when benefits outweigh risks.

VI. REFERENCES

1. Aubagio [package insert]. Cambridge, MA: Genzyme Corporation; December 2022.
2. Teriflunomide [package insert]. East Windsor, NJ: Aurobindo Pharma USA, Inc.; January 2023.

Reference number(s)
1746-A

SPECIALTY GUIDELINE MANAGEMENT

AUSTEDO (deutetrabenazine)
AUSTEDO XR (deutetrabenazine extended release)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
A. Treatment of chorea associated with Huntington's disease in adults
B. Treatment of tardive dyskinesia in adults

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary for both initial approval and continuation of therapy prior authorization reviews (where applicable): Documentation of score of items 1 to 7 of the Abnormal Involuntary Movement Scale (AIMS).

III. CRITERIA FOR INITIAL APPROVAL

A. Tardive dyskinesia
Authorization of 6 months may be granted for treatment of tardive dyskinesia when the baseline AIMS score for items 1 to 7 is obtained.

B. Chorea associated with Huntington's disease
Authorization of 6 months may be granted for treatment of chorea associated with Huntington's disease when both of the following criteria are met:
1. Member demonstrates characteristic motor examination features
2. Member meets one of the following conditions:
   i. Laboratory results indicate an expanded *HTT* CAG repeat sequence of at least 36
   ii. Member has a positive family history for Huntington's disease

IV. CONTINUATION OF THERAPY

A. Tardive dyskinesia
Authorization of 12 months may be granted for treatment of tardive dyskinesia when the member's tardive dyskinesia symptoms have improved as indicated by a decreased AIMS score (items 1 to 7) from baseline.

B. Chorea associated with Huntington's disease
Authorization of 12 months may be granted for treatment of chorea associated with Huntington's disease when the disease has improved or stabilized.

V. REFERENCES

1. Austedo [package insert]. Parsippany, NJ: Teva Neuroscience, Inc. February 2023.
2. Frank S, Testa CM, Stamler D, et al. Effect of deutetrabenazine on chorea among patients with Huntington disease: A randomized clinical trial. Huntington Study Group. *JAMA.* 2016;316(1):40-50.
3. Fernandez HH, Factor SA, Hauser RA, et al. Randomized controlled trial of deutetrabenazine for tardive dyskinesia: The ARM-TD study. *Neurology.* 2017;88:2003-10.
4. Anderson KE, Stamler D, Davis MD, et al. Deutetrabenazine for treatment of involuntary movements in patients with tardive dyskinesia (AIM-TD): a double-blind, randomized, placebo-controlled, phase 3 trial. *Lancet Psychiatry.* 2017;4: 595-604.
5. American Psychiatric Association. (2021). *Practice Guideline for the Treatment of Patients With Schizophrenia, third edition.* https://doi.org/10.1176/appi.books.9780890424841

STEP THERAPY CRITERIA

BRAND NAME
(generic)

AUVELITY
(dextromethorphan/bupropion hydrochloride)

Status: CVS Caremark® Criteria
Type: Initial Step Therapy with Quantity Limit;
Post Step Therapy Prior Authorization with Quantity Limit

POLICY

FDA-APPROVED INDICATIONS
Auvelity is indicated for the treatment of major depressive disorder (MDD) in adults.

SCREEN OUT LOGIC with QUANTITY LIMIT*
Include Rx and OTC products unless otherwise stated.

If the patient has filled a prescription for at least a 30 day supply of a serotonin and norepinephrine reuptake inhibitor (SNRI), a selective serotonin reuptake inhibitor (SSRI), mirtazapine OR bupropion (except generic for Zyban) within the past 180 days under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit.** If the patient does not meet the screen out logic, then the claim will reject with a message indicating that a prior authorization (PA) is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

**If the patient meets the screen out logic, then the initial limit criteria will apply. If the patient is requesting more than the initial quantity limit the claim will reject with a message indicating that a PA is required.

INITIAL LIMIT QUANTITY

Drug	1 Month Limit*	3 Month Limit*
Auvelity	60 tablets / 25 days	180 tablets / 75 days

**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*

COVERAGE CRITERIA
The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for the treatment of major depressive disorder (MDD) in an adult patient

Quantity Limits apply.
60 tablets per 25 days* or 180 tablets per 75 days*
**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*

Duration of Approval (DOA):

- 5562-E: DOA: 12 months

REFERENCES

1. Auvelity [package insert]. New York, NY: Axsome Therapeutics, Inc.; December 2022.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Waltham, MA: UpToDate, Inc.; 2023. https://online.lexi.com. Accessed May 24, 2023.
3. Micromedex (electronic version). Merative, Ann Arbor, Michigan, USA. Available at: https://www.micromedexsolutions.com/ (cited: 05/24/2023).
4. American Psychiatric Association (2010). Practice Guideline for the Treatment of Patients with Major Depressive Disorder. Available from: https://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/mdd.pdf. Accessed May 24, 2023.

Reference number(s)
3918-A, 6042-A

SPECIALTY GUIDELINE MANAGEMENT

AVEED (testosterone undecanoate injection)

POLICY

I. INDICATION

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
Aveed is indicated for testosterone replacement therapy in adult males for conditions associated with a deficiency or absence of endogenous testosterone.

1. Primary hypogonadism (congenital or acquired): testicular failure due to cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, orchiectomy, Klinefelter's syndrome, chemotherapy, or toxic damage from alcohol or heavy metals. These men usually have low serum testosterone concentrations and gonadotropins (follicle-stimulating hormone [FSH], luteinizing hormone [LH]) above the normal range.
2. Hypogonadotropic hypogonadism (congenital or acquired): gonadotropin or luteinizing hormone-releasing hormone (LHRH) deficiency, or pituitary-hypothalamic injury from tumors, trauma, or radiation. These men have low testosterone serum concentrations but have gonadotropins in the normal or low range.

Aveed should only be used in patients who require testosterone replacement therapy and in whom the benefits of the product outweigh the serious risks of pulmonary oil microembolism and anaphylaxis.

Limitations of use:

- Safety and efficacy of Aveed in men with "age-related hypogonadism" (also referred to as "late-onset hypogonadism") have not been established.
- Safety and efficacy of Aveed in males less than 18 years old have not been established.

B. Compendial Uses
Gender dysphoria (also known as transgender and gender diverse (TGD) persons)

All other indications are considered experimental/investigational and not medically necessary.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the prior authorization review: For primary hypogonadism or hypogonadotropic hypogonadism, pretreatment morning serum total testosterone concentrations

III. EXCLUSIONS

Coverage will not be provided for members with any of the following exclusions: Use for age-related hypogonadism or late-onset hypogonadism

IV. PRESCRIBER SPECIALITIES

For gender dysphoria, the medication must be prescribed by or in consultation with a provider specialized in the care of transgender youth (e.g., pediatric endocrinologist, family or internal medicine physician, obstetrician-gynecologist) that has collaborated care with a mental health provider for members less than 18 years of age.

V. CRITERIA FOR INITIAL APPROVAL

A. Primary hypogonadism or hypogonadotropic hypogonadism

Authorization of 12 months may be granted for treatment of primary hypogonadism or hypogonadotropic hypogonadism when all of the following criteria are met:

1. Member is a biological male or a person that self identifies as male.
2. Member is at least 18 years of age.
3. Member has at least two confirmed low morning serum total testosterone concentrations based on the reference laboratory range or current practice guidelines.

B. Gender dysphoria

1. Authorization of 12 months may be granted for gender dysphoria when all of the following criteria are met:
   i. The member has a diagnosis of gender dysphoria.
   ii. The member is able to make an informed decision to engage in hormone therapy.
   iii. The member's comorbid conditions are reasonably controlled.
   iv. The member has been educated on any contraindications and side effects to therapy.
   v. The member has been informed of fertility preservation options.
2. Authorization of 12 months may be granted for gender dysphoria in an adolescent member when all of the following criteria are met:
   i. The member has a diagnosis of gender dysphoria.
   ii. The member is able to make an informed decision to engage in hormone therapy.
   iii. The member has reached Tanner stage 2 of puberty or greater.
   iv. The member's comorbid conditions are reasonably controlled.
   v. The member has been educated on any contraindications and side effects to therapy.
   vi. The member has been informed of fertility preservation options.

VI. CONTINUATION OF THERAPY

A. Primary hypogonadism or hypogonadotropic hypogonadism

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for primary hypogonadism or hypogonadotropic hypogonadism when all of the following criteria are met:

1. Member is a biological male or a person that self identifies as male.
2. Member is at least 18 years of age.
3. Before the start of therapy, the member had at least two confirmed low morning serum total testosterone concentrations based on the reference laboratory range or current practice guidelines.

B. Gender dysphoria

1. Authorization of 12 months may be granted for continued treatment for gender dysphoria in members requesting reauthorization when all of the following criteria are met:
   i. The member has a diagnosis of gender dysphoria.
   ii. The member is able to make an informed decision to engage in hormone therapy.
   iii. The member's comorbid conditions are reasonably controlled.
   iv. The member has been educated on any contraindications and side effects to therapy.
   v. Before the start of therapy, the member has been informed of fertility preservation options.
2. Authorization of 12 months may be granted for continued treatment for gender dysphoria in adolescent members requesting reauthorization when all of the following criteria are met:
   i. The member has a diagnosis of gender dysphoria.
   ii. The member is able to make an informed decision to engage in hormone therapy.
   iii. The member has previously reached Tanner stage 2 of puberty or greater.
   iv. The member's comorbid conditions are reasonably controlled.
   v. The member has been educated on any contraindications and side effects to therapy.
   vi. Before the start of therapy, the member has been informed of fertility preservation options.

VII. OTHER

Per state regulatory guidelines around gender dysphoria, age restrictions may apply.

VIII. REFERENCES

1. Aveed [package insert]. Malvern, PA: Endo Pharmaceuticals Solutions Inc.; August 2021.
2. Bhasin S, Brito JP, Cunninghan GR, et al. Testosterone Therapy in Men with Hypogonadism: An Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab*. 2018;103(5):1715-1744.
3. Hembree WC, Cohen-Kettenis PT, Gooren L, et al. Endocrine Treatment of Gender-Dysphoric/Gender-Incongruent Persons: An Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab.* 2017:102(11):3869–3903.
4. Gender Identity Research and Education Society. Guidance for GPs and other clinicians on the treatment of gender variant people. UK Department of Health. Published March 10, 2008.
5. Standards of care for the health of transsexual, transgender, and gender-nonconforming people, 8th version. ©2022 World Professional Association for Transgender Health. Available at http://www.wpath.org.
6. IBM Micromedex® DRUGDEX® (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com/ (cited: February 1, 2023).
7. Health Care for Transgender and Gender Diverse Individuals. ©2021 The American College of Obstetricians and Gynecologists. Available at: https://www.acog.org/clinical/clinical-guidance/committee-opinion/articles/2021/03/health-care-for-transgender-and-gender-diverse-individuals.

Reference number(s)
1837-A

SPECIALTY GUIDELINE MANAGEMENT

AVONEX (interferon beta-1a)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Avonex is indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.

All other indications are considered experimental/investigational and not medically necessary.

II. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with a neurologist.

III. CRITERIA FOR INITIAL APPROVAL

A. Relapsing forms of multiple sclerosis
Authorization of 12 months may be granted to members who have been diagnosed with a relapsing form of multiple sclerosis (including relapsing-remitting and secondary progressive disease for those who continue to experience relapse).

B. Clinically isolated syndrome
Authorization of 12 months may be granted to members for the treatment of clinically isolated syndrome of multiple sclerosis.

IV. CONTINUATION OF THERAPY

For all indications: Authorization of 12 months may be granted for members who are experiencing disease stability or improvement while receiving Avonex.

V. OTHER

Members will not use Avonex concomitantly with other disease modifying multiple sclerosis agents (Note: Ampyra and Nuedexta are not disease modifying).

VI. REFERENCES

1. Avonex [package insert]. Cambridge, MA: Biogen Inc.; November 2021.

Reference number
3491-A

SPECIALTY GUIDELINE MANAGEMENT

AYVAKIT (avapritinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. Gastrointestinal Stromal Tumor (GIST)
      Ayvakit is indicated for the treatment of adults with unresectable or metastatic GIST harboring a platelet-derived growth factor receptor alpha (PDGFRA) exon 18 mutation, including PDGFRA D842V mutations.
   2. Advanced Systemic Mastocytosis (AdvSM)
      Ayvakit is indicated for the treatment of adult patients with advanced systemic mastocytosis (AdvSM). AdvSM includes patients with aggressive systemic mastocytosis (ASM), systemic mastocytosis with an associated hematological neoplasm (SM-AHN), and mast cell leukemia (MCL).
   3. Indolent Systemic Mastocytosis (ISM)
      Ayvakit is indicated for the treatment of adult patients with indolent systemic mastocytosis (ISM).

      Limitations of Use: Ayvakit is not recommended for the treatment of patients with ISM or AdvSM with platelet counts of less than 50 X 10^9/L.

B. Compendial Uses
   1. Myeloid/lymphoid neoplasms with eosinophilia and FIP1L1-PDGFRA rearrangement
   2. GIST

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
A. For GIST: PDGFRA exon 18 mutation testing (e.g., polymerase chain reaction [PCR]-based assay, next-generation sequencing [NGS]-based assay) results (where applicable).
B. For myeloid and/or lymphoid neoplasms with eosinophilia: Testing or analysis confirming FIP1L1-PDGFRA rearrangement and PDGFRA D842V mutation

III. CRITERIA FOR INITIAL APPROVAL

A. Gastrointestinal Stromal Tumor (GIST)
Authorization of 12 months may be granted for treatment of gastrointestinal stromal tumor (GIST) when any of the following criteria are met:
   1. The member meets all of the following criteria:

a. The disease is unresectable, recurrent/progressive or metastatic
b. The disease harbors a platelet-derived growth factor receptor alpha (PDGFRA) exon 18 mutation that is insensitive to imatinib, including the PDGFRA D842V mutation
c. The requested drug will be used as a single agent for first-line therapy.

2. The member meets all of the following criteria:
   a. The disease is unresectable, recurrent/progressive, or metastatic
   b. The member has failed at least four FDA-approved therapies (e.g., imatinib, sunitinib, regorafenib, ripretinib)
   c. The requested drug will be used as a single agent
3. The requested drug will be used for palliation of symptoms if previously tolerated and effective.
4. The member meets all of the following criteria:
   a. The requested drug will be used for neoadjuvant therapy to decrease surgical morbidity
   b. The disease harbors a PDGFRA exon 18 mutation that is insensitive to imatinib, including the PDGFRA D842V mutation
   c. The requested drug will be used as a single agent

B. Myeloid/Lymphoid Neoplasms with Eosinophilia

Authorization of 12 months may be granted for treatment of myeloid and/or lymphoid neoplasms with eosinophilia when all of the following criteria are met:

1. The disease harbors a PDGFRA D842V mutation which is resistant to imatinib.
2. The disease is FIP1L1-PDGFRA rearrangement-positive.

C. Advanced Systemic Mastocytosis (AdvSM), including Aggressive Systemic Mastocytosis (ASM), Systemic Mastocytosis with an Associated Hematological Neoplasm (SM-AHN) and Mast Cell Leukemia (MCL)

Authorization of 12 months may be granted for treatment of AdvSM, ASM, SM-AHN and MCL as a single agent when the member's platelet count is greater than or equal to 50 X 10^9/L.

D. Indolent Systemic Mastocytosis (ISM)

Authorization of 12 months may be granted for treatment of indolent systemic mastocytosis (ISM) when the member's platelet count is greater than or equal to 50 X 10^9/L.

IV. CONTINUATION OF THERAPY

A. GIST

Authorization of 12 months may be granted for continued treatment of GIST when the member is receiving clinical benefit and there is no evidence of generalized (widespread, systemic) disease progression or unacceptable toxicity while on the current regimen.

B. Myeloid/Lymphoid Neoplasms with Eosinophilia or AdvSM including ASM, SM-AHN, MCL

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

C. Indolent Systemic Mastocytosis (ISM)

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization when there is no evidence of unacceptable toxicity.

V. REFERENCES

1. Ayvakit [package insert]. Cambridge, MA: Blueprint Medicines Corporation; May 2023.
2. The NCCN Drugs & Biologics Compendium © 2022 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed August 4, 2022.

Reference number
2280-A

SPECIALTY GUIDELINE MANAGEMENT

VIDAZA (azacitidine)
azacitidine

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
1. Myelodysplastic syndromes (MDS): azacitidine/Vidaza is indicated for treatment of adult patients with the following French-American-British (FAB) myelodysplastic syndrome subtypes: refractory anemia (RA) or refractory anemia with ringed sideroblasts (RARS) (if accompanied by neutropenia or thrombocytopenia or requiring transfusions), refractory anemia with excess blasts (RAEB), refractory anemia with excess blasts in transformation (RAEB-T), and chronic myelomonocytic leukemia (CMMoL).
2. Juvenile myelomonocytic leukemia (JMML): azacitidine/Vidaza is indicated for treatment of pediatric patients aged 1 month and older with newly diagnosed juvenile myelomonocytic leukemia (JMML).

B. Compendial Uses
1. Acute myeloid leukemia (AML)
2. Accelerated phase or blast phase myelofibrosis
3. Blastic plasmacytoid dendritic cell neoplasm (BPDCN)
4. Myelodysplastic syndrome (MDS)/Myeloproliferative Neoplasms (MPN) Overlap Neoplasms

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Myelodysplastic syndromes (MDS)
Authorization of 12 months may be granted for the treatment of MDS.

B. Acute myeloid leukemia (AML)
Authorization of 12 months may be granted for the treatment of AML.

C. Accelerated phase or blast phase myelofibrosis
Authorization of 12 months may be granted for the treatment of accelerated phase or blast phase myelofibrosis.

D. Blastic plasmacytoid dendritic cell neoplasm (BPDCN)
Authorization of 12 months may be granted for the treatment of BPDCN when used in combination with venetoclax in either of the following settings:
1. For the treatment of relapsed or refractory disease.
2. For the treatment of systemic disease with palliative intent.

E. Myelodysplastic syndrome (MDS)/Myeloproliferative Neoplasms (MPN) Overlap Neoplasms
Authorization of 12 months may be granted for the treatment of MDS/MPN overlap neoplasms (i.e., chronic myelomonocytic leukemia (CMML), juvenile myelomonocytic leukemia (JMML), BCR-ABL negative atypical chronic myeloid leukemia (aCML), unclassifiable MDS/MPN, or MDS/MPN with ring sideroblasts and thrombocytosis).

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.
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IV. REFERENCES

1. Vidaza [package insert]. Summit, NJ: Celgene Corporation; May 2022.
2. Azacitidine injection [package insert]. Parsippany, NJ: Actavis Pharma Inc.; July 2020.
3. National Comprehensive Cancer Network. The NCCN Drugs & Biologics Compendium. http://www.nccn.org. Accessed January 7, 2022.

Reference number(s)
3881-A

SPECIALTY GUIDELINE MANAGEMENT

BAFIERTAM (monomethyl fumerate)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Bafiertam is indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Relapsing forms of multiple sclerosis (MS)
Authorization of 12 months may be granted for to members who have been diagnosed with a relapsing form of multiple sclerosis (including relapsing-remitting and secondary progressive disease for those who continue to experience relapse).

B. Clinically isolated syndrome
Authorization of 12 months may be granted to members for the treatment of clinically isolated syndrome.

III. CONTINUATION OF THERAPY

For all indications: Authorization of 12 months may be granted to members who are experiencing disease stability or improvement while receiving Bafiertam.

IV. OTHER CRITERIA

Members will not use Bafiertam concomitantly with other disease modifying multiple sclerosis agents (Note: Ampyra and Nuedexta are not disease modifying).

V. REFERENCES

1. Bafiertam [package insert]. High Point, NC: Banner Life Sciences LLC; May 2021.

CVS caremark®

Reference number(s)
2965-A

SPECIALTY GUIDELINE MANAGEMENT

BALVERSA (erdafitinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication
Balversa is indicated for the treatment of adult patients with locally advanced or metastatic urothelial carcinoma (mUC) that has:
1. susceptible FGFR3 or FGFR2 genetic alterations, and
2. progressed during or following at least one line of prior platinum-containing chemotherapy, including within 12 months of neoadjuvant or adjuvant platinum-containing chemotherapy.

B. Compendial Use
Urothelial Carcinoma
1. Bladder cancer
2. Primary carcinoma of the urethra
3. Upper genitourinary (GU) tract tumors
4. Urothelial carcinoma of the prostate

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: Fibroblast growth factor receptor 3 (FGFR3) or Fibroblast growth factor receptor 2 (FGFR2) mutation status

III. CRITERIA FOR INITIAL APPROVAL

A. Urothelial carcinoma – Bladder cancer
Authorization of 12 months may be granted for treatment of bladder cancer with FGFR3 or FGFR2 genetic alterations as a single agent when used as subsequent therapy for any of the following:
1. Stage II disease if tumor is present following reassessment of tumor status 2-3 months after primary treatment with concurrent chemoradiotherapy, radiotherapy alone or transurethral resection of bladder tumor (TURBT)
2. Locally advanced or metastatic disease
3. Metastatic or local recurrence post-cystectomy
4. Muscle invasive local recurrence or persistent disease in a preserved bladder

B. Urothelial Carcinoma – Primary Carcinoma of the Urethra

Authorization of 12 months may be granted for the treatment of primary carcinoma of the urethra with FGFR3 or FGFR2 genetic alterations as a single agent when used as subsequent therapy for locally advanced, recurrent or metastatic disease.

C. Urothelial Carcinoma – Upper Genitourinary (GU) Tract Tumors
Authorization of 12 months may be granted for the treatment of upper genitourinary (GU) tract tumors with FGFR3 or FGFR2 genetic alterations as a single agent when used as subsequent therapy for locally advanced or metastatic disease.

D. Urothelial Carcinoma – Urothelial Carcinoma of the Prostate
Authorization of 12 months may be granted for the treatment of urothelial carcinoma of the prostate with FGFR3 or FGFR2 genetic alterations as a single agent when used as subsequent therapy for locally advanced or metastatic disease.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

V. REFERENCES

1. Balversa [package insert]. Horsham, PA: Janssen Products, LP; April 2022.
2. The NCCN Drugs & Biologics Compendium® © 2022 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed July 6, 2022.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME*
(generic)

BANZEL
(rufinamide)

Status: CVS Caremark Criteria ***Ref# 863-A***
Type: Initial Prior Authorization ***Ref# 496-A***

** Drugs that are listed in the target drug box include both brand and generic and all dosages forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Banzel is indicated for adjunctive treatment of seizures associated with Lennox-Gastaut Syndrome in pediatric patients 1 year of age and older and in adults.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for adjunctive treatment of seizures associated with Lennox-Gastaut Syndrome in a patient one year of age or older

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Banzel is indicated for adjunctive treatment of seizures associated with Lennox-Gastaut Syndrome in pediatric patients 1 year of age and older and in adults.[1-3]

REFERENCES

1. Banzel [package insert]. Woodcliff Lake, NJ: Eisai Inc.; December 2021.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2021; Accessed March 17, 2022.
3. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed March 17, 2022.

Written by:	UM Development (SE)
Date Written:	12/2009
Revised:	(KD) 04/2010 (CAS Adapted); (CY) 03/2011 (Added Banzel Susp/Banzel MDC-1 06-2010(2)); (JK) 06/2011, (TM) 06/2012. (PL) 10/2012 (MDC-2); (MS) 05/2013, 10/2013; (GS/CF) 05/2014; (CF) 05/2015; (KM) 05/2016 (no clinical changes), (SE) 06/2016 (created separate Med D); (SF) 05/2017; (KC) 05/2018 (combined 863-A and 4966-A), 05/2019 (removed MDC from title, no clinical changes), 05/2020 (no clinical changes); (CJH) 05/2021 (no clinical changes), (DFW) 05/2022 (no clinical changes)
Reviewed:	Medical Affairs (WLF) 12/2009; (KP) 06/2011, 06/2012; (DC) 05/2013; (KP) 10/2013; (LMS) 05/2014; (DNC) 05/2015; (ME) 05/2017; (CHART) 05/28/2020, 05/27/2021, 05/26/2022 External Review: 02/2010, 10/2010, 10/2011, 10/2012, 10/2013, 10/2014, 10/2015, 10/2016, 10/2017, 10/2018, 10/2019, 10/2020, 08/2021, 08/2022

CVS caremark®

CRITERIA FOR APPROVAL

1	Is the requested drug being prescribed for adjunctive treatment of seizures associated with Lennox-Gastaut Syndrome in a patient one year of age or older?	Yes	No

Mapping Instructions (863-A)			
	Yes	**No**	**DENIAL REASONS – DO NOT USE FOR MEDICARE PART D**
1.	Approve, 36 months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you meet all of these conditions: - You are 1 year of age or older - You have seizures associated with Lennox-Gastaut Syndrome - You are using it along with another seizure drug Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]

Mapping Instructions (496-A)			
	Yes	**No**	**DENIAL REASONS – DO NOT USE FOR MEDICARE PART D**
1.	Approve, 12 months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you meet all of these conditions: - You are 1 year of age or older - You have seizures associated with Lennox-Gastaut Syndrome - You are using it along with another seizure drug Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]

Reference number
1764-A

SPECIALTY GUIDELINE MANAGEMENT

BENLYSTA (belimumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Benlysta is indicated for the treatment of:
A. Patients aged 5 years and older with active, autoantibody-positive, systemic lupus erythematosus (SLE) who are receiving standard therapy.
B. Adult patients with active lupus nephritis who are receiving standard therapy.

Limitations of Use
The efficacy of Benlysta has not been evaluated in patients with severe active central nervous system lupus. Benlysta has not been studied in combination with other biologics. Use of Benlysta is not recommended in these situations.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
A. Initial requests: Medical records (e.g., chart notes, lab reports) documenting the presence of autoantibodies relevant to SLE (e.g., ANA, anti-ds DNA, anti-Sm, antiphospholipid antibodies, complement proteins), or kidney biopsy supporting the diagnosis (where applicable).
B. Continuation requests: Medical records (e.g., chart notes, lab reports) documenting disease stability or improvement.

III. EXCLUSIONS

Coverage will not be provided for members with any of the following exclusions:
A. Severe active central nervous system (CNS) lupus (including seizures that are attributed to CNS lupus, psychosis, organic brain syndrome, cerebrovascular accident, cerebritis, or CNS vasculitis requiring therapeutic intervention within 60 days before initiation of belimumab) in a member initiating therapy with Benlysta.
B. Member is using Benlysta in combination with other biologics.

IV. CRITERIA FOR INITIAL APPROVAL

A. Systemic lupus erythematosus (SLE)

Authorization of 12 months may be granted for treatment of active SLE when all of the following criteria are met:

1. Prior to initiating therapy, the member is positive for autoantibodies relevant to SLE (e.g., ANA, anti-ds DNA, anti-Sm, antiphospholipid antibodies, complement proteins)
2. The member is receiving a stable standard treatment for SLE with any of the following (alone or in combination):
   i. Glucocorticoids (e.g., prednisone, methylprednisolone, dexamethasone)
   ii. Antimalarials (e.g., hydroxychloroquine)
   iii. Immunosuppressants (e.g., azathioprine, methotrexate, mycophenolate, cyclosporine, cyclophosphamide)

B. Active lupus nephritis

Authorization of 12 months may be granted for the treatment of active lupus nephritis when all of the following criteria are met:

1. Prior to initiating therapy, the member is positive for autoantibodies relevant to SLE (e.g., ANA, anti-ds DNA, anti-Sm, antiphospholipid antibodies, complement proteins) or lupus nephritis was confirmed on kidney biopsy.
2. Member has clinically active lupus renal disease and is receiving a stable standard induction and maintenance treatment for lupus nephritis (e.g., cyclophosphamide, mycophenolate mofetil, azathioprine, glucocorticoids).

V. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section IV who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition.

VI. REFERENCES

1. Benlysta [package insert]. Philadelphia, PA: GlaxoSmithKline LLC; March 2021.
2. Fanouriakis A, Kostopoulou M, Alunno A, et al. 2019 Update of the EULAR Recommendations for the Management of Systemic Lupus Erythematosus. *Ann Rheum Dis*. 2019;78:736-745.
3. Rovin BH, Parikh SV, Hebert LA, et al. Lupus nephritis: induction therapy in severe lupus nephritis – should MMF be considered the drug of choice? *Clin J Am Soc Nephrol.* 2013;8(1):147-153.
4. Hahn BH, McMahon MA, Wilkinson A, et al. American College of Rheumatology guidelines for screening, treatment, and management of lupus nephritis. *Arthritis Care & Research*. 2012;64(6):797-808.
5. Furie R, Rovin BH, Houssiau F, et al. Two-Year, Randomized, Controlled Trial of Belimumab in Lupus Nephritis. N Engl J Med. 2020;383(12):1117-1128.
6. Aringer M, Costenbader K, Daikh D, et al. 2019 European League Against Rheumatism/American College of Rheumatology classification criteria for systemic lupus erythematosus. *Ann Rheum Dis.* 2019;78:1151-1159.
7. Rovin BH, Adler SG, Barratt J, et al. Kidney Disease: Improving Global Outcomes (KDIGO) Golmerular Disease Work Group. KDIGO 2021 Clinical Practice Guideline for the Management of Glomerular Diseases. *Kidney Int.* 2021 Oct; 100(4S):S1-S276.
8. Gordon C, Amissah-Arthru MB, Gayed M, et al. The British Society for Rheumatology guideline for the management of systemic lupus erythematosus in adults. *Rheumatology (Oxford)*. 2018; 57(1):e1-e45.

QUANTITY LIMIT CRITERIA

DRUG CLASS	**ANTI-ANXIETY AGENTS**
BRAND NAME* (generic)	
	ALPRAZOLAM INTENSOL (alprazolam oral solution concentrate)
	(alprazolam orally disintegrating tablet)
	ATIVAN (lorazepam)
	(chlordiazepoxide)
	(clonazepam orally disintegrating tablet)
	DIAZEPAM INTENSOL (diazepam oral solution concentrate)
	(diazepam oral solution)
	KLONOPIN (clonazepam)
	(lorazepam oral concentrate solution)
	LOREEV XR (lorazepam extended-release)
	(oxazepam)
	TRANXENE (clorazepate)
	VALIUM (diazepam)
	XANAX (alprazolam)
	XANAX XR (alprazolam extended-release)

Status: CVS Caremark Criteria

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Alprazolam Intensol Oral Solution

Anxiety Disorders

Alprazolam Intensol Oral Solution is indicated for the management of anxiety disorder (a condition corresponding most closely to the APA Diagnostic and Statistical Manual [DSM-III-R] diagnosis of generalized anxiety disorder) or the short-term relief of symptoms of anxiety. Anxiety or tension associated with the stress of everyday life usually does not require treatment with an anxiolytic.

Generalized anxiety disorder is characterized by unrealistic or excessive anxiety and worry (apprehensive expectation) about two or more life circumstances, for a period of 6 months or longer, during which the person has been bothered more days than not by these concerns. At least 6 of the following 18 symptoms are often present in these patients: Motor Tension (trembling, twitching, or feeling shaky; muscle tension, aches, or soreness; restlessness; easy fatigability); Autonomic Hyperactivity (shortness of breath or smothering sensations; palpitations or accelerated heart rate; sweating, or cold clammy hands; dry mouth; dizziness or light-headedness; nausea, diarrhea, or other abdominal distress; flushes or chills; frequent urination; trouble swallowing or 'lump in throat'); Vigilance and Scanning (feeling keyed up or on edge; exaggerated startle response; difficulty concentrating or 'mind going blank' because of anxiety; trouble falling or staying asleep; irritability). These symptoms must not be secondary to another psychiatric disorder or caused by some organic factor.

Anxiety associated with depression is responsive to Alprazolam Intensol Oral Solution.

Panic Disorder

Alprazolam Intensol Oral Solution is also indicated for the treatment of panic disorder, with or without agoraphobia. Studies supporting this claim were conducted in patients whose diagnoses corresponded closely to the DSM-III-R/IV criteria for panic disorder.

Panic disorder (DSM-IV) is characterized by recurrent unexpected panic attacks, i.e., a discrete period of intense fear or discomfort in which four (or more) of the following symptoms develop abruptly and reach a peak within 10 minutes: (1) palpitations, pounding heart, or accelerated heart rate; (2) sweating; (3) trembling or shaking; (4) sensations of shortness of breath or smothering; (5) feeling of choking; (6) chest pain or discomfort; (7) nausea or abdominal distress; (8) feeling dizzy, unsteady, lightheaded, or faint; (9) derealization (feelings of unreality) or depersonalization (being detached from oneself); (10) fear of losing control; (11) fear of dying; (12) paresthesias (numbness or tingling sensations); (13) chills or hot flushes.

Demonstrations of the effectiveness of Alprazolam Intensol Oral Solution by systematic clinical study are limited to 4 months duration for anxiety disorder and 4 to 10 weeks duration for panic disorder; however, patients with panic disorder have been treated on an open basis for up to 8 months without apparent loss of benefit. The physician should periodically reassess the usefulness of the drug for the individual patient.

Alprazolam Orally Disintegrating Tablet

Generalized Anxiety Disorder

Alprazolam orally disintegrating tablets are indicated for the treatment of generalized anxiety disorder.

The efficacy of alprazolam in the treatment of generalized anxiety disorder was demonstrated in 5 short-term, placebo-controlled trials.

Panic Disorder

Alprazolam orally disintegrating tablets are also indicated for the treatment of panic disorder, with or without agoraphobia.

The efficacy of alprazolam in the treatment of panic disorder was established in 2 short-term, placebo-controlled trials.

Demonstrations of the effectiveness of alprazolam by systematic clinical study are limited to 4 months in duration for generalized anxiety disorder and 4 to 10 weeks duration for panic disorder; however, patients with panic disorder have been treated on an open basis for up to 8 months without apparent loss of benefit. The physician should periodically reassess the usefulness of the drug for the individual patient.

Ativan and Lorazepam Oral Concentrate

Ativan (lorazepam) and lorazepam oral concentrate are indicated for the management of anxiety disorders or for the short-term relief of the symptoms of anxiety or anxiety associated with depressive symptoms. Anxiety or tension associated with the stress of everyday life usually does not require treatment with an anxiolytic.

The effectiveness of Ativan (lorazepam) and lorazepam oral concentrate in long-term use, that is, more than 4 months, has not been assessed by systematic clinical studies. The physician should periodically reassess the usefulness of the drug for the individual patient.

Chlordiazepoxide
Chlordiazepoxide hydrochloride capsules are indicated for the management of anxiety disorders or for the short-term relief of symptoms of anxiety, withdrawal symptoms of acute alcoholism, and preoperative apprehension and anxiety. Anxiety or tension associated with the stress of everyday life usually does not require treatment with an anxiolytic.
The effectiveness of chlordiazepoxide hydrochloride capsules in long term use, that is, more than 4 months, has not been assessed by systematic clinical studies. The physician should periodically reassess the usefulness of the drug for the individual patient.

Klonopin, Clonazepam Orally Disintegrating Tablet
Seizure Disorders
Klonopin and clonazepam orally disintegrating tablets are useful alone or as an adjunct in the treatment of the Lennox-Gastaut syndrome (petit mal variant), akinetic and myoclonic seizures. In patients with absence seizures (petit mal) who have failed to respond to succinimides, Klonopin and clonazepam orally disintegrating tablets may be useful. In some studies, up to 30% of patients have shown a loss of anticonvulsant activity, often within 3 months of administration. In some cases, dosage adjustment may reestablish efficacy.
Panic Disorder
Klonopin and clonazepam orally disintegrating tablets are indicated for the treatment of panic disorder, with or without agoraphobia, as defined in DSM-V. Panic disorder is characterized by the occurrence of unexpected panic attacks and associated concern about having additional attacks, worry about the implications or consequences of the attacks, and/or a significant change in behavior related to the attacks. The efficacy of Klonopin and clonazepam orally disintegrating tablets was established in two 6- to 9-week trials in panic disorder patients whose diagnoses corresponded to the DSM-IIIR category of panic disorder.
Panic disorder (DSM-V) is characterized by recurrent unexpected panic attacks, i.e., a discrete period of intense fear or discomfort in which four (or more) of the following symptoms develop abruptly and reach a peak within 10 minutes: (1) palpitations, pounding heart or accelerated heart rate; (2) sweating; (3) trembling or shaking; (4) sensations of shortness of breath or smothering; (5) feeling of choking; (6) chest pain or discomfort; (7) nausea or abdominal distress; (8) feeling dizzy, unsteady, lightheaded or faint; (9) derealization (feelings of unreality) or depersonalization (being detached from oneself); (10) fear of losing control; (11) fear of dying; (12) paresthesias (numbness or tingling sensations); (13) chills or hot flushes.
The effectiveness of Klonopin and clonazepam orally disintegrating tablets in long-term use, that is, for more than 9 weeks, has not been systematically studied in controlled clinical trials. The physician who elects to use Klonopin and clonazepam orally disintegrating tablets for extended periods should periodically reevaluate the long-term usefulness of the drug for the individual patient.

Loreev XR
Loreev XR is indicated for the treatment of anxiety disorders in adults who are receiving stable, evenly divided, three times daily dosing with lorazepam tablets.

Oxazepam
Oxazepam is indicated for the management of anxiety disorders or for the short-term relief of the symptoms of anxiety. Anxiety or tension associated with the stress of everyday life usually does not require treatment with an anxiolytic. Anxiety associated with depression is also responsive to oxazepam therapy.
This product has been found particularly useful in the management of anxiety, tension, agitation, and irritability in older patients.
Alcoholics with acute tremulousness, inebriation, or with anxiety associated with alcohol withdrawal are responsive to therapy.
The effectiveness of oxazepam in long-term use, that is, more than 4 months, has not been assessed by systematic clinical studies. The physician should periodically reassess the usefulness of the drug for the individual patient.

Tranxene
Tranxene is indicated for the management of anxiety disorders or for the short-term relief of the symptoms of anxiety. Anxiety or tension associated with the stress of everyday life usually does not require treatment with an anxiolytic.

Tranxene tablets are indicated as adjunctive therapy in the management of partial seizures.
The effectiveness of Tranxene tablets in long-term management of anxiety, that is, more than 4 months, has not been assessed by systematic clinical studies. Long-term studies in epileptic patients, however, have shown continued therapeutic activity. The physician should reassess periodically the usefulness of the drug for the individual patient.
Tranxene tablets are indicated for the symptomatic relief of acute alcohol withdrawal.

Valium, Diazepam Intensol, Diazepam Oral Solution
Valium, Diazepam Intensol, and diazepam oral solution are indicated for the management of anxiety disorders or for the short-term relief of the symptoms of anxiety. Anxiety or tension associated with the stress of everyday life usually does not require treatment with an anxiolytic.
In acute alcohol withdrawal, Valium, Diazepam Intensol, and diazepam oral solution may be useful in the symptomatic relief of acute agitation, tremor, impending or acute delirium tremens and hallucinosis.
Valium, Diazepam Intensol, and diazepam oral solution are a useful adjunct for the relief of skeletal muscle spasm due to reflex spasm to local pathology (such as inflammation of the muscles or joints, or secondary to trauma); spasticity caused by upper motor neuron disorders (such as cerebral palsy and paraplegia); athetosis; and stiff-man syndrome.
Oral Valium, Diazepam Intensol, and diazepam oral solution may be used adjunctively in convulsive disorders, although it has not proved useful as the sole therapy.
The effectiveness of Valium, Diazepam Intensol, and diazepam oral solution in long-term use, that is, more than 4 months, has not been assessed by systematic clinical studies. The physician should periodically reassess the usefulness of the drug for the individual patient.

Xanax
Xanax is indicated for the acute treatment of generalized anxiety disorder in adults and for the treatment of panic disorder with or without agoraphobia in adults.

Xanax XR
Xanax XR is indicated for the treatment of panic disorder with or without agoraphobia, in adults.

RATIONALE

Benzodiazepine Maximum Daily Dose Chart[1-16]		
Brand Name	**Generic Name**	**Maximum Dose/24 hours**
Ativan, lorazepam oral concentrate solution	lorazepam	10 mg
Chlordiazepoxide	chlordiazepoxide	300 mg
Klonopin, clonazepam ODT	clonazepam	20 mg
Loreev XR	lorazepam extended-release	10 mg
Oxazepam	oxazepam	120 mg
Tranxene	clorazepate	90 mg
Valium, Diazepam Intensol, diazepam oral solution	diazepam	40 mg
Xanax, Alprazolam Intensol Oral Solution, Alprazolam ODT	alprazolam	10 mg
Xanax XR	alprazolam extended-release	10 mg

Ativan (lorazepam) and Lorazepam Oral Concentrate
The usual range is 2 to 6 mg/day given in divided doses, the largest dose being taken before bedtime, but the daily dosage may vary from 1 to 10 mg/day. For anxiety, most patients require an initial dose of 2 to 3 mg/day given two times a day or three times a day. For insomnia due to anxiety or transient situational stress, a single daily dose of 2 to 4 mg may be given, usually at bedtime.[3,8]

The limit will accommodate the treatment of anxiety and insomnia at recommended doses. The initial quantity limit will be set at 150 Ativan (lorazepam) tablets per month and 150 milliliters of lorazepam oral concentrate (2 mg/mL) per month to allow for up to 10 mg per day.

Chlordiazepoxide
For the relief of mild and moderate anxiety disorders and symptoms of anxiety, the usual daily dose is 5 mg or 10 mg, 3 or 4 times daily. For the relief of severe anxiety disorders and symptoms of anxiety, the usual daily dose is 20 mg or 25 mg, 3 or 4 times daily. For preoperative apprehension and anxiety, 5 to 10 mg, 3 or 4 times daily on days preceding surgery. If used as preoperative medication, 50 to 100 mg IM 1 hour prior to surgery. For the relief of withdrawal symptoms of acute alcoholism, the parenteral form is usually used initially. If the drug is administered orally, then the suggested initial dose is 50 to 100 mg, to be followed by repeated doses as needed until agitation is controlled — up to 300 mg per day.[4]

The limit will accommodate the treatment of anxiety and alcohol withdrawal symptoms at recommended doses. The initial quantity limit will be set at 360 chlordiazepoxide capsules per month to allow for up to 300 mg per day.

Klonopin (clonazepam) and Clonazepam Orally Disintegrating Tablet
The initial dose for adults with seizure disorders should not exceed 1.5 mg/day divided into three doses. Dosage may be increased in increments of 0.5 to 1 mg every 3 days until seizures are adequately controlled or until side effects preclude any further increase. Maintenance dosage must be individualized for each patient depending upon response. Maximum recommended daily dose is 20 mg. The initial dose for adults with panic disorder is 0.25 mg twice daily. An increase to the target dose for most patients of 1 mg/day may be made after 3 days. It is possible that some individual patients may benefit from doses of up to a maximum dose of 4 mg/day.[5,7]

The limit will accommodate the treatment of panic disorder and seizure disorders at recommended doses. The initial quantity limit will be set at 300 Klonopin (clonazepam) tablets per month and 300 clonazepam ODT per month to allow for a maximum dose of up to 20 mg per day.

Loreev XR (lorazepam extended-release)
Loreev XR is initiated in patients who are being treated with lorazepam tablets, administered three times daily in evenly divided doses (refer to the Prescribing Information of lorazepam tablets for the recommended dosage of lorazepam tablets). Discontinue lorazepam tablets and administer the first dose of Loreev XR in the morning the day after the final dose of lorazepam tablets. The recommended once daily dosage of Loreev XR is equal to the total daily dose of lorazepam tablets, which may vary from 1 to 10 mg/day. For example, the recommended dosage for patients who have been receiving lorazepam tablets at a dosage of 1 mg three times daily is Loreev XR 3 mg once daily in the morning.[3,9]

The limit will accommodate the treatment of anxiety at recommended doses. The initial quantity limit will be set at 90 Loreev XR (lorazepam extended-release) 3 mg capsules per month and 150 Loreev XR (lorazepam extended-release) capsules per month for all other strengths to allow for the upper limits of dosing up to 10 mg per day.

Oxazepam
For mild-to-moderate anxiety, with associated tension, irritability, agitation, or related symptoms of functional origin or secondary to organic disease, the usual dosage is 10 to 15 mg, 3 or 4 times daily. For severe anxiety syndromes, agitation, or anxiety associated with depression, the usual dosage is 15 to 30 mg, 3 or 4 times daily. If necessary, increase cautiously to 15 mg, 3 or 4 times daily. For alcoholics with acute inebriation, tremulousness, or anxiety on withdrawal, the usual dose is 15 to 30 mg, 3 or 4 times daily.[10]

The limit will accommodate the treatment of anxiety and alcohol withdrawal syndrome. The initial quantity limit will be set at 120 oxazepam capsules per month to allow for up to 120 mg per day.

Tranxene (clorazepate)
For the symptomatic relief of anxiety, the usual daily dose is 30 mg. The dose should be adjusted gradually within the range of 15 to 60 mg daily in accordance with the response of the patient. For the symptomatic relief of acute alcohol withdrawal, the maximum recommended total daily dose is 90 mg. As an adjunct to antiepileptic drugs, the maximum recommended initial dose in patients over 12 years old is 7.5 mg three times a day. Dosage should not exceed 90 mg/day.[11]

The limit will accommodate the treatment of anxiety, alcohol withdrawal, and adjunctive therapy to antiepileptic drugs. The initial quantity limit will be set at 180 Tranxene (clorazepate) tablets per month to allow for a maximum dose of up to 90 mg per day.

Valium (diazepam), Diazepam Intensol, Diazepam Oral Solution
For the management of anxiety disorders and relief of symptoms of anxiety, the usual adult daily dose is, depending upon severity of symptoms, 2 mg to 10 mg, 2 to 4 times daily. For symptomatic relief in acute alcohol withdrawal, the usual daily dose is 10 mg, 3 or 4 times during the first 24 hours, reducing to 5 mg, 3 or 4 times daily as needed. For adjunctive use in the relief of skeletal muscle spasm, the usual daily dose is 2 mg to 10 mg, 3 or 4 times daily. For adjunctive use in convulsive disorders, the usual daily dose is 2 mg to 10 mg, 2 to 4 times daily.[6,12]

The limit will accommodate all FDA-approved indications. The initial quantity limit will be set at 120 Valium (diazepam) tablets per month, 1200 milliliters of diazepam oral solution (5 mg/5 ml) per month, and 240 milliliters of Diazepam Intensol (5 mg/ml) per month to allow for a maximum dose of up to 40 mg per day.

Xanax (alprazolam), Alprazolam Intensol Oral Solution, Alprazolam Orally Disintegrating Tablet
Treatment for patients with anxiety should be initiated with a dose of 0.25 to 0.5 mg given three times daily. The dose may be increased to achieve a maximum therapeutic effect, at intervals of 3 to 4 days, to a maximum daily dose of 4 mg, given in divided doses. The lowest possible effective dose should be employed and the need for continued treatment reassessed frequently. The risk of dependence may increase with dose and duration of treatment. The successful treatment of many panic disorder patients has required the use of alprazolam at doses greater than 4 mg daily. In controlled trials conducted to establish the efficacy of alprazolam in panic disorder, doses in the range of 1 to 10 mg daily were used. Occasional patients required as much as 10 mg a day to achieve a successful response.[1,2,13]

The limit will accommodate the treatment of anxiety and panic disorder. The initial quantity limit will be set at 150 Xanax (alprazolam) tablets or alprazolam orally disintegrating tablets per month and 300 milliliters of Alprazolam Intensol (1 mg/ml) per month to allow for the upper limits of dosing for panic disorder up to 10 mg per day.

Xanax XR (alprazolam extended-release)
The recommended starting oral dosage for Xanax XR is 0.5 mg to 1 mg once daily. Depending on the response, the dose may be increased at intervals of every 3 to 4 days in increments of no more than 1 mg once daily. The recommended dosage range is between 3 mg to 6 mg once daily. Dosage should be individualized for maximum beneficial effect. Controlled trials of Xanax XR Tablets for the treatment of panic disorder included dosages in the range of 1 mg to 10 mg per day. Most patients showed a response in the dosage range of 3 mg to 6 mg per day. Occasional patients required as much as 10 mg a day to achieve a successful response.[14] Dosage generally should be increased until an acceptable therapeutic response is achieved, intolerance occurs, or a maximum dosage of 10 mg once daily is achieved.[15]

The limit will accommodate the treatment of panic disorder. The initial quantity limit will be set at 90 Xanax XR (alprazolam extended-release) 3 mg tablets per month and 150 Xanax XR (alprazolam extended-release) tablets per month for all other strengths to allow for the upper limits of dosing up to 10 mg per day.

Combined use of two or more benzodiazepines is not supported in the literature and therefore is not recommended. Therefore, these limits will accumulate together across all drugs and strengths up to the highest quantity listed depending on the order that the claims are processed.

If the patient is requesting more than the initial quantity limit, the claim will reject with a message indicating that quantity limits are exceeded.

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Written by:	UM Development (RP)
Date Written:	06/2011
Revised:	(RP) 09/2011 (added Niravam, removed clonazepam), 10/2011 (added diazepam oral solutions), 05/2012 (added lorazepam and alprazolam oral solutions); (JK) (removed ** for VF in limit criteria box); (MS) 05/2013; (CF) 05/2014, 05/2015, 05/2016, 05/2017 (no clinical changes); (KC) 05/2018; (CF) 03/2019 (removed brand Niravam); (MAC) 03/2020 (no changes); (CJH) 02/2021 (no clinical changes); (AW) 09/2021 (added Loreev XR); (SLF) 02/2022 (added Loreev 1.5mg)
Reviewed:	Medical Affairs: (WF) 06/2011, 09/2011; (KP) 10/2011; (LB) 05/2012; (KP) 05/2013; (LMS) 05/2014; (ADA) 05/2015; (ME) 05/2016; (DNC) 05/2018, 03/2019; (CHART) 03/26/2020, 02/25/2021, 09/23/2021, 02/24/2022, 03/31/2022 External Review: 10/2011, 10/2012, 08/2013, 06/2014, 08/2014, 08/2015, 08/2016, 08/2017, 08/2018, 08/2019, 06/2021, 10/2021 (FYI), 04/2022 (FYI)

LIMIT CRITERIA

Limits should accumulate across all drugs and strengths up to the highest quantity listed depending on the order the claims are processed.

	1 Month Limit*	3 Month Limit*
Alprazolam Intensol solution (1 mg/mL)	300 mL / 25 days	900 mL / 75 days
Alprazolam ODT (0.25, 0.5, 1, 2 mg)	150 tablets / 25 days	450 tablets / 75 days
Ativan (0.5, 1, 2 mg)	150 tablets / 25 days	450 tablets / 75 days
Chlordiazepoxide (5, 10, 25 mg)	360 capsules / 25 days	1080 capsules / 75 days
Clonazepam ODT (0.125, 0.25, 0.5, 1, 2 mg)	300 tablets / 25 days	900 tablets / 75 days
Diazepam solution (5 mg/5 mL)	1200 mL / 25 days	3600 mL / 75 days
Diazepam Intensol solution (5 mg/mL)	240 mL / 25 days	720 mL / 75 days
Klonopin (0.5, 1, 2 mg)	300 tablets / 25 days	900 tablets / 75 days
Lorazepam Intensol solution (2 mg/mL)	150 mL / 25 days	450 mL / 75 days
Loreev XR (1, 1.5, 2 mg)	150 capsules / 25 days	450 capsules / 75 days
Loreev XR (3 mg)	90 capsules / 25 days	270 capsules / 75 days
Oxazepam (10, 15, 30 mg)	120 capsules / 25 days	360 capsules / 75 days
Tranxene (3.75, 7.5, 15 mg)	180 tablets / 25 days	540 tablets / 75 days
Valium (2, 5, 10 mg)	120 tablets / 25 days	360 tablets / 75 days
Xanax (0.25, 0.5, 1, 2 mg)	150 tablets / 25 days	450 tablets / 75 days
Xanax XR (0.5, 1, 2 mg)	150 tablets / 25 days	450 tablets / 75 days
Xanax XR (3 mg)	90 tablets / 25 days	270 tablets / 75 days

**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*

QUANTITY LIMIT CRITERIA

DRUG CLASS	**ANTI-ANXIETY AGENTS**
BRAND NAME (generic)	
	ALPRAZOLAM INTENSOL (alprazolam oral solution concentrate)
	(alprazolam orally disintegrating tablet)
	ATIVAN (lorazepam)
	(chlordiazepoxide)
	(clonazepam orally disintegrating tablet)
	DIAZEPAM INTENSOL (diazepam oral solution concentrate)
	(diazepam oral solution)
	KLONOPIN (clonazepam)
	(lorazepam oral concentrate solution)
	LOREEV XR (lorazepam extended-release)
	(oxazepam)
	TRANXENE (clorazepate)
	VALIUM (diazepam)
	XANAX (alprazolam)
	XANAX XR (alprazolam extended-release)

Status: CVS Caremark Criteria
Type: Quantity Limit

POLICY

FDA-APPROVED INDICATIONS

Alprazolam Orally Disintegrating Tablet

Generalized Anxiety Disorder

Alprazolam orally disintegrating tablets, USP are indicated for the treatment of generalized anxiety disorder.

The efficacy of alprazolam in the treatment of generalized anxiety disorder was demonstrated in 5 short-term, placebo-controlled trials.

Panic Disorder

Alprazolam orally disintegrating tablets, USP are also indicated for the treatment of panic disorder, with or without agoraphobia.

The efficacy of alprazolam in the treatment of panic disorder was established in 2 short-term, placebo-controlled trials.

Demonstrations of the effectiveness of alprazolam by systematic clinical study are limited to 4 months in duration for generalized anxiety disorder and 4 to 10 weeks duration for panic disorder; however, patients with panic disorder have been treated on an open basis for up to 8 months without apparent loss of benefit. The physician should periodically reassess the usefulness of the drug for the individual patient.

Ativan, Lorazepam Oral Concentrate

Ativan (lorazepam) and lorazepam oral concentrate are indicated for the management of anxiety disorders or for the short-term relief of the symptoms of anxiety or anxiety associated with depressive symptoms. Anxiety or tension associated with the stress of everyday life usually does not require treatment with an anxiolytic.

The effectiveness of Ativan (lorazepam) and lorazepam oral concentrate in long-term use, that is, more than 4 months, has not been assessed by systematic clinical studies. The physician should periodically reassess the usefulness of the drug for the individual patient.

Chlordiazepoxide

Chlordiazepoxide hydrochloride capsules are indicated for the management of anxiety disorders or for the short-term relief of symptoms of anxiety, withdrawal symptoms of acute alcoholism, and preoperative apprehension and anxiety. Anxiety or tension associated with the stress of everyday life usually does not require treatment with an anxiolytic.

The effectiveness of chlordiazepoxide hydrochloride capsules in long term use, that is, more than 4 months, has not been assessed by systematic clinical studies. The physician should periodically reassess the usefulness of the drug for the individual patient.

Klonopin, Clonazepam Orally Disintegrating Tablet

Seizure Disorders

Klonopin and clonazepam orally disintegrating tablets are useful alone or as an adjunct in the treatment of the Lennox-Gastaut syndrome (petit mal variant), akinetic and myoclonic seizures. In patients with absence seizures (petit mal) who have failed to respond to succinimides, Klonopin and clonazepam orally disintegrating tablets may be useful.

Some loss of effect may occur during the course of clonazepam treatment.

Panic Disorder

Klonopin and clonazepam orally disintegrating tablets are indicated for the treatment of panic disorder, with or without agoraphobia, as defined in DSM-V. Panic disorder is characterized by the occurrence of unexpected panic attacks and associated concern about having additional attacks, worry about the implications or consequences of the attacks, and/or a significant change in behavior related to the attacks.

The efficacy of Klonopin and clonazepam orally disintegrating tablets was established in two 6- to 9-week trials in panic disorder patients whose diagnoses corresponded to the DSM-IIIR category of panic disorder.

Panic disorder (DSM-V) is characterized by recurrent unexpected panic attacks, i.e., a discrete period of intense fear or discomfort in which four (or more) of the following symptoms develop abruptly and reach a peak within 10 minutes: (1) palpitations, pounding heart or accelerated heart rate; (2) sweating; (3) trembling or shaking; (4) sensations of shortness of breath or smothering; (5) feeling of choking; (6) chest pain or discomfort; (7) nausea or abdominal distress; (8) feeling dizzy, unsteady, lightheaded or faint; (9) derealization (feelings of unreality) or depersonalization (being detached from

oneself); (10) fear of losing control; (11) fear of dying; (12) paresthesias (numbness or tingling sensations); (13) chills or hot flushes.

The effectiveness of Klonopin and clonazepam orally disintegrating tablets in long-term use, that is, for more than 9 weeks, has not been systematically studied in controlled clinical trials. The physician who elects to use Klonopin and clonazepam orally disintegrating tablets for extended periods should periodically reevaluate the long-term usefulness of the drug for the individual patient.

Loreev XR
Loreev XR is indicated for the treatment of anxiety disorders in adults who are receiving stable, evenly divided, three times daily dosing with lorazepam tablets.

Oxazepam
Oxazepam capsules are indicated for the management of anxiety disorders or for the short-term relief of the symptoms of anxiety. Anxiety or tension associated with the stress of everyday life usually does not require treatment with an anxiolytic.

Anxiety associated with depression is also responsive to oxazepam therapy.

This product has been found particularly useful in the management of anxiety, tension, agitation, and irritability in older patients.

Alcoholics with acute tremulousness, inebriation, or with anxiety associated with alcohol withdrawal are responsive to therapy.

The effectiveness of oxazepam in long-term use, that is, more than 4 months, has not been assessed by systematic clinical studies. The physician should periodically reassess the usefulness of the drug for the individual patient.

Tranxene
Tranxene is indicated for the management of anxiety disorders or for the short-term relief of the symptoms of anxiety. Anxiety or tension associated with the stress of everyday life usually does not require treatment with an anxiolytic.

Tranxene tablets are indicated as adjunctive therapy in the management of partial seizures.

The effectiveness of Tranxene tablets in long-term management of anxiety, that is, more than 4 months, has not been assessed by systematic clinical studies. Long-term studies in epileptic patients, however, have shown continued therapeutic activity. The physician should reassess periodically the usefulness of the drug for the individual patient.

Tranxene tablets are indicated for the symptomatic relief of acute alcohol withdrawal.

Valium, Diazepam Intensol, Diazepam Oral Solution
Valium, Diazepam Intensol, and diazepam oral solution are indicated for the management of anxiety disorders or for the short-term relief of the symptoms of anxiety. Anxiety or tension associated with the stress of everyday life usually does not require treatment with an anxiolytic.

In acute alcohol withdrawal, Valium, Diazepam Intensol, and diazepam oral solution may be useful in the symptomatic relief of acute agitation, tremor, impending or acute delirium tremens and hallucinosis.

Valium, Diazepam Intensol, and diazepam oral solution are a useful adjunct for the relief of skeletal muscle spasm due to reflex spasm to local pathology (such as inflammation of the muscles or joints, or secondary to trauma); spasticity caused by upper motor neuron disorders (such as cerebral palsy and paraplegia); athetosis; and stiff-man syndrome.

Oral Valium, Diazepam Intensol, and diazepam oral solution may be used adjunctively in convulsive disorders, although it has not proved useful as the sole therapy.

The effectiveness of Valium, Diazepam Intensol, and diazepam oral solution in long-term use, that is, more than 4 months, has not been assessed by systematic clinical studies. The physician should periodically reassess the usefulness of the drug for the individual patient.

Xanax, Alprazolam Intensol Oral Solution
Xanax and Alprazolam Intensol are indicated for the:

- acute treatment of generalized anxiety disorder (GAD) in adults.
- treatment of panic disorder (PD) with or without agoraphobia in adults.

Xanax XR
Xanax XR is indicated for the treatment of panic disorder with or without agoraphobia, in adults.

INITIAL LIMIT QUANTITY

Limits should accumulate across all drugs and strengths up to the highest quantity listed depending on the order the claims are processed.

Drug	1 Month Limit*	3 Month Limit*
Alprazolam Intensol solution (1 mg/mL)	300 mL / 25 days	900 mL / 75 days
Alprazolam ODT (0.25 mg, 0.5 mg, 1 mg, 2 mg)	150 tablets / 25 days	450 tablets / 75 days
Ativan (0.5 mg, 1 mg, 2 mg)	150 tablets / 25 days	450 tablets / 75 days
Chlordiazepoxide (5 mg, 10 mg, 25 mg)	360 capsules / 25 days	1080 capsules / 75 days
Clonazepam ODT (0.125 mg, 0.25 mg, 0.5 mg , 1 mg, 2 mg)	300 tablets / 25 days	900 tablets / 75 days
Clorazepate (3.75 mg, 7.5 mg, 15 mg)	180 tablets / 25 days	540 tablets / 75 days
Diazepam solution (5 mg/5 mL)	1200 mL / 25 days	3600 mL / 75 days
Diazepam Intensol solution (5 mg/mL)	240 mL / 25 days	720 mL / 75 days
Klonopin (0.5 mg, 1 mg, 2 mg)	300 tablets / 25 days	900 tablets / 75 days
Lorazepam Intensol solution (2 mg/mL)	150 mL / 25 days	450 mL / 75 days
Loreev XR (1 mg, 1.5 mg, 2 mg)	150 capsules / 25 days	450 capsules / 75 days
Loreev XR (3 mg)	90 capsules / 25 days	270 capsules / 75 days
Oxazepam (10 mg, 15 mg, 30 mg)	120 capsules / 25 days	360 capsules / 75 days
Tranxene (7.5 mg)	180 tablets / 25 days	540 tablets / 75 days
Valium (2 mg, 5 mg, 10 mg)	120 tablets / 25 days	360 tablets / 75 days
Xanax (0.25 mg , 0.5 mg, 1 mg, 2 mg)	150 tablets / 25 days	450 tablets / 75 days
Xanax XR (0.5 mg, 1 mg, 2 mg)	150 tablets / 25 days	450 tablets / 75 days
Xanax XR (3 mg)	90 tablets / 25 days	270 tablets / 75 days

**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*

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Reference number(s)
1602-A

SPECIALTY GUIDELINE MANAGEMENT

BERINERT (C1 esterase inhibitor [human])

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication
Berinert is indicated for the treatment of acute abdominal, facial, or laryngeal hereditary angioedema (HAE) attacks in adult and pediatric patients.

B. Compendial Use
Short-term preprocedural prophylaxis for HAE attacks

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
A. For initial authorization, the following should be documented:
   1. C1 inhibitor functional and antigenic protein levels
   2. F12, angiopoietin-1, plasminogen, kininogen-1 (KNG1), heparan sulfate-glucosamine 3-O-sulfotransferase 6 (HS3ST6), or myoferlin (MYOF) gene mutation testing, if applicable
   3. Chart notes confirming family history of angioedema and the angioedema was refractory to a trial of high-dose antihistamine therapy, if applicable
B. For continuation of therapy, chart notes demonstrating a reduction in severity and/or duration of attacks

III. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with a prescriber who specializes in the management of HAE.

IV. CRITERIA FOR INITIAL APPROVAL

Hereditary Angioedema (HAE)

A. Preprocedural Prophylaxis
Authorization of 30 days may be granted for short-term preprocedural prophylaxis (i.e., prior to surgical or major dental procedures) when either of the following criteria is met at the time of diagnosis:
   1. Member has C1 inhibitor deficiency or dysfunction as confirmed by laboratory testing and meets one of the following criteria:
      i. C1 inhibitor (C1-INH) antigenic level below the lower limit of normal as defined by the laboratory performing the test, or

ii. Normal C1-INH antigenic level and a low C1-INH functional level (functional C1-INH less than 50% or C1-INH functional level below the lower limit of normal as defined by the laboratory performing the test).

2. Member has normal C1 inhibitor as confirmed by laboratory testing and meets one of the following criteria:
   i. Member has an F12, angiopoietin-1, plasminogen, kininogen-1 (KNG1), heparan sulfate-glucosamine 3-O-sulfotransferase 6 (HS3ST6), or myoferlin (MYOF) gene mutation as confirmed by genetic testing, or
   ii. Member has a documented family history of angioedema and the angioedema was refractory to a trial of high-dose antihistamine therapy (i.e., cetirizine at 40 mg per day or the equivalent) for at least one month.

B. Acute Attacks

Authorization of 6 months may be granted for treatment of acute HAE attacks when the requested medication will not be used in combination with any other medication used for the treatment of acute HAE attacks and either of the following criteria is met at the time of diagnosis:

1. Member has C1 inhibitor deficiency or dysfunction as confirmed by laboratory testing and meets one of the following criteria:
   i. C1 inhibitor (C1-INH) antigenic level below the lower limit of normal as defined by the laboratory performing the test, or
   ii. Normal C1-INH antigenic level and a low C1-INH functional level (functional C1-INH less than 50% or C1-INH functional level below the lower limit of normal as defined by the laboratory performing the test).
2. Member has normal C1 inhibitor as confirmed by laboratory testing and meets one of the following criteria:
   i. Member has an F12, angiopoietin-1, plasminogen, kininogen-1 (KNG1), heparan sulfate-glucosamine 3-O-sulfotransferase 6 (HS3ST6), or myoferlin (MYOF) gene mutation as confirmed by genetic testing, or
   ii. Member has a documented family history of angioedema and the angioedema was refractory to a trial of high-dose antihistamine therapy (i.e., cetirizine at 40 mg per day or the equivalent) for at least one month.

V. CONTINUATION OF THERAPY

Hereditary Angioedema

A. Preprocedural Prophylaxis

All members (including new members) requesting authorization for continued short-term preprocedural prophylaxis (i.e., prior to surgical or major dental procedures) must meet all initial authorization criteria.

B. Acute Attacks

Authorization of 6 months may be granted for continued treatment of acute HAE attacks when all of the following criteria are met:

1. Member meets the criteria for initial approval.
2. Member has experienced a reduction in severity and/or duration of acute attacks.
3. Prophylaxis should be considered based on the attack frequency, attack severity, comorbid conditions, and member's quality of life.

VI. REFERENCES

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QUANTITY LIMIT CRITERIA

DRUG CLASS **LONG ACTING BETA2-ADRENERGIC AGONIST, COMBINATIONS ORAL INHALATION**

BRAND NAME (generic)

LONG-ACTING BETA2-ADRENERGIC AGONIST:

ARCAPTA NEOHALER (indacaterol)

BROVANA (arformoterol tartrate)

PERFOROMIST (formoterol)

SEREVENT DISKUS (salmeterol)

STRIVERDI RESPIMAT (olodaterol)

LONG-ACTING BETA2-ADRENERGIC AGONIST / ANTICHOLINERGIC:

ANORO ELLIPTA (umeclidinium/vilanterol)

BEVESPI AEROSPHERE (glycopyrrolate/formoterol)

DUAKLIR PRESSAIR (aclidinium/formoterol)

STIOLTO RESPIMAT (tiotropium bromide/olodaterol)

UTIBRON NEOHALER (glycopyrrolate/indacaterol)

LONG-ACTING BETA2-ADRENERGIC AGONIST / CORTICOSTEROID:

ADVAIR DISKUS (fluticasone propionate/salmeterol)

ADVAIR HFA (fluticasone propionate/salmeterol)

AIRDUO DIGIHALER
(fluticasone propionate/salmeterol)

AIRDUO RESPICLICK
(fluticasone propionate/salmeterol)

BREO ELLIPTA
(fluticasone furoate/vilanterol)

DULERA
(mometasone/formoterol)

SYMBICORT
(budesonide/formoterol)

SYMBICORT AEROSPHERE
(budesonide/formoterol)

LONG-ACTING BETA2-ADRENERGIC AGONIST / ANTICHOLINERGIC / CORTICOSTEROID:

BREZTRI AEROSPHERE
(budesonide/glycopyrrolate/formoterol fumarate)

TRELEGY ELLIPTA
(fluticasone furoate/umeclidinium/vilanterol)

Status: CVS Caremark® Criteria
Type: Quantity Limit

POLICY

FDA-APPROVED INDICATIONS
Long-Acting Beta2-Adrenergic Agonist:
Arcapta Neohaler
Arcapta Neohaler is indicated for long-term, once-daily maintenance bronchodilator treatment of airflow obstruction in patients with chronic obstructive pulmonary disease (COPD).
Limitations of Use
Arcapta Neohaler is not indicated to treat acute deteriorations of COPD.
Arcapta Neohaler is not indicated to treat asthma. The safety and effectiveness of Arcapta Neohaler in asthma have not been established.

Brovana
Brovana (arformoterol tartrate) Inhalation Solution is indicated for the long-term, twice daily (morning and evening) maintenance treatment of bronchoconstriction in patients with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and emphysema. Brovana Inhalation Solution is for use by nebulization only.
Limitations of Use
Brovana Inhalation solution is not indicated to treat acute deteriorations of chronic obstructive pulmonary disease.

Brovana Inhalation Solution is not indicated to treat asthma. The safety and effectiveness of Brovana Inhalation Solution in asthma have not been established.

Perforomist
Perforomist (formoterol fumarate) Inhalation Solution is indicated for the long-term, twice daily (morning and evening) administration in the maintenance treatment of bronchoconstriction in patients with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and emphysema.
Limitations of Use
Perforomist Inhalation Solution is not indicated to treat acute deteriorations of chronic obstructive pulmonary disease.
Perforomist Inhalation Solution is not indicated to treat asthma. The safety and effectiveness of Perforomist Inhalation Solution in asthma have not been established.

Serevent Diskus
Treatment of Asthma
Serevent Diskus is indicated for the treatment of asthma and in the prevention of bronchospasm only as concomitant therapy with an ICS in patients aged 4 years and older with reversible obstructive airway disease, including patients with symptoms of nocturnal asthma. LABA, such as salmeterol, the active ingredient in Serevent Diskus, as monotherapy (without ICS) increase the risk of asthma-related death. Use of Serevent Diskus for the treatment of asthma without concomitant use of an ICS is contraindicated. Use Serevent Diskus only as additional therapy for patients with asthma who are currently taking but are inadequately controlled on an ICS. Do not use Serevent Diskus for patients whose asthma is adequately controlled on low- or medium-dose ICS.
Pediatric and Adolescent Patients
Available data from controlled clinical trials suggest that LABA as monotherapy increase the risk of asthma-related hospitalization in pediatric and adolescent patients. For pediatric and adolescent patients with asthma who require addition of a LABA to an ICS, a fixed-dose combination product containing both an ICS and a LABA should ordinarily be used to ensure adherence with both drugs. In cases where use of a separate ICS and a LABA is clinically indicated, appropriate steps must be taken to ensure adherence with both treatment components. If adherence cannot be assured, a fixed-dose combination product containing both an ICS and a LABA is recommended.
Limitations of Use
Serevent Diskus is NOT indicated for the relief of acute bronchospasm.
Prevention of Exercise-Induced Bronchospasm
Serevent Diskus is also indicated for prevention of exercise-induced bronchospasm (EIB) in patients aged 4 years and older. Use of Serevent Diskus as a single agent for the prevention of EIB may be clinically indicated in patients who do not have persistent asthma. In patients with persistent asthma, use of Serevent Diskus for the prevention of EIB may be clinically indicated, but the treatment of asthma should include an ICS.
Maintenance Treatment of Chronic Obstructive Pulmonary Disease
Serevent Diskus is indicated for the long-term twice-daily administration in the maintenance treatment of bronchospasm associated with chronic obstructive pulmonary disease (COPD) (including emphysema and chronic bronchitis).
Limitations of Use
Serevent Diskus is NOT indicated for the relief of acute bronchospasm.

Striverdi Respimat
Striverdi Respimat is a long-acting beta2-agonist indicated for long-term, once-daily maintenance bronchodilator treatment of airflow obstruction in patients with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and/or emphysema.
Limitations of Use
Striverdi Respimat is not indicated to treat acute deteriorations of COPD.
Striverdi Respimat is not indicated to treat asthma. The safety and effectiveness of Striverdi Respimat in asthma have not been established.

Long-Acting Beta2-Adrenergic Agonist / Anticholinergic:
Anoro Ellipta
Anoro Ellipta is indicated for the maintenance treatment of patients with chronic obstructive pulmonary disease (COPD).
Limitations of Use

Anoro Ellipta is NOT indicated for the relief of acute bronchospasm or for the treatment of asthma. The safety and efficacy of Anoro Ellipta in asthma have not been established.

Bevespi Aerosphere
Bevespi Aerosphere is indicated for the maintenance treatment of patients with chronic obstructive pulmonary disease (COPD).
Limitations of Use
Bevespi Aerosphere is not indicated for the relief of acute bronchospasm or for the treatment of asthma.

Duaklir Pressair
Duaklir Pressair is a combination of aclidinium bromide (an anticholinergic) and formoterol fumarate (a LABA) indicated for the maintenance treatment of patients with chronic obstructive pulmonary disease (COPD).
Limitations of Use
Duaklir Pressair is not indicated for the relief of acute bronchospasm or for the treatment of asthma.

Stiolto Respimat
Stiolto Respimat is a combination of tiotropium and olodaterol indicated for long-term, once-daily maintenance treatment of patients with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and/or emphysema.
Limitations of Use
Stiolto Respimat is not indicated to treat acute deteriorations of COPD.
Stiolto Respimat is not indicated to treat asthma. The safety and effectiveness of Stiolto Respimat in asthma have not been established.

Utibron Neohaler
Utibron Neohaler is indicated for the long-term, maintenance treatment of airflow obstruction in patients with chronic obstructive pulmonary disease (COPD).
Limitations of Use
Utibron Neohaler is not indicated for the relief of acute bronchospasm or for the treatment of asthma. The safety and effectiveness of Utibron in asthma have not been established.

Long-Acting Beta2-Adrenergic Agonist / Corticosteroid:
Advair Diskus
Treatment of Asthma
Advair Diskus is indicated for the twice-daily treatment of asthma in patients aged 4 years and older. Advair Diskus should be used for patients not adequately controlled on a long-term asthma control medication such as an inhaled corticosteroid (ICS) or whose disease warrants initiation of treatment with both an ICS and long-acting beta2-adrenergic agonist (LABA).
Maintenance Treatment of Chronic Obstructive Pulmonary Disease
Advair Diskus 250/50 is indicated for the twice-daily maintenance treatment of airflow obstruction in patients with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and/or emphysema. Advair Diskus 250/50 is also indicated to reduce exacerbations of COPD in patients with a history of exacerbations. Advair Diskus 250/50 twice daily is the only approved dosage for the treatment of COPD because an efficacy advantage of the higher strength Advair Diskus 500/50 over Advair Diskus 250/50 has not been demonstrated.
Limitations of Use
Advair Diskus is NOT indicated for the relief of acute bronchospasm.

Advair HFA
Advair HFA is indicated for treatment of asthma in adult and adolescent patients aged 12 years and older. Advair HFA should be used for patients not adequately controlled on a long-term asthma control medication such as an inhaled corticosteroid (ICS) or whose disease warrants initiation of treatment with both an ICS and long-acting beta2-adrenergic agonist (LABA).
Limitations of Use
Advair HFA is not indicated for the relief of acute bronchospasm.

AirDuo Digihaler

AirDuo Digihaler is indicated for the treatment of asthma in adult and pediatric patients aged 12 years and older. AirDuo Digihaler should be used for patients not adequately controlled on a long term asthma control medication such as an inhaled corticosteroid or whose disease warrants initiation of treatment with both an inhaled corticosteroid and long acting beta2-adrenergic agonist (LABA).
Limitations of Use
AirDuo Digihaler is not indicated for the relief of acute bronchospasm.

AirDuo Respiclick
AirDuo Respiclick is indicated for the treatment of asthma in adult and pediatric patients aged 12 years and older. AirDuo Respiclick should be used for patients not adequately controlled on a long-term asthma control medication such as an inhaled corticosteroid or whose disease warrants initiation of treatment with both an inhaled corticosteroid and long acting beta2-adrenergic agonist (LABA).
Limitations of Use
AirDuo Respiclick is not indicated for the relief of acute bronchospasm.

Breo Ellipta
Maintenance Treatment of Chronic Obstructive Pulmonary Disease
Breo Ellipta 100/25 is indicated for the long-term, once-daily, maintenance treatment of airflow obstruction in patients with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and/or emphysema. Breo Ellipta 100/25 is also indicated to reduce exacerbations of COPD in patients with a history of exacerbations. Breo Ellipta 100/25 once daily is the only strength indicated for the treatment of COPD.
Treatment of Asthma
Breo Ellipta is indicated for the once-daily treatment of asthma in patients aged 18 years and older. Breo Ellipta should be used for patients not adequately controlled on a long-term asthma control medication such as an inhaled corticosteroid (ICS) or whose disease warrants initiation of treatment with both an ICS and long-acting beta2-adrenergic agonist (LABA).
Limitations of Use
Breo Ellipta is NOT indicated for the relief of acute bronchospasm.

Dulera
Dulera is indicated for the twice-daily treatment of asthma in patients 5 years of age and older. Dulera should be used for patients not adequately controlled on a long-term asthma-control medication such as an inhaled corticosteroid (ICS) or whose disease warrants initiation of treatment with both an ICS and long-acting beta2-adrenergic agonist (LABA).
Limitations of Use
Dulera is NOT indicated for the relief of acute bronchospasm.

Symbicort
Treatment of Asthma
Symbicort is indicated for the treatment of asthma in patients 6 years of age and older. Symbicort should be used for patients not adequately controlled on a long-term asthma-control medication such as an inhaled corticosteroid (ICS) or whose disease warrants initiation of treatment with both an inhaled corticosteroid and long-acting beta2-adrenergic agonist (LABA).
Maintenance Treatment of Chronic Obstructive Pulmonary Disease (COPD)
Symbicort 160/4.5 is indicated for the maintenance treatment of airflow obstruction in patients with chronic obstructive pulmonary disease (COPD) including chronic bronchitis and/or emphysema. Symbicort 160/4.5 is also indicated to reduce exacerbations of COPD. Symbicort 160/4.5 is the only strength indicated for the treatment of COPD.
Limitations of Use
Symbicort is NOT indicated for the relief of acute bronchospasm.

Symbicort Aerosphere
Symbicort Aerosphere is indicated for the maintenance treatment of patients with chronic obstructive pulmonary disease (COPD).
Limitations of Use
Symbicort Aerosphere is NOT indicated for the relief of acute bronchospasm or for the treatment of asthma.

Long-Acting Beta2-Adrenergic Agonist / Anticholinergic / Corticosteroid:

Breztri Aerosphere
Breztri Aerosphere is indicated for the maintenance treatment of patients with chronic obstructive pulmonary disease (COPD).
Limitations of Use
Breztri Aerosphere is NOT indicated for the relief of acute bronchospasm or for the treatment of asthma.

Trelegy Ellipta
Maintenance Treatment of Chronic Obstructive Pulmonary Disease
Trelegy Ellipta is indicated for the maintenance treatment of patients with chronic obstructive pulmonary disease (COPD).

Maintenance Treatment of Asthma
Trelegy Ellipta is indicated for the maintenance treatment of asthma in patients aged 18 years and older.
Limitations of Use
Trelegy Ellipta is NOT indicated for the relief of acute bronchospasm.

LIMIT CRITERIA LONG-ACTING BETA2-ADRENERGIC AGONIST:
Limits do not accumulate together; patient is allowed the maximum limit for each drug and strength
PLEASE NOTE: Since manufacturer package sizes may vary, it is the discretion of the dispensing pharmacy to fill quantities per package size up to these quantity limits. In such cases the filling limit and day supply may be less than what is indicated.

Medication	Maintenance Dose	Maximum Daily Dose	Package Size	1 Month Limit* 3 Months Limit*
Arcapta Neohaler (indacaterol)	inhalation of the powder contents of 1 capsule once daily	1 capsule	30 capsules per box	1 package (30 capsules) / 25 days 3 packages (30 capsules each) / 75 days
Brovana (arformoterol tartrate)	nebulization of 1 vial (2 mL) twice daily	2 vials (2 mL each)	30 vials (2 mL each) per carton	2 packages (60 vials x 2 mL) / 25 days 6 packages (180 vials x 2 mL) / 75 days
			60 vials (2mL each) per carton	1 package (60 vials x 2 mL) / 25 days 3 packages (180 vials x 2 mL) / 75 days
Perforomist (formoterol)	nebulization of 1 vial (2 mL) twice daily	2 vials (2 mL each)	30 vials (2 mL each) per carton	2 packages (60 vials x 2 mL) / 25 days 6 packages (180 vials x 2 mL) / 75 days
			60 vials (2 mL each) per carton	1 package (60 vials x 2 mL) / 25 days 3 packages (180 vials x 2 mL) / 75 days
Serevent Diskus (salmeterol)	1 inhalation twice daily	2 inhalations	60 blisters per inhaler	1 package (60 blisters) / 25 days 3 packages (60 blisters each) / 75 days
Striverdi Respimat (olodaterol)	2 inhalations once daily	2 inhalations	60 inhalations per 4 gm cartridge	1 package (4 gm) / 25 days 3 packages (4 gm each) / 75 days

**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*

LIMIT CRITERIA LONG-ACTING BETA2-ADRENERGIC AGONIST / ANTICHOLINERGIC:
Limits do not accumulate together; patient is allowed the maximum limit for each drug and strength
PLEASE NOTE: Since manufacturer package sizes may vary, it is the discretion of the dispensing pharmacy to fill quantities per package size up to these quantity limits. In such cases the filling limit and day supply may be less than what is indicated.

Medication	Maintenance Dose	Maximum Daily Dose	Package Size	1 Month Limit* 3 Months Limit*
Anoro Ellipta (umeclidinium/ vilanterol)	1 inhalation once daily	1 inhalation	30 inhalations (60 blisters) per inhaler	1 package (60 blisters) / 25 days 3 packages (60 blisters each) / 75 days

Bevespi Aerosphere (glycopyrrolate/ formoterol)	2 inhalations twice daily	4 inhalations	120 inhalations per 10.7 gm canister	1 package (10.7 gm) / 25 days 3 packages (10.7 gm each) / 75 days
Duaklir Pressair (aclidinium/ formoterol)	1 inhalation twice daily	2 inhalations	60 inhalations per inhaler	1 package / 25 days 3 packages / 75 days
Stiolto Respimat (tiotropium bromide/ olodaterol)	2 inhalations once daily	2 inhalations	60 inhalations per 4 gm cartridge	1 package (4 gm) / 25 days 3 packages (4 gm each) / 75 days
Utibron Neohaler (glycopyrrolate/ indacaterol)	1 inhalation twice daily	2 inhalations	60 capsules per box	1 package (60 capsules) / 25 days 3 packages (60 capsules each) / 75 days
**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*				

LIMIT CRITERIA LONG-ACTING BETA2-ADRENERGIC AGONIST / CORTICOSTEROID:
Limits do not accumulate together; patient is allowed the maximum limit for each drug and strength
PLEASE NOTE: Since manufacturer package sizes may vary, it is the discretion of the dispensing pharmacy to fill quantities per package size up to these quantity limits. In such cases the filling limit and day supply may be less than what is indicated.

Medication	**Maintenance Dose**	**Maximum Daily Dose**	**Package Size**	**1 Month Limit* 3 Months Limit***
Advair Diskus (fluticasone propionate/ salmeterol)	1 inhalation twice daily	2 inhalations	60 blisters per inhaler	1 package (60 blisters) / 25 days 3 packages (60 blisters each) / 75 days
Advair HFA (fluticasone propionate/ salmeterol)	2 inhalations twice daily	4 inhalations	120 inhalations per 12 gm canister	1 package (12 gm) / 25 days 3 packages (12 gm each) / 75 days
AirDuo Digihaler (fluticasone propionate/ salmeterol)	1 inhalation twice daily	2 inhalations	60 inhalations per inhaler	1 package / 25 days 3 packages / 75 days
AirDuo Respiclick (fluticasone propionate/ salmeterol)	1 inhalation twice daily	2 inhalations	60 inhalations per inhaler	1 package / 25 days 3 packages / 75 days
Breo Ellipta (fluticasone furoate/ vilanterol)	1 inhalation once daily	1 inhalation	30 inhalations (60 blisters) per inhaler	1 package (60 blisters) / 25 days 3 packages (60 blisters each) / 75 days
Dulera (mometasone/ formoterol)	2 inhalations twice daily	4 inhalations	120 inhalations per 13 gm canister	1 package (13 gm) / 25 days 3 packages (13 gm each) / 75 days
Symbicort (budesonide/ formoterol)	2 inhalations twice daily	4 -12 inhalations	120 inhalations per 10.2 gm canister	3 packages (10.2 gm each) / 25 days 9 packages (10.2 gm each) / 75 days
Symbicort Aerosphere (budesonide/ formoterol)	2 inhalations twice daily	4 inhalations	120 inhalations per 10.7 gm canister	1 package (10.7 gm each) / 25 days 3 packages (10.7 gm each) / 75 days
**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*				

LIMIT CRITERIA LONG-ACTING BETA2-ADRENERGIC AGONIST / ANTICHOLINERGIC / CORTICOSTEROID:
Limits do not accumulate together; patient is allowed the maximum limit for each drug and strength

PLEASE NOTE: Since manufacturer package sizes may vary, it is the discretion of the dispensing pharmacy to fill quantities per package size up to these quantity limits. In such cases the filling limit and day supply may be less than what is indicated.				
Medication	**Maintenance Dose**	**Maximum Daily Dose**	**Package Size**	**1 Month Limit* 3 Months Limit***
Breztri Aerosphere (budesonide/ glycopyrrolate/ formoterol fumarate)	2 inhalations twice daily	4 inhalations	120 inhalations per 10.7 gm canister	1 package (10.7 gm) / 25 days 3 packages (10.7 gm each) / 75 days
Trelegy Ellipta (fluticasone furoate/ umeclidinium/ vilanterol)	1 inhalation once daily	1 inhalation	30 inhalations (60 blisters) per inhaler	1 package (60 blisters) / 25 days 3 packages (60 blisters each) / 75 days
**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*				

REFERENCES

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3. AirDuo Digihaler [package insert]. Parsippany, NJ: Teva Pharmaceuticals USA, Inc.; April 2022.
4. AirDuo Respiclick [package insert]. Parsippany, NJ: Teva Pharmaceuticals USA, Inc.; April 2022.
5. Anoro Ellipta [package insert]. Research Triangle Park, NC: GlaxoSmithKline; August 2020.
6. Arcapta Neohaler [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; July 2021.
7. Bevespi Aerosphere [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; November 2020.
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QUANTITY LIMIT CRITERIA

DRUG CLASS	**SHORT ACTING BETA2-ADRENERGIC AGONIST ORAL INHALATION**
BRAND NAME* **(generic)**	**(albuterol inhalation solution)**
	PROAIR DIGIHALER **(albuterol)**
	PROAIR HFA **(albuterol)**
	PROAIR RESPICLICK **(albuterol)**
	PROVENTIL HFA **(albuterol)**
	VENTOLIN HFA **(albuterol)**
	XOPENEX SOLUTION **(levalbuterol)**
	XOPENEX CONCENTRATE **(levalbuterol)**
	XOPENEX HFA **(levalbuterol)**

Status: CVS Caremark Criteria
Type: Quantity Limit ***Ref # 1086-H***

**Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Albuterol Inhalation Solution 0.63mg/3mL (0.021%) and 1.25mg/3mL (0.042%)
Albuterol sulfate inhalation solution is indicated for the relief of bronchospasm in patients 2 to 12 years of age with asthma (reversible obstructive airway disease).

Albuterol Inhalation Solution 0.083% (2.5mg/3mL)
Albuterol sulfate inhalation solution is indicated for the relief of bronchospasm in patients 2 years of age and older with reversible obstructive airway disease and acute attacks of bronchospasm.

Albuterol Inhalation Solution 0.5% (2.5mg / 0.5mL)
0.5mL Vial

Albuterol sulfate inhalation solution is indicated for the relief of bronchospasm in patients 12 years of age and older with reversible obstructive airway disease and acute attacks of bronchospasm.
20mL Bottle
Albuterol sulfate inhalation solution is indicated for the relief of bronchospasm in patients 2 years of age and older with reversible obstructive airway disease and acute attacks of bronchospasm.

ProAir Digihaler
Bronchospasm
ProAir Digihaler is indicated for the treatment or prevention of bronchospasm in patients 4 years of age and older with reversible obstructive airway disease.
Exercise-Induced Bronchospasm
ProAir Digihaler is indicated for the prevention of exercise-induced bronchospasm in patients 4 years of age and older.

ProAir HFA
Bronchospasm
ProAir HFA Inhalation Aerosol is indicated for the treatment or prevention of bronchospasm in patients 4 years of age and older with reversible obstructive airway disease.
Exercise-Induced Bronchospasm
Proair HFA Inhalation Aerosol is indicated for the prevention of exercise-induced bronchospasm in patients 4 years of age and older.

ProAir Respiclick
Bronchospasm
ProAir Respiclick is indicated for the treatment or prevention of bronchospasm in patients 4 years of age and older with reversible obstructive airway disease.
Exercise-Induced Bronchospasm
ProAir Respiclick is indicated for the prevention of exercise-induced bronchospasm in patients 4 years of age and older.

Proventil HFA
Proventil HFA Inhalation Aerosol is indicated in adults and children 4 years of age and older for the treatment or prevention of bronchospasm with reversible obstructive airway disease and for the prevention of exercise-induced bronchospasm.

Ventolin HFA
Bronchospasm
Ventolin HFA is indicated for the treatment or prevention of bronchospasm in adult and pediatric patients aged 4 years and older with reversible obstructive airway disease.
Exercise-Induced Bronchospasm
Ventolin HFA is indicated for the prevention of exercise-induced bronchospasm in adult and pediatric patients aged 4 years and older.

Xopenex Solution
Xopenex (levalbuterol HCl) Inhalation Solution is indicated for the treatment or prevention of bronchospasm in adults, adolescents, and children 6 years of age and older with reversible obstructive airway disease.

Xopenex Concentrate
Xopenex (levalbuterol HCl) Inhalation Solution Concentrate is indicated for the treatment or prevention of bronchospasm in adults, adolescents, and children 6 years of age and older with reversible obstructive airway disease.

Xopenex HFA
Xopenex HFA is indicated for the treatment or prevention of bronchospasm in adults, adolescents, and children 4 years of age and older with reversible obstructive airway disease.

RATIONALE
The 1-month limit is a quantity sufficient at maximum recommended dosage for 30-day supply and the 3-month limit is 3 times the 1-month limit. If the patient is requesting more than the initial quantity limit, the claim will reject with a message indicating that quantity limits are exceeded.

More frequent administration, higher doses, or a larger number of inhalations is not recommended. If a previously effective dosage regimen fails to provide the usual response, this may be a marker of destabilization of asthma and requires reevaluation of the patient and the treatment regimen, giving special consideration to the possible need for anti-inflammatory treatment (e.g., corticosteroids).

Albuterol Sulfate Inhalation Solution[1]
0.63mg/3mL (0.021%) and 1.25mg/3mL (0.042%)
The usual starting dosage for patients 2 to 12 years of age is 1.25mg or 0.63mg of albuterol sulfate inhalation solution administered 3 or 4 times daily, as needed, by nebulization. Patients 6 to 12 years of age with more severe asthma, weight >40kg, or patients 11 to 12 years of age may achieve a better initial response with the 1.25mg dose.
Albuterol Sulfate Inhalation Solution 0.63mg and 1.25mg, are supplied as 3mL unit-dose vials available in cartons containing 25 vials and 30 vials.

Albuterol Sulfate Inhalation Solution[2]
0.083% (2.5mg/3mL)
The usual dosage for adults and for children weighing at least 15kg is 2.5mg of albuterol (one vial) administered three to four times daily by nebulization. Children weighing < 15kg who require < 2.5mg/dose (i.e., less than a full vial) should use albuterol inhalation solution, 0.5% instead of albuterol inhalation solution, 0.083%.
Albuterol Sulfate Inhalation Solution 0.083%, 2.5mg/3mL, equivalent to 0.5mL albuterol 0.5% (2.5mg albuterol) diluted to 3mL, is supplied in cartons of 25 vials, 30 vials, and 60 vials.

Albuterol Sulfate Inhalation Solution[3,4]
0.5% (2.5mg / 0.5mL)
20mL Bottle
For children 2 to 12 years of age, initial dosing should be based upon body weight (0.1 to 0.15 mg/kg per dose), with subsequent dosing titrated to achieve the desired clinical response. Dosing should not exceed 2.5mg three to four times daily by nebulization. The appropriate volume of the 0.5% inhalation solution should be diluted in sterile normal saline solution to a total volume of 3mL prior to administration via nebulization.

Approximate Weight (kg)	Dose (mg)	Volume of Inhalation Solution
10-15	1.25	0.25 mL
>15	2.5	0.5 mL

0.5mL Vial and 20mL Bottle
The usual dosage for adults and children 12 years of age and older is 2.5mg of albuterol (one unit-of-use vial) administered three to four times daily by nebulization. To administer 2.5mg of albuterol, dilute 0.5mL of the 0.5% inhalation solution with 2.5mL of sterile normal saline solution.
Albuterol Sulfate Inhalation Solution, 0.5%, 2.5mg / 0.5mL, is supplied in bottles of 20mL in a box of one, and as 30 vials (0.5mL each) per carton.

ProAir Digihaler[5]
For bronchospasm, the recommended dosage is 2 inhalations every 4 to 6 hours by oral inhalation. In some patients, 1 inhalation every 4 hours may be sufficient.
For exercise-induced bronchospasm, the recommended dosage is 2 inhalations 15 to 30 minutes before exercise by oral inhalation.
ProAir Digihaler inhalation powder is supplied as an inhaler in a box of one (net contents of 0.65gm) and provides 200 actuations.

ProAir HFA[6]
For treatment of acute episodes of bronchospasm or prevention of symptoms associated with bronchospasm, the usual dosage for adults and children 4 years and older is two inhalations repeated every 4 to 6 hours. In some patients, one inhalation every 4 hours may be sufficient.
For exercise-induced bronchospasm, the usual dosage for adults and children 4 years of age or older is two inhalations 15 to 30 minutes before exercise.

ProAir HFA Inhalation Aerosol is supplied as an 8.5 gm canister in a box of one and provides 200 actuations.

ProAir Respiclick[7]
The recommended dosage for bronchospasm is 2 inhalations every 4 to 6 hours by oral inhalation. In some patients, 1 inhalation every 4 hours may be sufficient.
The recommended dosage for exercise-induced bronchospasm is 2 inhalations 15 to 30 minutes before exercise by oral inhalation.
ProAir Respiclick inhalation powder is supplied as an inhaler in a box of one (net contents of 0.65gm) and provides 200 actuations.

Proventil HFA[8]
For treatment of acute episodes of bronchospasm or prevention of asthmatic symptoms, the usual dosage for adults and children 4 years of age and older is two inhalations repeated every 4 to 6 hours. In some patients, one inhalation every 4 hours may be sufficient.
For exercise-induced bronchospasm prevention, the usual dosage for adults and children 4 years of age and older is two inhalations 15 to 30 minutes before exercise.
Proventil HFA Inhalation Aerosol is supplied as a canister with a net weight of 6.7gm containing 200 inhalations.

Ventolin HFA[9]
For treatment of acute episodes of bronchospasm or prevention of symptoms associated with bronchospasm, the usual dosage for adults and pediatric patients aged 4 years and older is 2 inhalations repeated every 4 to 6 hours; in some patients, 1 inhalation every 4 hours may be sufficient.
For the prevention of exercise-induced bronchospasm, the usual dosage for adults and pediatric patients aged 4 years and older is 2 inhalations 15 to 30 minutes before exercise.
Ventolin HFA is supplied as an 18gm canister containing 200 actuations, and as an 8gm canister containing 60 actuations.

Xopenex Solution[10]
For children 6 to 11 years old, the recommended dosage of Xopenex Inhalation Solution is 0.31mg administered three times a day, by nebulization. Routine dosing should not exceed 0.63 mg three times a day.
For adults and adolescents 12 years of age and older, the recommended starting dosage of Xopenex Inhalation Solution for patients is 0.63mg administered three times a day, by nebulization. Patients 12 years of age and older with more severe asthma or patients who do not respond adequately to a dose of 0.63 mg of Xopenex Inhalation Solution may benefit from a dosage of 1.25 mg three times a day.
Xopenex Inhalation Solution is available in 3mL vials in strengths of 0.31mg, 0.63mg, and 1.25mg in a carton containing 24 unit-dose vials. Levalbuterol Inhalation Solution is also available as 25 vials and 30 vials (3mL each) per carton.

Xopenex Concentrate[11]
For children 6 to 11 years old, the recommended dosage of Xopenex Inhalation Solution Concentrate is 0.31mg administered three times a day, by nebulization. Routine dosing should not exceed 0.63 mg three times a day.
For adults and adolescents 12 years of age and older, the recommended starting dosage of Xopenex Inhalation Solution Concentrate is 0.63mg administered three times a day, every 6 to 8 hours, by nebulization.
Patients 12 years of age and older with more severe asthma or patients who do not respond adequately to a dose of 0.63mg of Xopenex Inhalation Solution may benefit from a dosage of 1.25mg three times a day.
For dosages less than 1.25mg, the non-concentrate (i.e., Xopenex Inhalation Solution, 3 mL) formulation must be used.
Xopenex Inhalation Solution Concentrate is to be diluted with sterile normal saline before administration by nebulization.
Xopenex Inhalation Solution Concentrate is supplied in 0.5mL unit-dose vials containing 1.25mg of levalbuterol and is available in cartons of 30 vials.

Xopenex HFA[12]
For treatment of acute episodes of bronchospasm or prevention of asthmatic symptoms, the recommended dosage of Xopenex HFA for adults and children 4 years of age and older is 2 inhalations (90 mcg of levalbuterol free base) repeated every 4 to 6 hours; in some patients, 1 inhalation (45 mcg of levalbuterol free base) every 4 hours may be sufficient.
Xopenex HFA is supplied as a canister with a net weight of 15gm containing 200 metered actuations.

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2. Albuterol 0.083% inhalation solution [package insert]. Columbia, SC: The Ritedose Corporation; September 2018.
3. Albuterol 0.5% inhalation solution (0.5mL)[package insert]. Orlando, FL: Nephron Pharmaceuticals Corporation; February 2019.
4. Albuterol sulfate inhalation solution, 0.5% (20mL) [package insert]. Amityville, NY: HI-Tech Pharmacal Co., Inc.; February 2017.
5. ProAir Digihaler [package insert]. Parsippany, NJ: Teva Pharmaceuticals USA, Inc.; October 2020.
6. ProAir HFA [package insert]. Parsippany, NJ: Teva Pharmaceuticals USA, Inc.; August 2020.
7. ProAir Respiclick [package insert]. Parsippany, NJ: Teva Pharmaceuticals USA, Inc.; April 2021.
8. Proventil HFA [package insert]. Princeton, NJ: Sandoz Inc..; December 2020.
9. Ventolin HFA [package insert]. Research Triangle Park, NC: GlaxoSmithKline; August 2021.
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11. Xopenex inhalation solution concentrate [package insert]. Lake Forest, IL: Akorn, Inc.; December 2018.
12. Xopenex HFA [package insert]. Marlborough, MA: Sunovion Pharmaceuticals, Inc.; February 2017.
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Written by: UM Development (KB)
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Reviewed: (MG) 06/2003, 11/2004, 03/2005 (Xopenex HFA and Albuterol HFA added); (NB) 03/2006, 09/2006 (Advair HFA added); (CT) 03/2007(2) (Perforomist added), 02/2008, 02/2009, 09/2009 (updated Xopenex soln limit 02/2009(2)), (MS) 01/2010; (RP) 02/2011, 07/2011 (Arcapta Neohaler added), 06/2012, (TM) 02/2013, 05/2013 (add Breo Ellipta), (TM) 11/2013 (separate short and long acting), 11/2014, (TM) 04/2015; (MS) 11/2015 (no clinical changes), (TM) 11/2016 (no clinical changes), 11/2017 (no clinical changes), (TM) 11/2018 (no clinical changes), (TM) 12/2018 (add ProAir Digihaler), (TM) 11/2019 (no clinical changes), (TM) 11/2020 (no clinical changes); (RZ) 09/2021 (no clinical changes)
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External Review: 08/2003, 12/2004, 11/2005, 06/2006, 06/2007, 06/2008, 06/2009, 06/2011, 10/2011, 10/2012, 06/2013, 01/2014, 02/2015, 02/2016, 02/2017, 02/2018, 02/2019 (FYI), 02/2019, 02/2020, 02/2021, 02/2022

LIMIT CRITERIA

Limits do not accumulate together; patient is allowed the maximum limit for each drug and strength

PLEASE NOTE: Since manufacturer package sizes may vary, it is the discretion of the dispensing pharmacy to fill quantities per package size up to these quantity limits. In such cases the filling limit and day supply may be less than what is indicated.

Medication*	Maintenance Dose	Maximum Daily Dose	Package Size	1 Month Limit* 3 Months Limit*
Albuterol 0.63mg / 3mL, 1.25mg / 3mL (0.021%, 0.042%) Inhalation Soln	nebulization of 1 vial (3mL) three to four times daily	4 vials (3mL each)	25 vials (3mL each) per carton	5 packages (125 vials x 3mL) / 25 days 15 packages (375 vials x 3mL) / 75 days
			30 vials (3mL each) per carton	4 packages (120 vials x 3mL) / 25 days 12 packages (360 vials x 3mL) / 75 days
Albuterol 0.083%, 2.5mg / 3mL Inhalation Solution	nebulization of 1 vial (3mL) three to four times daily	4 vials (3mL each)	25 vials (3mL each) per carton	5 packages (125 vials x 3mL) / 25 days 15 packages (375 vials x 3mL) / 75 days
			30 vials (3mL each) per carton	4 packages (120 vials x 3mL) / 25 days 12 packages (360 vials x 3mL) / 75 days
			60 vials (3mL each) per carton	2 packages (120 vials x 3mL) / 25 days 6 packages (360 vials x 3mL) / 75 days
Albuterol 0.5%, 2.5mg / 0.5mL Inhalation Solution	nebulization of 0.25mL-0.5mL three to four times daily	2mL	20mL per bottle	3 packages (20mL each) / 25 days 9 packages (20mL each) / 75 days
			30 vials (0.5mL each) per carton	4 packages (120 vials x 0.5mL) / 25 days 12 packages (360vials x 0.5mL) / 75 days

ProAir Digihaler (albuterol)	1-2 inhalations every 4 to 6 hours	12 inhalations	200 inhalations per inhaler	2 packages / 25 days 6 packages / 75 days
ProAir HFA (albuterol)	1-2 inhalations every 4 to 6 hours	12 inhalations	200 inhalations per 8.5gm canister	2 packages (8.5gm each) / 25 days 6 packages (8.5gm each) / 75 days
ProAir RespiClick (albuterol)	1-2 inhalations every 4 to 6 hours	12 inhalations	200 inhalations per inhaler	2 packages / 25 days 6 packages / 75 days
Proventil HFA (albuterol)	1-2 inhalations every 4 to 6 hours	12 inhalations	200 inhalations per 6.7gm canister	2 packages (6.7gm each) / 25 days 6 packages (6.7gm each) / 75 days
Ventolin HFA (albuterol)	1-2 inhalations every 4 to 6 hours	12 inhalations	60 inhalations per 8gm canister	6 packages (8gm each) / 25 days 18 packages (8gm each) / 75 days
			200 inhalations per 18gm canister	2 packages (18gm each) / 25 days 6 packages (18gm each) / 75 days
Xopenex 0.31mg,0.63mg, 1.25 mg / 3 mL (levalbuterol)	nebulization of 1 vial (3mL) three times daily	3 vials (3mL each)	24 vials (3mL each) per carton	4 packages (96 vials x 3mL) / 25 days 12 packages (288 vials x 3mL) / 75 days
			25 vials (3mL each) per carton	4 packages (100 vials x 3mL) / 25 days 12 packages (300 vials x 3mL) / 75 days
			30 vials (3mL each) per carton	3 packages (90 vials x 3mL) / 25 days 9 packages (270 vials x 3mL) / 75 days
Xopenex Concentrate 1.25mg / 0.5mL (levalbuterol)	nebulization of 1 vial (0.5mL) three times daily	3 vials (0.5mL each)	30 vials (0.5mL each) per carton	3 packages (90 vials x 0.5mL) / 25 days 9 packages (270 vials x 0.5mL) / 75 days
Xopenex HFA (levalbuterol)	1-2 inhalations every 4 to 6 hours	12 inhalations	200 inhalations per 15gm canister	2 packages (15gm each) / 25 days 6 packages (15gm each) / 75 days
**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*				

Reference number(s)
1840-A

SPECIALTY GUIDELINE MANAGEMENT

BETASERON (interferon beta-1b)
EXTAVIA (interferon beta-1b)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Betaseron and Extavia are indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.

All other indications are considered experimental/investigational and not medically necessary.

II. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with a neurologist.

III. CRITERIA FOR INITIAL APPROVAL

A. Relapsing forms of multiple sclerosis
Authorization of 12 months may be granted to members who have been diagnosed with a relapsing form of multiple sclerosis (including relapsing-remitting and secondary progressive disease for those who continue to experience relapse).

B. Clinically isolated syndrome
Authorization of 12 months may be granted to members for the treatment of clinically isolated syndrome of multiple sclerosis.

IV. CONTINUATION OF THERAPY

For all indications: Authorization of 12 months may be granted for members who are experiencing disease stability or improvement while receiving Betaseron or Extavia.

V. OTHER

Members will not use Betaseron or Extavia concomitantly with other disease modifying multiple sclerosis agents (Note: Ampyra and Nuedexta are not disease modifying).

VI. REFERENCES

1. Betaseron [package insert]. Whippany, NJ: Bayer HealthCare Pharmaceuticals Inc.; November 2021.
2. Extavia [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; November 2021.

Reference number(s)
1795-A

SPECIALTY GUIDELINE MANAGEMENT

Targretin (bexarotene) capsules
bexarotene capsules (generic)
Targretin (bexarotene) gel 1%
bexarotene gel 1% (generic)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
1. Targretin/bexarotene capsules are indicated for the treatment of cutaneous manifestations of cutaneous T-cell lymphoma (CTCL) in patients who are refractory to at least one prior systemic therapy.
2. Targretin gel is indicated for the topical treatment of cutaneous lesions in patients with CTCL (Stage IA and IB) who have refractory or persistent disease after other therapies or who have not tolerated other therapies.

B. Compendial Uses
1. Targretin/bexarotene capsules
   a. Mycosis fungoides (MF)
   b. Sézary syndrome (SS)
   c. Primary cutaneous CD30+ T-cell lymphoproliferative disorders:
      i. Primary cutaneous anaplastic large cell lymphoma (ALCL)
      ii. Lymphomatoid papulosis (LyP)
2. Targretin gel
   a. Mycosis fungoides (MF)
   b. Sézary syndrome (SS)
   c. Chronic or smoldering adult T-cell leukemia/lymphoma (ATLL)
   d. Primary cutaneous B-cell lymphoma:
      i. Primary cutaneous marginal zone lymphoma
      ii. Primary cutaneous follicle center lymphoma

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Targretin/bexarotene Capsules

1. Mycosis Fungoides (MF)/Sézary Syndrome (SS)
Authorization of 12 months may be granted for treatment of MF or SS.

2. Primary Cutaneous Anaplastic Large Cell Lymphoma (ALCL)/Lymphomatoid Papulosis (LyP)[4]

Authorization of 12 months may be granted for treatment of primary cutaneous ALCL or LyP as a single agent.

B. Targretin Gel

1. Mycosis Fungoides (MF)/Sézary syndrome (SS)
Authorization of 12 months may be granted for treatment of MF or SS.

2. Adult T-cell Leukemia/Lymphoma (ATLL)
Authorization of 12 months may be granted for treatment of chronic or smoldering ATLL.

3. Primary Cutaneous B-cell Lymphoma
Authorization of 12 months may be granted for treatment of primary cutaneous marginal zone lymphoma or primary cutaneous follicle center lymphoma.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

IV. REFERENCES

1. Targretin capsules [package insert]. St. Petersburg, FL: Catalent Pharma Solutions LLC; April 2020.
2. Targretin gel [package insert]. San Antonio, TX: DPT Laboratories, Ltd.; February 2020.
3. Bexarotene capsule [package insert]. Bridgewater, NJ: Amneal Pharmaceuticals LLC; December 2022.
4. Bexarotene gel [package insert]. Bridgewater, NJ: Amneal Pharmaceuticals LLC; April 2022.
5. The NCCN Drugs & Biologics Compendium® © 2023 National Comprehensive Cancer Network, Inc. Available at: https://www.nccn.org. Accessed January 3, 2023.

Reference number(s)
1649-A

SPECIALTY GUIDELINE MANAGEMENT

TRACLEER (bosentan)
bosentan (generic)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Indicated for the treatment of pulmonary arterial hypertension (PAH) (World Health Organization [WHO] Group 1):

A. In adults to improve exercise ability and to decrease clinical worsening. Studies establishing effectiveness included predominantly patients with WHO Functional Class II-IV symptoms and etiologies of idiopathic or heritable PAH, PAH associated with connective tissue diseases, and PAH associated with congenital heart disease with left-to-right shunts.
B. In pediatric patients aged 3 years and older with idiopathic or congenital PAH to improve pulmonary vascular resistance (PVR), which is expected to result in an improvement in exercise ability.

All other indications are considered experimental/investigational and not medically necessary.

II. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with a pulmonologist or cardiologist.

III. CRITERIA FOR INITIAL APPROVAL

Pulmonary Arterial Hypertension (PAH)
Authorization of 12 months may be granted for treatment of PAH when ALL of the following criteria are met:

A. Member has PAH defined as WHO Group 1 class of pulmonary hypertension (refer to Appendix).
B. PAH was confirmed by either criterion (1) or criterion (2) below:
    1. Pretreatment right heart catheterization with all of the following results:
        i. mPAP > 20 mmHg
        ii. PCWP ≤ 15 mmHg
        iii. PVR ≥ 3 Wood units
    2. For infants less than one year of age, PAH was confirmed by Doppler echocardiogram if right heart catheterization cannot be performed.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for members with an indication listed in Section III who are currently receiving the requested medication through a paid pharmacy or medical benefit, and who are experiencing benefit from therapy as evidenced by disease stability or disease improvement.

V. APPENDIX

WHO Classification of Pulmonary Hypertension

1 PAH

1.1 Idiopathic (PAH)
1.2 Heritable PAH
1.3 Drug- and toxin-induced PAH
1.4. PAH associated with:
- 1.4.1 Connective tissue diseases
- 1.4.2 HIV infection
- 1.4.3 Portal hypertension
- 1.4.4 Congenital heart diseases
- 1.4.5 Schistosomiasis

1.5 PAH long-term responders to calcium channel blockers
1.6 PAH with overt features of venous/capillaries (PVOD/PCH) involvement
1.7 Persistent PH of the newborn syndrome

2 PH due to left heart disease

2.1 PH due to heart failure with preserved LVEF
2.2 PH due to heart failure with reduced LVEF
2.3 Valvular heart disease
2.4 Congenital/acquired cardiovascular conditions leading to post-capillary PH

3 PH due to lung diseases and/or hypoxia

3.1 Obstructive lung disease
3.2 Restrictive lung disease
3.3 Other lung disease with mixed restrictive/obstructive pattern
3.4 Hypoxia without lung disease
3.5 Developmental lung disorders

4 PH due to pulmonary artery obstruction

4.1 Chronic thromboembolic PH
4.2 Other pulmonary artery obstructions
- 4.2.1 Sarcoma (high or intermediate grade) or angiosarcoma
- 4.2.2 Other malignant tumors
  - Renal carcinoma
  - Uterine carcinoma
  - Germ cell tumours of the testis
  - Other tumours
- 4.2.3 Non-malignant tumours
  - Uterine leiomyoma
- 4.2.4 Arteritis without connective tissue disease
- 4.2.5 Congenital pulmonary artery stenosis
- 4.2.6 Parasites
  - Hydatidosis

5 PH with unclear and/or multifactorial mechanisms

5.1 Hematologic disorders: Chronic hemolytic anemia, myeloproliferative disorders
5.2 Systemic and metabolic disorders: Pulmonary Langerhans cell histiocytosis, Gaucher disease, glycogen storage disease, neurofibromatosis, sarcoidosis

5.3 Others: chronic renal failure with or without hemodialysis, fibrosing mediastinitis
5.4 Complex congenital heart disease

VI. REFERENCES

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Reference number(s)
2171-A

SPECIALTY GUIDELINE MANAGEMENT

BOSULIF (bosutinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
Adult patients with:
1. Newly-diagnosed chronic phase (CP) Philadelphia chromosome-positive chronic myelogenous leukemia (Ph+ CML)
2. Chronic phase, accelerated phase (AP), or blast phase (BP) Ph+ CML with resistance or intolerance to prior therapy

B. Compendial Uses
1. Primary treatment of patients with advanced phase CML (accelerated phase or blast phase)
2. Follow-up therapy for CML patients after hematopoietic stem cell transplant (HSCT)
3. Ph+ B-cell acute lymphoblastic leukemia or lymphoblastic lymphoma (Ph+ B-ALL/LL)
4. Maintenance therapy for Ph+ B-ALL/LL patients after HSCT
5. Myeloid/lymphoid neoplasms with eosinophilia and ABL1 rearrangement in chronic phase
6. Lymphoid, myeloid or mixed lineage neoplasms with eosinophilia and ABL1 rearrangement in blast phase

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

The following information is necessary to initiate the prior authorization review:
A. Prior to initiation of therapy for treatment of CML or Ph+ B-ALL/LL: results of cytogenetic and/or molecular testing for detection of the Ph chromosome or the BCR-ABL gene
B. For members requesting initiation of therapy with the requested medication for treatment of CML or Ph+ B-ALL/LL after experiencing resistance to prior tyrosine kinase inhibitor (TKI) therapy: results of BCR-ABL1 mutation testing including T315I, G250E, V299L, F317L mutations
C. For members requesting initiation of therapy with the requested medication for treatment of myeloid and/or lymphoid neoplasms with eosinophilia: results of testing or analysis confirming ABL1 rearrangement

III. CRITERIA FOR INITIAL APPROVAL

A. Chronic Myeloid Leukemia (CML)

Authorization of 7 months may be granted for treatment of CML that has been confirmed by detection of the Ph chromosome or BCR-ABL gene by cytogenetic and/or molecular testing when any of the following criteria are met:

1. Member has not received prior therapy with a tyrosine kinase inhibitor (TKI) (e.g., dasatinib, imatinib, nilotinib, ponatinib)
2. Member experienced toxicity or intolerance to prior therapy with a TKI
3. Member experienced resistance to prior therapy with a TKI and results of BCR-ABL1 mutation testing are negative for all of the following: T315I, G250E, V299L, and F317L
4. Member has received HSCT for CML and results of BCR-ABL1 mutation testing are negative for all of the following: T315I, G250E, V299L, and F317L

B. Ph+ B-Cell Acute Lymphoblastic Leukemia (B-ALL)/Lymphoblastic Lymphoma (B-LL)

Authorization of 12 months may be granted for treatment Ph+ B-ALL/LL that has been confirmed by detection of Ph chromosome or BCR-ABL gene by cytogenetic and/ or molecular testing when any of the following criteria are met:

1. Member has not received prior therapy with a TKI (e.g., dasatinib, imatinib, nilotinib, ponatinib)
2. Member experienced intolerance or toxicity to prior therapy with a TKI
3. Member experienced resistance to prior therapy with a TKI and results of BCR-ABL1 mutation testing are negative for all of the following: T315I, G250E, V299L, and F317L
4. Member has received HSCT for Ph+ B-ALL/LL and results of BCR-ABL1 mutation testing are negative for all of the following: T315I, G250E, V299L, and F317L

C. Myeloid/Lymphoid Neoplasms with Eosinophilia

Authorization of 12 months may be granted for treatment of myeloid and/or lymphoid neoplasms with eosinophilia and ABL1 rearrangement in the chronic phase or blast phase.

IV. CONTINUATION OF THERAPY

A. CML

Authorization may be granted for continued treatment of CML that has been confirmed by detection of Ph chromosome or BCR-ABL gene by cytogenetic and/ or molecular testing when either of the following criteria are met:

1. Authorization of 12 months may be granted when any of the following criteria is met:
   a. BCR-ABL1 is less than or equal to 10% and there is no evidence of disease progression or unacceptable toxicity while on the current regimen for members who have been receiving the requested medication for 6 months or greater
   b. Member has received HSCT and there is no evidence of unacceptable toxicity or disease progression while on the current regimen
2. Authorization of up to 7 months may be granted when the member has completed less than 6 months of therapy with the requested medication.

B. Ph+ B-ALL/LL

Authorization of 12 months may be granted for continued treatment of B-ALL/LL when there is no evidence of unacceptable toxicity or disease progression while on the current regimen and either of the following criteria is met:

1. Member has Ph+ B-ALL/LL that has been confirmed by detection of Ph chromosome or BCR-ABL gene by cytogenetic and/ or molecular testing
2. Member has received HSCT for B-ALL/LL

C. Myeloid/Lymphoid Neoplasms with Eosinophilia
Authorization of 12 months may be granted for continued treatment in members requesting reauthorization when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

V. REFERENCES

1. Bosulif [package insert]. New York, NY: Pfizer Inc.; October 2021.
2. The NCCN Drugs & Biologics Compendium® © 2022 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed April 6, 2022.
3. NCCN Clinical Practice Guidelines in Oncology® Chronic Myeloid Leukemia (Version 3.2022). © 2022 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed April 6, 2022.
4. NCCN Clinical Practice Guidelines in Oncology® Acute Lymphoblastic Leukemia (Version 1.2022). © 2022 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed April 6, 2022.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME*
(generic)

CIALIS 2.5 mg, 5 mg
(tadalafil)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization with Quantity Limit ***Ref # 865-C***

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Erectile Dysfunction
Cialis is indicated for the treatment of erectile dysfunction (ED).
Benign Prostatic Hyperplasia
Cialis is indicated for the treatment of the signs and symptoms of benign prostatic hyperplasia (BPH).
Erectile Dysfunction and Benign Prostatic Hyperplasia
Cialis is indicated for the treatment of ED and the signs and symptoms of BPH (ED/BPH).

Limitation of Use
If Cialis is used with finasteride to initiate BPH treatment, such use is recommended for up to 26 weeks because the incremental benefit of Cialis decreases from 4 weeks until 26 weeks, and the incremental benefit of Cialis beyond 26 weeks is unknown.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for daily use for symptomatic benign prostatic hyperplasia (BPH) [Note: Examples of signs and symptoms of BPH are incomplete emptying, weak stream, straining, urinary frequency, intermittency, or urgency.]

Quantity Limits apply.

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Cialis is indicated for the treatment of erectile dysfunction (ED), for the treatment of the signs and symptoms of benign prostatic hyperplasia (BPH), and for the treatment of ED and the signs and symptoms of BPH (ED/BPH).[1-3] However, the diagnosis of ED will not be included in these criteria for approval. Cialis is not indicated for use in pediatric patients. Safety and efficacy in patients below the age of 18 years have not been established.

According to the American Urological Association (AUA) BPH guidelines, the most prevalent and generally first line approach to the treatment of male lower urinary tract symptoms secondary/attributed to BPH (LUTS/BPH) is behavioral and lifestyle modifications followed by medical therapy, including alpha-adrenergic antagonists (alpha blockers), 5-alpha reductase inhibitors (5ARIs), phosphodiesterase 5 selective inhibitors (PDE5s), anticholinergics, and beta-3 agonists - which may be utilized alone, or in combination to take advantage of their different mechanisms of action. Clinicians should offer one of the following alpha blockers as a treatment option for patients with bothersome, moderate to severe LUTS/BPH: alfuzosin, doxazosin, silodosin, tamsulosin, or terazosin. 5-ARIs alone or in combination with alpha blockers are recommended as a treatment option to prevent progression of LUTS/BPH and/or reduce the risks of urinary retention and need for future prostate-related surgery.[4] For patients with LUTS/BPH irrespective of comorbid erectile dysfunction

(ED), 5 mg daily tadalafil should be discussed as a treatment option. In clinical studies, tadalafil improved lower urinary tract symptoms associated with BPH (e.g., urinary frequency, urgency, nocturia, straining, incomplete emptying, weak urinary stream) but generally did not affect peak urinary flow rate or postvoid residual volume.[2]

The recommended dose of Cialis for once daily use for BPH is 5 mg, taken at approximately the same time every day. For BPH, a starting dose of 2.5 mg is recommended for creatinine clearance 30 to 50 mL/min.[1-3] The quantity for approval for Cialis 2.5 mg and 5 mg will be 30 tablets per month.

REFERENCES

1. Cialis [package insert]. Indianapolis, IN: Eli Lilly and Company; June 2020.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2022; Accessed March 31, 2022.
3. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed March 31, 2022.
4. Management of Lower Urinary Tract Symptoms Attributed to Benign Prostatic Hyperplasia: AUA Guideline Part I Initial Work-up and Medical Management. J.Urol. October 2021; Vol 206, 806-817.

Written by:	UM Development (SE)
Date Written:	10/2011
Revised:	(TM) 05/2012; (PL) 10/2012 (extended duration); (TM) 04/2013; (CT) 04/2014; (CF) 04/2015; (JH) 04/2016; (KM) 04/2017 (removed contraindication question, added limit question); (KC) 04/2018 (no clinical changes); (KC/CF) 04/2019 (no clinical changes); (KC) 04/2020 (no clinical changes), 08/2020 (updated note in diagnosis question), 04/2021 (no clinical changes); (PM) 10/2021 (updated short descriptions), (VLS) 03/2022 (no clinical changes)
Reviewed:	Medical Affairs: (KP) 10/2011; (DR) 05/2012; (DC) 04/2013; (KP) 04/2014; (ADA) 04/2015; (TP) 04/2016; (JG) 04/2017; (CHART) 04/30/20, 09/03/20, 04/22/21, (CHART) 04/28/2022 External Review: 11/2011, 06/2012, 08/2013, 08/2014, 08/2015, 08/2016, 08/2017, 08/2018, 08/2019, 08/2020, 08/2021, 08/2022

CRITERIA FOR APPROVAL

1	Is the requested drug being prescribed for daily use for symptomatic benign prostatic hyperplasia (BPH)? [Note: Examples of signs and symptoms of BPH are incomplete emptying, weak stream, straining, urinary frequency, intermittency, or urgency.] [If no, then no further questions.]	Yes	No
2	Does the patient require MORE than the plan allowance of 1 tablet per day? [RPh Note: If yes, then deny and enter a partial approval for 30 tablets / 25 days or 90 tablets / 75 days of Cialis 2.5 mg or Cialis 5 mg.]	Yes	No

Guidelines for Approval	
Duration of Approval	**36 months**
Quantity for Approval	**30 tablets per 25 days* 90 tablets per 75 days***
Set 1	
Yes to question(s)	**No to question(s)**
1	2

**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*

Mapping Instructions				
	Yes	**No**	**DENIAL REASONS (Non-Medicaid, Non-Medicare Part D)**	**DENIAL REASONS (Medicaid)**
1.	Go to 2	Deny	Coverage for this medication is denied for the following reason(s). We reviewed the information we received about your condition and circumstances. We used the policy (INSERT CRITERIA NAME) when making this decision. The policy states that this medication may be approved when the member is requesting the medication for daily use for symptomatic benign prostatic hyperplasia (BPH). Based on the policy and the information we have, the request is denied. The request was denied because the information provided to us indicates that you are not requesting the medication for the treatment of symptomatic benign prostatic hyperplasia (BPH). [Short Description: No approvable diagnosis]	You do not meet the requirements of your plan. Your plan covers this drug when you have benign prostatic hyperplasia (BPH) that is causing symptoms. Your request has been denied based on the information we have. [Short Description: No approvable diagnosis - Medicaid]
2.	Deny	Approve, 36 months 30 tablets per 25 days* 90 tablets per 75 days*	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 30 tablets per month of the requested drug and strength. Your request has been partially approved. You have been approved for the maximum quantity that your plan covers for a duration of 36 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity]	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 30 tablets per month of the requested drug and strength. Your request has been partially approved. You have been approved for the maximum quantity that your plan covers for a duration of 36 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity - Medicaid]

** The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*

Reference number
2616-A

SPECIALTY GUIDELINE MANAGEMENT

BRAFTOVI (encorafenib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met, and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication
1. Braftovi is indicated, in combination with binimetinib, for the treatment of patients with unresectable or metastatic melanoma with a BRAF V600E or V600K mutation, as detected by an FDA-approved test.

2. Braftovi is indicated, in combination with cetuximab, for the treatment of adult patients with metastatic colorectal cancer (CRC) with a BRAF V600E mutation, as detected by an FDA-approved test, after prior therapy.

Limitations of use: Braftovi is not indicated for treatment of patients with wild-type BRAF melanoma or wild-type BRAF CRC.

B. Compendial Uses
1. Glioma, BRAF V600 activating mutation-positive
2. Meningioma, BRAF V600 activating mutation-positive
3. Astrocytoma, BRAF V600 activating mutation-positive
4. Colorectal cancer, advanced disease
5. Colorectal cancer, unresectable metachronous metastases
6. Cutaneous melanoma

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of BRAF mutation documentation is necessary to initiate the prior authorization review.

III. CRITERIA FOR INITIAL APPROVAL

A. Cutaneous Melanoma
Authorization of 12 months may be granted for treatment of cutaneous melanoma with a BRAF V600 activating mutation (e.g., V600E or V600K) in any of the following settings:
1. Unresectable or metastatic disease when used either:
   i. in combination with binimetinib (Mektovi), or
   ii. as a single agent if BRAF/MEK inhibitor combination therapy is contraindicated
2. Adjuvant treatment of resected stage III disease in combination with binimetinib (Mektovi) when the member has had an unacceptable toxicity to dabrafenib (Tafinlar) in combination with trametinib (Mekinist) or dabrafenib/trametinib are less desirable based on side-effect profiles.

3. Limited resectable local satellite/in-transit recurrent disease in combination with binimetinib (Mektovi) when the member has had an unacceptable toxicity to dabrafenib (Tafinlar) in combination with trametinib (Mekinist) or dabrafenib/trametinib are less desirable based on side-effect profiles

B. Central Nervous System Cancer
Authorization of 12 months may be granted for treatment of BRAF V600 mutation-positive (e.g., BRAF V600E or V600K) gliomas, meningiomas, or astrocytomas.

C. Colorectal Cancer
Authorization of 12 months may be granted for treatment of colorectal cancer (including appendiceal adenocarcinoma) when the following criteria are met:
1. Braftovi is used in combination with either cetuximab (Erbitux) or panitumumab (Vectibix).
2. Tumor is positive for BRAF V600E mutation.
3. Either of the following:
   a. Will be used as subsequent therapy for advanced or metastatic disease
   b. Will be used as primary treatment for unresectable metachronous metastases and previous adjuvant FOLFOX (fluorouracil, leucovorin, and oxaliplatin) or CapeOX (capecitabine and oxaliplatin) within the past 12 months

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

V. REFERENCES

1. Braftovi [package insert]. Boulder, CO: Array BioPharma, Inc.; February 2022.
2. The NCCN Drugs & Biologics Compendium® © 2022 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed November 11, 2022.
3. Usubalieva A, Pierson CR, Kavran CA, et al. Primary Meningeal Pleomorphic Xanthoastrocytoma With Anaplastic Features: A Report of 2 Cases, One With *BRAFV600E* Mutation and Clinical Response to the *BRAF* Inhibitor Dabrafenib. *Journal of neuropathology and experimental neurology*. 2015;74(10):960-969. doi:10.1097/NEN.0000000000000240.
4. Mordechai O, Postovsky S, Vlodavsky E, et al. Metastatic Rhabdoid Meningioma with *BRAF* V600E Mutation and Good Response to Personalized Therapy: Case Report and Review of the Literature. *Pediatric Hematology and Oncology*. 2015; 32:3, 207-211, DOI: 10.3109/08880018.2014.936058
5. Lassaletta, A, Guerreiro Stucklin, A, Ramaswamy, V, et al. Profound clinical and radiological response to BRAF inhibition in a 2-month-old diencephalic child with hypothalamic/chiasmatic glioma. *Pediatric Blood and Cancer*. 2016; 63: 2038-2041. doi:10.1002/pbc.26086.
6. Meletah SK, Pavlick D, Brennan T, et al. Personalized Treatment for a Patient with a BRAF V600E Mutation using Dabrafenib and a Tumor Treatment Fields Device in a High-Grade Glioma Arising from Ganglioglioma. *Journal of the National Comprehensive Cancer Network.* 2016; 14(11): 1345-1350.

STEP THERAPY CRITERIA

BRAND NAME
(generic)

BREXAFEMME
(ibrexafungerp)

Status: CVS Caremark Criteria
Type: Initial Step Therapy with Quantity Limit;
Post Step Therapy Prior Authorization with Quantity Limit

POLICY

FDA-APPROVED INDICATIONS
Brexafemme is indicated in adult and post-menarchal pediatric females for:
- Treatment of vulvovaginal candidiasis (VVC)
- Reduction in the incidence of recurrent vulvovaginal candidiasis (RVVC).

INITIAL STEP THERAPY with QUANTITY LIMIT*
***Include Rx and OTC products unless otherwise stated.*

If the patient has filled a prescription for at least a 1-day supply of generic fluconazole within the past 180 days under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit.** If the patient does not meet the initial step therapy criteria, then the claim will reject with a message indicating that a prior authorization (PA) is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

**If the patient meets the initial step therapy criteria, then the initial limit criteria will apply. If the patient is requesting more than the initial quantity limit the claim will reject with a message indicating that a PA is required.

****INITIAL LIMIT CRITERIA**
Limits should accumulate across all drugs and strengths up to highest quantity listed depending on the order the claims are processed.

Drug	Limit*
Brexafemme (ibrexafungerp)	4 tablets / 7 days

**** This drug is for short-term, acute use.***

COVERAGE CRITERIA
The requested drug will be covered with prior authorization when the following criteria are met:
- The requested drug is being prescribed for the treatment of vulvovaginal candidiasis (VVC)

OR
- The requested drug is being prescribed for reduction in the incidence of recurrent vulvovaginal candidiasis (RVVC)

AND
- The requested drug is being prescribed for an adult or post-menarchal pediatric patient

AND
  - The patient has experienced an inadequate treatment response to a course of therapy with fluconazole

  OR
  - The patient has experienced an intolerance to fluconazole

  OR

- The patient has a contraindication that would prohibit a trial of fluconazole

AND

- The requested drug is not being used in a footbath

Quantity Limits apply.
Vulvovaginal candidiasis: 4 tablets per 7 days
Recurrent vulvovaginal candidiasis: 4 tablets per 25 days* or 12 tablets per 75 days*
**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*

REFERENCES

1. Brexafemme [package insert]. Jersey City, NJ: SCYNEXIS, Inc.; November 2022.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2022; Accessed December 5, 2022.
3. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed December 5, 2022.
4. Pappas PG, Kauffman CA, Andes DR, et al. Clinical practice guideline for the management of candidiasis: 2016 update by the infectious diseases society of America. *Clin Infect Dis*. 2016;62(4):e1-e50.
5. Paladine HL, Desai UA. Vaginitis: diagnosis and treatment. *Am Fam Physician*. 2018;97(5):321-329.

Reference number(s)
4338-A

SPECIALTY GUIDELINE MANAGEMENT

BRONCHITOL (mannitol inhalation powder)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Bronchitol is indicated as add-on maintenance therapy to improve pulmonary function in adult patients 18 years and older with Cystic Fibrosis. Use Bronchitol only for adults who have passed the Bronchitol Tolerance Test.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Cystic Fibrosis
Authorization of 12 months may be granted for treatment of cystic fibrosis when all of the following criteria are met:
A. Bronchitol will be used as add-on maintenance therapy for cystic fibrosis.
B. The member has passed the Bronchitol Tolerance Test and did not experience any of the following during the test:
    1. Bronchospasm
    2. Decrease in FEV1
    3. Decrease in oxygen saturation
C. The member is at least 18 years of age.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II who are experiencing benefit from therapy as evidenced by disease stability or disease improvement (e.g., improvement in FEV1 from baseline).

IV. REFERENCES

1. Bronchitol [package insert]. Cary, NC: Chiesi USA, Inc.; October 2020.

CVS caremark®

Reference number(s)
3411-A

SPECIALTY GUIDELINE MANAGEMENT

BRUKINSA (zanubrutinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication
Brukinsa is a kinase inhibitor indicated for the treatment of adult patients with:
1. Mantle cell lymphoma (MCL) who have received at least one prior therapy.
2. Waldenstrom's macroglobulinemia (WM).
3. Relapsed or refractory marginal zone lymphoma (MZL) who have received at least one anti-CD20-based regimen.
4. Chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL)

B. Compendial Use
1. Mantle Cell Lymphoma
2. Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma
3. Gastric MALT Lymphoma (Extranodal Marginal Zone Lymphoma of the Stomach)/Non-gastric MALT Lymphoma (Extranodal Marginal Zone Lymphoma of Nongastric Sites)
4. Nodal Marginal Zone Lymphoma
5. Splenic Marginal Zone Lymphoma
6. Waldenstrom Macroglobulinemia/Lymphoplasmacytic lymphoma/Bing-Neel Syndrome

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
Test results confirming TP53 mutation, where applicable

III. CRITERIA FOR INITIAL APPROVAL

A. Mantle Cell Lymphoma
Authorization of 12 months may be granted for treatment of mantle cell lymphoma when any of the following criteria are met:
1. The requested medication will be used as a single agent when the member has received at least one prior therapy.
2. The requested medication will be used as a component of TRIANGLE regimen for members with TP53 mutations for induction therapy.
TRIANGLE regimen = alternating RCHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone) + Brukinsa/RDHAP (rituximab, dexamethasone, and cytarabine) + platinum (carboplatin, cisplatin, or oxaliplatin) regimen
3. The requested medication will be used in combination with rituximab for maintenance therapy.

B. Chronic Lymphocytic Leukemia (CLL)/Small Lymphocytic Lymphoma (SLL)
Authorization of 12 months may be granted for treatment of CLL/SLL when used as a single agent.

C. Marginal Zone Lymphoma
Authorization of 12 months may be granted for treatment of marginal zone lymphoma, including gastric MALT lymphoma (extranodal marginal zone lymphoma of the stomach), non-gastric MALT lymphoma (extranodal marginal zone lymphoma of nongastric sites), nodal marginal zone lymphoma and splenic marginal zone lymphoma, when used as subsequent therapy for members who have received an anti-CD20 based-regimen (e.g., rituximab or obinutuzumab).

D. Waldenstrom Macroglobulinemia/Lymphoplasmacytic Lymphoma/Bing-Neel Syndrome
Authorization of 12 months may be granted for treatment of Waldenstrom macroglobulinemia/Lymphoplasmacytic lymphoma when used as a single agent or for the treatment of Bing-Neel syndrome when used as a single agent or in combination with rituximab.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

V. REFERENCES

1. Brukinsa [package insert]. San Mateo, CA: BeiGene USA, Inc.; April 2023.
2. The NCCN Drugs & Biologics Compendium® © 2023 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed June 2, 2023.
3. Eskelund CW, Dahl C, Hansen JW, et al. TP53 mutations identify younger mantle cell lymphoma patients who do not benefit from intensive chemoimmunotherapy. *Blood.* 2017;130(17):1903-1910.

QUANTITY LIMIT PRIOR AUTHORIZATION CRITERIA

BRAND NAME*
(generic)
(buprenorphine sublingual tablets)

Status: CVS Caremark Criteria ***REG***
Type: Quantity Limit; Post Limit Prior Authorization ***Ref # 2328-HJ***

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS
Buprenorphine sublingual tablets are indicated for the treatment of opioid dependence and are preferred for induction. Buprenorphine sublingual tablets should be used as part of a complete treatment plan to include counseling and psychosocial support.

INITIAL QUANTITY LIMIT*

Limits do not accumulate together; patient is allowed the maximum limit for each drug and strength.

Drug	1 Month Limit**
Buprenorphine sublingual tablets	90 tablets / 25 days

***The duration of 25 days is used for a 30-day fill period to allow time for refill processing.*

**If the patient is requesting more than the initial quantity limit, then the claim will reject with a message indicating that the quantity limit is exceeded.*

DURATION LIMIT*

Drug	Duration Limit (per 3 months)
Buprenorphine sublingual tablets	30-day supply

**If the patient is requesting more than a cumulative 30-day supply within the past 3 months, then the claim will reject with a message indicating that a prior authorization is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.*

COVERAGE CRITERIA
- The requested drug will be covered with prior authorization when the following criteria are met:
  - The requested drug is being prescribed for induction therapy and/or subsequent maintenance therapy for treatment of opioid use disorder

  AND
  - The patient is pregnant or breastfeeding

Quantity limits apply.

RATIONALE
For induction, the dosage of buprenorphine should be individualized based on the type and degree of opioid use disorder and the timing of last use. For maintenance, the typical dosing range of buprenorphine is 4 to 24 mg once daily. Doses higher than this have not been demonstrated to provide any clinical advantage.[1-3] Buprenorphine sublingual tablets are

available in 2 mg and 8 mg strengths, therefore initial quantity limits will be set to allow 90 tablets per month to allow for a maximum of 24 mg per day at the highest available strength.

If the patient is requesting more than the initial quantity limit of 90 tablets per month, then the claim will reject with a message indicating that the quantity limit is exceeded. Also, if the patient is requesting more than a cumulative 30-day supply within the past 3 months, then the claim will reject with a message indicating that a prior authorization is required. The prior authorization (PA) criteria would then be applied to requests submitted for evaluation to the PA unit. The initial quantity limit and duration limit will allow the patient to complete the first 30 days of treatment without requiring prior authorization.

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Buprenorphine sublingual tablets are indicated for the treatment of opioid dependence and are preferred for induction. Buprenorphine sublingual tablets should be used as part of a complete treatment plan to include counseling and psychosocial support; however, treatment can be initiated prior to these additional services starting.[1-3]

Buprenorphine is an effective treatment recommended for patients who have opioid use disorder, are able to give informed consent, and have no specific contraindications for agonist treatment. Treatment with buprenorphine has the following four goals: 1) To suppress opioid withdrawal, 2) To block the effects of illicit opioids, 3) To reduce opioid craving and stop or reduce the use of illicit opioids, 4) To promote and facilitate patient engagement in recovery-oriented activities including psychosocial intervention.[4]

At initiation, the risk of precipitated withdrawal can be reduced by using a lower initial dose of buprenorphine. An initial dose of 2-4 mg and observation of the patient for signs of precipitated withdrawal is recommended. If 60-90 minutes have passed without the onset of withdrawal symptoms, then additional dosing can be done in increments of 2-8 mg. Once it has been established that the initial dose is well tolerated, the buprenorphine dose can be increased fairly rapidly to a dose that provides stable effects for 24 hours and is clinically effective.[4]

After initiation, evidence suggests that buprenorphine doses of 16 mg or more per day or more may be more effective than lower doses at suppressing illicit opioid use. The FDA generally recommends dosing to a limit of 24 mg per day, noting that there is limited evidence regarding the relative efficacy of higher doses. In addition, the use of higher doses may increase the risk of diversion. There is no recommended time limit for treatment with buprenorphine. Clinicians should not encourage patients to discontinue and detoxification only strategies should not be used as a standard. While research is limited, available research generally suggests that longer duration of treatment results in better outcomes.[4]

Providers should discuss treatment options as well as risks and benefits with the patient and document the decision in her chart. For women who are pregnant or breastfeeding and have opioid use disorder, opioid agonist treatment with methadone or buprenorphine is the most appropriate treatment, taking into consideration effects on the fetus, neonatal opioid withdrawal syndrome, and impacts on perinatal care and parenting of young children.[4]

There is a growing body of evidence comparing outcomes related to methadone and buprenorphine treatment during pregnancy. Infants born to mothers treated with buprenorphine had shorter hospital stays (10 vs. 17.5 days), had shorter treatment durations for neonatal opioid withdrawal syndrome (NOWS) (4.1 vs. 9.9 days), and required a lower cumulative dose of morphine (1.1 vs. 10.4 mg) to treat NOWS compared to infants born to mothers on treatment with methadone. However, in this trial, mothers treated with buprenorphine were more likely to drop out of treatment compared to mothers treated with methadone. Larger studies are needed comparing the safety and effectiveness of buprenorphine versus methadone in the obstetric population.[4]

While the evidence on the safety and efficacy of naloxone in pregnant women remains limited, the combination buprenorphine/naloxone product is frequently used and the consensus of the guideline committee is that the combination product is safe and effective for this population. Naloxone is minimally absorbed when these medications are taken as prescribed.[4] However, according to the U.S. Department of Health and Human Services' Treatment Improvement Protocol (TIP) 63 guidelines, the buprenorphine monoproduct (without naloxone) has been recommended for the treatment of pregnant women because of the danger to the fetus of precipitated opioid withdrawal if the combination product were to be injected. Although there are some publications with small sample sizes that indicate that the combination product appears to be safe in pregnancy the safety data are insufficient at this time to recommend its use. This is an area of some

uncertainty. An expert panel on the treatment of OUD in pregnancy was unable to agree whether pregnant women should be treated with the monoproduct or combination product.[5] Because of this less than definitive consensus, buprenorphine sublingual tablets will be approved for a duration of 12 months when being prescribed for induction therapy and/or subsequent maintenance therapy for treatment of opioid use disorder for pregnant and breastfeeding patients.

Buprenorphine sublingual tablets are available in 2 mg and 8 mg strengths, therefore the post limit quantity will allow pregnant and breastfeeding patients 90 buprenorphine tablets per month when being prescribed for induction therapy and/or subsequent maintenance therapy for treatment of opioid use disorder to allow for a maximum of 24 mg per day at the highest available strength.

The American Academy of Pediatrics recommends exclusive breastfeeding for about 6 months, followed by continued breastfeeding as complementary foods are introduced, with continuation of breastfeeding for 1 year or longer as mutually desired by mother and infant.[6] Buprenorphine sublingual tablets will be approved for a duration of 12 months when being prescribed for induction therapy and/or subsequent maintenance therapy for treatment of opioid use disorder for pregnant and breastfeeding patients.

According to the U.S. Department of Health and Human Services' Treatment Improvement Protocol (TIP) 63 guidelines, patients who responded well to buprenorphine in the past should be considered for this treatment. In addition, unsuccessful treatment experiences with buprenorphine in the past do not necessarily indicate that buprenorphine will be ineffective again. Motivation and circumstances change over time.[5] Setting a limit regarding the number of reauthorizations is beyond the scope of this program, and the decision to request reauthorization will be left at the discretion of prescribers.

REFERENCES

1. Buprenorphine sublingual tablets [package insert]. Parsippany, NJ: Teva Pharmaceuticals; August 2021.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2021; Accessed November 9, 2021.
3. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed November 9, 2021.
4. American Society of Addiction Medicine National Practice Guideline For the Treatment of Opioid Use Disorder. https://www.asam.org/docs/default-source/quality-science/npg-jam-supplement.pdf?sfvrsn=a00a52c2_2. Accessed November 2021.
5. U.S. Department of Health and Human Services. Substance Abuse and Mental Health Services Administration (SAMHSA). TIP 63: Medications for Opioid Use Disorder - A Treatment Improvement Protocol. https://store.samhsa.gov/system/files/sma18-5063fulldoc.pdf . Accessed November 2021.
6. Eidelman AI, Schanler RJ; American Academy of Pediatrics Section on Breastfeeding. Breastfeeding and the use of human milk. Pediatrics. 2012;129 (3):827-843.

Written by:	UM Development (CF/JH)
Date Written:	10/2017
Revised:	11/2017, 04/2018 (non-clinical change to question order and denial reasons); (JG) 07/2018 (no clinical changes); (CF) 11/2018 (no clinical changes), 11/2019 (opioid dependence updated to opioid use disorder); (DS) 11/2020 (no clinical changes; clarified limits do not accumulate), 11/2021 (no clinical changes)
Reviewed:	Medical Affairs: (DNC) 10/2017, 11/2017; (CHART) 11/27/2019, 02/27/2020 (FYI for CPO rec – opioid use disorder), 12/03/2020, 12/02/2021 External Review: 10/2017, 08/2018, 02/2019, 02/2020, 02/2021, 02/2022

CRITERIA FOR APPROVAL

1	Is the requested drug being prescribed for induction therapy and/or subsequent maintenance therapy for treatment of opioid use disorder? [If no, then no further questions.]	Yes	No

2	Is the patient pregnant or breastfeeding? [If no, then no further questions.]	Yes	No
3	Does the patient require use of MORE than the plan allowance of 90 tablets per month? [RPh Note: If yes, then deny and enter a partial approval for 90 tablets per month of buprenorphine.]	Yes	No

Mapping Instructions			
	Yes	**No**	**DENIAL REASONS – DO NOT USE FOR MEDICARE PART D**
1.	Go to 2	Deny	You do not meet the requirements of your plan. Your plan covers up to 90 tablets of the requested drug to allow the first 30 days of treatment without requiring prior authorization. Your plan covers additional quantities of this drug when it is being used to start and/or keep up with addiction treatment. Your request has been denied based on the information we have. [Short Description: No approvable diagnosis.]
2.	Go to 3	Deny	You do not meet the requirements of your plan. Your plan covers up to 90 tablets of the requested drug to allow the first 30 days of treatment without requiring prior authorization. Your plan covers additional quantities of this drug when you are pregnant or breastfeeding and using buprenorphine to start and/or keep up with addiction treatment. Your request has been denied based on the information we have. [Short Description: Not pregnant or breastfeeding.]
3.	Deny	Approve, 12 months 90 tablets per 25 days* or 270 tablets per 75 days*	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 90 tablets per month of the requested drug and strength. Your request has been partially approved. You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity.]

**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*

PRIOR AUTHORIZATION CRITERIA

BRAND NAME*
(generic)

(buprenorphine sublingual tablets)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization with Quantity Limits ***Ref # 780-C***

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Buprenorphine sublingual tablets are indicated for the treatment of opioid dependence and are preferred for induction. Buprenorphine sublingual tablets should be used as part of a complete treatment plan to include counseling and psychosocial support.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being used as part of a complete program for the treatment of opioid use disorder [Note: Complete treatment programs may include the following: A) Behavioral therapies (e.g., individual therapy, group counseling, family behavior therapy, cognitive behavioral therapy, motivational enhancement, motivational incentives, mutual support), B) Medical history, physical exam, and screening laboratory tests as needed (e.g., HIV and hepatitis C screening), C) Diversion control protocols such as observed dosing, pill counts, testing for buprenorphine's metabolite (nor-buprenorphine), D) Random urine testing for opioids and other illicit substances, E) Use of the Prescription Drug Monitoring Program (PDMP) if available in state.]
  AND
  - The patient is pregnant or breastfeeding **AND**
  - The requested drug is being prescribed for induction therapy and/or subsequent maintenance therapy for treatment of opioid use disorder
    OR
  - The requested drug is being prescribed for INDUCTION THERAPY for transition from opioid use to treatment of opioid use disorder

Quantity limits apply.

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Buprenorphine sublingual tablets are indicated for the treatment of opioid dependence and are preferred for induction. Buprenorphine sublingual tablets should be used as part of a complete treatment plan to include counseling and psychosocial support; however, treatment can be initiated prior to these additional services starting.[1-4]

Buprenorphine is an effective treatment recommended for patients who have opioid use disorder, are able to give informed consent, and have no specific contraindications for agonist treatment. Treatment with buprenorphine has the following four goals: 1) To suppress opioid withdrawal, 2) To block the effects of illicit opioids, 3) To reduce opioid craving and stop or reduce the use of illicit opioids, 4) To promote and facilitate patient engagement in recovery-oriented activities including psychosocial intervention.[4]

CVS caremark®

According to the American Society of Addiction Medicine (ASAM) National Practice Guidelines, patients on buprenorphine-containing opioid agonist therapy should receive a comprehensive assessment including physical examination and screening for hepatitis and human immunodeficiency virus (HIV) prior to beginning medication treatment. Clinicians should take steps to reduce the chance of buprenorphine diversion. Recommended strategies may include frequent office visits (e.g., weekly in early treatment); drug testing, including testing for buprenorphine and metabolites; and recall visits for medication counts. Accessing Prescription Drug Monitoring Program (PDMP) data is advisable to check for other medications that the patient may be receiving.[4]

To improve outcomes, buprenorphine therapy is recommended to be combined with behavioral therapies. Research shows that when treating opioid use disorder, a combination of medication and behavioral therapies is the most effective, but this should not be a limitation to the initiation of treatment. Behavioral therapies help patients engage in the treatment process, modify their attitudes and behaviors related to drug and alcohol use, and increase healthy life skills. These treatments can also enhance the effectiveness of medications and help people stay in treatment longer. Treatment programs that combine pharmacological and behavioral therapy services increase the likelihood of cessation relative to programs without these services. There are a number of treatment strategies that can be used in combination with medications to successfully address opioid use disorder. These include individual therapy, group counseling, family behavior therapy, cognitive behavioral therapy, motivational enhancement, and motivational incentives (contingency management).[6]

At initiation, the risk of precipitated withdrawal can be reduced by using a lower initial dose of buprenorphine. An initial dose of 2-4 mg and observation of the patient for signs of precipitated withdrawal is recommended. If 60-90 minutes have passed without the onset of withdrawal symptoms, then additional dosing can be done in increments of 2-8 mg. Once it has been established that the initial dose is well tolerated, the buprenorphine dose can be increased fairly rapidly to a dose that provides stable effects for 24 hours and is clinically effective.[4]

After initiation, evidence suggests that buprenorphine doses of 16 mg or more per day or more may be more effective than lower doses at suppressing illicit opioid use. The FDA generally recommends dosing to a limit of 24 mg per day, noting that there is limited evidence regarding the relative efficacy of higher doses. In addition, the use of higher doses may increase the risk of diversion. There is no recommended time limit for treatment with buprenorphine. Clinicians should not encourage patients to discontinue and detoxification only strategies should not be used as a standard. While research is limited, available research generally suggests that longer duration of treatment results in better outcomes.[4] Buprenorphine sublingual tablets are available in 2 mg and 8 mg strengths, therefore non-pregnant patients undergoing induction will be approved for 21 tablets every 3 months to allow for a maximum of 24 mg per day at the highest available strength. Typical induction lasts 1 to 3 days and rarely over 7 days. This quantity and duration of approval will allow the patient to have 7 days of induction therapy every 3 months. If there is further need for induction, a buprenorphine combination product may be used.

Providers should discuss treatment options as well as risks and benefits with the patient and document the decision in her chart. For women who are pregnant or breastfeeding, opioid agonist treatment with methadone or buprenorphine is the most appropriate treatment, taking into consideration effects on the fetus, neonatal opioid withdrawal syndrome, and impacts on perinatal care and parenting of young children.[4]

There is a growing body of evidence comparing outcomes related to methadone and buprenorphine treatment during pregnancy. Infants born to mothers treated with buprenorphine had shorter hospital stays (10 vs. 17.5 days), had shorter treatment durations for neonatal opioid withdrawal syndrome (NOWS) (4.1 vs. 9.9 days), and required a lower cumulative dose of morphine (1.1 vs. 10.4 mg) to treat NOWS compared to infants born to mothers on treatment with methadone. However, in this trial, mothers treated with buprenorphine were more likely to drop out of treatment compared to mothers treated with methadone. Larger studies are needed comparing the safety and effectiveness of buprenorphine versus methadone in the obstetric population.[4]

While the evidence on the safety and efficacy of naloxone in pregnant women remains limited, the combination buprenorphine/naloxone product is frequently used and the consensus of the guideline committee is that the combination product is safe and effective for this population. Naloxone is minimally absorbed when these medications are taken as

prescribed.[4] However, according to the U.S. Department of Health and Human Services' Treatment Improvement Protocol (TIP) 63 guidelines, the buprenorphine monoproduct (without naloxone) has been recommended for the treatment of pregnant women because of the danger to the fetus of precipitated opioid withdrawal if the combination product were to be injected. Although there are some publications with small sample sizes that indicate that the combination product appears to be safe in pregnancy the safety data are insufficient at this time to recommend its use. This is an area of some uncertainty. An expert panel on the treatment of OUD in pregnancy was unable to agree whether pregnant women should be treated with the monoproduct or combination product.[5] Because of this less than definitive consensus, buprenorphine sublingual tablets will be approved for a duration of 12 months when being prescribed for induction therapy and/or subsequent maintenance therapy for treatment of opioid use disorder for pregnant and breastfeeding patients.

Buprenorphine sublingual tablets are available in 2 mg and 8 mg strengths, therefore the post limit quantity will allow pregnant and breastfeeding patients 90 buprenorphine tablets per month when being prescribed for induction therapy and/or subsequent maintenance therapy for treatment of opioid use disorder to allow for a maximum of 24 mg per day at the highest available strength.

The American Academy of Pediatrics recommends exclusive breastfeeding for about 6 months, followed by continued breastfeeding as complementary foods are introduced, with continuation of breastfeeding for 1 year or longer as mutually desired by mother and infant.[7] Buprenorphine sublingual tablets will be approved for a duration of 12 months when being prescribed for induction therapy and/or subsequent maintenance therapy for treatment of opioid use disorder for pregnant and breastfeeding patients.

According to the U.S. Department of Health and Human Services' Treatment Improvement Protocol (TIP) 63 guidelines, patients who responded well to buprenorphine in the past should be considered for this treatment. In addition, unsuccessful treatment experiences with buprenorphine in the past do not necessarily indicate that buprenorphine will be ineffective again. Motivation and circumstances change over time.[5] Setting a limit regarding the number of reauthorizations is beyond the scope of this program, and the decision to request reauthorization will be left at the discretion of prescribers.

A 7-day emergency supply is permitted for members requiring an immediate start of therapy for treatment of opioid use disorder while a prior authorization is being worked. The reject message displays "PA req call XXXXXXXXXX. For Emerg. Fill CALL 8009665772". When calling for an emergency fill, the Customer Care representative is instructed to ask if the buprenorphine is being used for treatment of opioid use disorder. If so, the representative will enter a one-time 7-day supply override in the system to allow the patient to get the medication while a prior authorization is being worked. The representative will also explain that the doctor must initiate the Prior Authorization process. Emergency supplies will be allowed with a prior authorization reject once every 90 days in the event of a relapse.

REFERENCES

1. Buprenorphine sublingual tablets [package insert]. Parsippany, NJ: Teva Pharmaceuticals; August 2021.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2021; Accessed November 9, 2021.
3. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed November 9, 2021.
4. American Society of Addiction Medicine National Practice Guideline For the Treatment of Opioid Use Disorder. https://www.asam.org/docs/default-source/quality-science/npg-jam-supplement.pdf?sfvrsn=a00a52c2_2. Accessed November 2021.
5. U.S. Department of Health and Human Services. Substance Abuse and Mental Health Services Administration (SAMHSA). TIP 63: Medications for Opioid Use Disorder - A Treatment Improvement Protocol. https://store.samhsa.gov/system/files/sma18-5063fulldoc.pdf. Accessed November 2021.
6. Medication Assisted Treatment for Substance Use Disorders – Informational Bulletin. http://www.medicaid.gov/Federal-Policy-Guidance/downloads/CIB-07-11-2014.pdf. Accessed November 2021.
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Written by:	UM Development (JH)
Date Written:	07/2003
Revised:	(NB) 02/2005, 02/2006; (SE) 03/2009,10/2009 (clarification); (CT) 12/2009; (KD) 04/2010 (added pregnancy information and Suboxone for induction); (SE) 07/2010 (added renewal criteria regarding use of other opioids/urine drug screen/changed duration of approval) 12-2009 (3), 07/2010 (added in QL question) 12-2009 (4), 09-2010 (removed QL and related question) 12-2009 (4); (CY) 03/2011 (added QL), 06/2011, 03/2012 (removed Suboxone, made separate document), 12/2012; (SE) 05/2013 (created commercial version), 09/2013; (CF) 09/2014, 05/2015 (added denial reasons), 09/2015; (CF/GB) 08/2016; (CF/JH) 01/2017 (no clinical changes), 04/2017 (added breastfeeding, clarified complete program question), 11/2017; (CF) 11/2018 (no clinical changes); 11/2019 (opioid dependence updated to opioid use disorder); (DS) 11/2020 (no clinical changes), 11/2021 (no clinical changes)
Reviewed:	Medical Affairs: 07/2003; (MM) 02/2005, 02/2006; (WLF) 03/2009, 12/2009, 04/2010; (KP) 07/2010, 07/2010, 06/2011, 11/2011, 03/2012; (DC) 12/2012; (KP) 10/2013; (LCB) 09/2014; (DNC) 09/2015, 04/2017, 11/2017, 02/2018; (CHART) 11/27/2019, 02/27/2020 (FYI for CPO rec – opioid use disorder), 12/03/2020, 12/02/2021 External Review: 05/2005, 06/2006, 04/2009, 05/2010, 06/2010, 10/2010, 10/2011, 08/2012, 02/2013, 04/2014, 12/2014, 12/2015, 12/2016, 04/2017, 02/2018, 02/2019, 02/2020, 02/2021, 02/2022

CRITERIA FOR APPROVAL

1	Is the requested drug being used as part of a complete program for the treatment of opioid use disorder? [Note: Complete treatment programs may include the following: A) Behavioral therapies (e.g., individual therapy, group counseling, family behavior therapy, cognitive behavioral therapy, motivational enhancement, motivational incentives, mutual support), B) Medical history, physical exam, and screening laboratory tests as needed (e.g., HIV and hepatitis C screening), C) Diversion control protocols such as observed dosing, pill counts, testing for buprenorphine's metabolite (nor-buprenorphine), D) Random urine testing for opioids and other illicit substances, E) Use of the Prescription Drug Monitoring Program (PDMP) if available in state.] [If no, then no further questions.]	Yes	No
2	Is the patient pregnant or breastfeeding? [If no, then skip to question 5.]	Yes	No
3	Is the requested drug being prescribed for induction therapy and/or subsequent maintenance therapy for treatment of opioid use disorder? [If no, then no further questions.]	Yes	No
4	Does the patient require use of MORE than the plan allowance of 90 tablets per month? [No further questions.] [RPh Note: If yes, then deny and enter a partial approval for 90 tablets per month of buprenorphine.]	Yes	No
5	Is the requested drug being prescribed for INDUCTION THERAPY for transition from opioid use to treatment of opioid use disorder? [If no, then no further questions.]	Yes	No
6	Does the patient require use of MORE than the plan allowance of 21 tablets in a three month period for induction therapy? [RPh Note: If yes, then deny and enter a partial approval for 21 tablets per 75 days of buprenorphine.]	Yes	No

Mapping Instructions			
	Yes	**No**	**DENIAL REASONS – DO NOT USE FOR MEDICARE PART D**
1.	Go to 2	Deny	You do not meet the requirements of your plan. Your plan covers this drug when it is being used as part of a program for the treatment of opioid use disorder. Your request has been denied based on the information we have. [Short Description: Not part of opioid use disorder program.]
2.	Go to 3	Go to 5	
3.	Go to 4	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you meet all of these conditions: - You are pregnant or breastfeeding - You are using buprenorphine to start and/or keep up with addiction treatment Your request has been denied based on the information we have. [Short Description: Pregnant/breastfeeding with no approvable diagnosis.]
4.	Deny	Approve, 12 months 90 tablets per 25 days* or 270 tablets per 75 days*	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 90 tablets per month of the requested drug and strength. Your request has been partially approved. You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity.]
5.	Go to 6	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you are using buprenorphine to start addiction treatment. Your request has been denied based on the information we have. [Short Description: No approvable diagnosis.]
6.	Deny	Approve, 3 months 21 tablets per 75 days*	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 21 tablets in a three month period of the requested drug and strength to start addiction treatment. Your request has been partially approved. You have been approved for the maximum quantity that your plan covers for a duration of 3 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max induction quantity.]

The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.

Reference number(s)
3411-A

SPECIALTY GUIDELINE MANAGEMENT

BRUKINSA (zanubrutinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication
Brukinsa is a kinase inhibitor indicated for the treatment of adult patients with:
1. Mantle cell lymphoma (MCL) who have received at least one prior therapy.
2. Waldenstrom's macroglobulinemia (WM).
3. Relapsed or refractory marginal zone lymphoma (MZL) who have received at least one anti-CD20-based regimen.
4. Chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL)

B. Compendial Use
1. Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma
2. Gastric MALT Lymphoma (Extranodal Marginal Zone Lymphoma of the Stomach)/Non-gastric MALT Lymphoma (Extranodal Marginal Zone Lymphoma of Nongastric Sites)
3. Nodal Marginal Zone Lymphoma
4. Splenic Marginal Zone Lymphoma
5. Waldenstrom Macroglobulinemia/Lymphoplasmacytic lymphoma/Bing-Neel Syndrome

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Mantle Cell Lymphoma
Authorization of 12 months may be granted for treatment of mantle cell lymphoma as a single agent when the member has received at least one prior therapy.

B. Chronic Lymphocytic Leukemia (CLL)/Small Lymphocytic Lymphoma (SLL)
Authorization of 12 months may be granted for treatment of CLL/SLL when used as a single agent.

C. Marginal Zone Lymphoma
Authorization of 12 months may be granted for treatment of marginal zone lymphoma, including gastric MALT lymphoma (extranodal marginal zone lymphoma of the stomach), non-gastric MALT lymphoma (extranodal marginal zone lymphoma of nongastric sites), nodal marginal zone lymphoma and splenic marginal zone lymphoma, when used as subsequent therapy for members who have received an anti-CD20 based-regimen (e.g., rituximab or obinutuzumab).

D. Waldenstrom Macroglobulinemia/Lymphoplasmacytic Lymphoma/Bing-Neel Syndrome

Authorization of 12 months may be granted for treatment of Waldenstrom macroglobulinemia/Lymphoplasmacytic lymphoma when used as a single agent or for the treatment of Bing-Neel syndrome when used as a single agent or in combination with rituximab.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

IV. REFERENCES

1. Brukinsa [package insert]. San Mateo, CA: BeiGene USA, Inc.; April 2023.
2. The NCCN Drugs & Biologics Compendium ® © 2023 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed June 2, 2023.

QUANTITY LIMIT CRITERIA

BRAND NAME*
(generic)

BUNAVAIL
(buprenorphine and naloxone buccal film)

CASSIPA
(buprenorphine and naloxone sublingual film)

SUBOXONE
(buprenorphine and naloxone sublingual tablet and film)

ZUBSOLV
(buprenorphine and naloxone sublingual tablet)

Status: CVS Caremark Criteria
Type: Quantity Limit ***Ref # 1553-H***

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Bunavail
Bunavail is indicated for the treatment of opioid dependence. Bunavail should be used as part of a complete treatment plan that includes counseling and psychosocial support.

Cassipa
Cassipa is indicated for the maintenance treatment of opioid dependence. Cassipa should be used as part of a complete treatment plan to include counseling and psychosocial support.

Suboxone Film
Suboxone sublingual film is indicated for treatment of opioid dependence. Suboxone sublingual film should be used as part of a complete treatment plan that includes counseling and psychosocial support.

Suboxone Tablet
Buprenorphine and Naloxone sublingual tablets are indicated for the maintenance treatment of opioid dependence. Buprenorphine and Naloxone sublingual tablets should be used as part of a complete treatment plan that includes counseling and psychosocial support.

Zubsolv
Zubsolv is indicated for treatment of opioid dependence. Zubsolv should be used as part of a complete treatment plan that includes counseling and psychosocial support.

RATIONALE
Bunavail (buprenorphine/naloxone buccal film), Cassipa (buprenorphine/naloxone sublingual film), Suboxone (buprenorphine/naloxone sublingual tablet and film), and Zubsolv (buprenorphine/naloxone sublingual tablet) are indicated for the treatment of opioid dependence and should be used as part of a complete treatment plan that includes counseling and psychosocial support; however, treatment can be initiated prior to these additional services starting.[1-7]

When using buprenorphine/naloxone products for induction, consideration should be given to the type of opioid use disorder (i.e., long- or short-acting opioid products), the time since last opioid use, concomitant non-pharmaceutical fentanyl use, and the severity of opioid use disorder.[1-7]

At initiation, the risk of precipitated withdrawal can be reduced by using a lower initial dose of buprenorphine. An initial dose of 2-4 mg and observation of the patient for signs of precipitated withdrawal is recommended. If 60-90 minutes have passed without the onset of withdrawal symptoms, then additional dosing can be done in increments of 2-8 mg. Once it has been established that the initial dose is well tolerated, the buprenorphine dose can be increased fairly rapidly to a dose that provides stable effects for 24 hours and is clinically effective.[8]

After initiation, evidence suggests that buprenorphine doses of 16 mg or more per day or more may be more effective than lower doses at suppressing illicit opioid use. The FDA generally recommends dosing to a limit of 24 mg per day, noting that there is limited evidence regarding the relative efficacy of higher doses. In addition, the use of higher doses may increase the risk of diversion. There is no recommended time limit for treatment with buprenorphine. Clinicians should not encourage patients to discontinue and detoxification only strategies should not be used as a standard. While research is limited, available research generally suggests that longer duration of treatment results in better outcomes.[8]

Bunavail
The maintenance dose of Bunavail is generally in the range of 2.1 mg/0.3 mg buprenorphine/naloxone to 12.6 mg/2.1 mg buprenorphine/naloxone per day depending on the individual patient and clinical response. The recommended target dosage of Bunavail during maintenance is 8.4 mg/1.4 mg buprenorphine/naloxone as a single daily dose. Dosages higher than 12.6 mg/2.1 mg buprenorphine/naloxone have not been demonstrated to provide any clinical advantage.[1,6,7]

Cassipa
Cassipa (16 mg/4 mg) should only be used after induction and stabilization of the patient, and when the patient has been titrated to a dose of 16 mg of buprenorphine using another marketed product. The dosage of buprenorphine and naloxone sublingual film may need to be adjusted to a level that holds the patient in treatment and suppresses opioid withdrawal signs and symptoms. Cassipa comes in a single dose and cannot be adjusted.[3,6,7]

Suboxone
The maintenance dose of Suboxone is generally in the range of 4 mg/1 mg buprenorphine/naloxone to 24 mg/6 mg buprenorphine/naloxone per day depending on the individual and clinical response. The recommended target dosage of Suboxone during maintenance is 16 mg/4mg buprenorphine/naloxone per day as a single daily dose. Dosages higher than 24 mg/6 mg buprenorphine/naloxone daily have not been demonstrated to provide a clinical advantage.[2,4,6,7]

Zubsolv
The maintenance dose of Zubsolv is generally in the range of 2.9 mg/0.71 mg buprenorphine/naloxone to 17.2 mg/4.2 mg buprenorphine/naloxone per day depending on the individual patient and clinical response. The recommended target dosage of Zubsolv during maintenance is 11.4 mg/2.9 mg buprenorphine/naloxone as a single daily dose. Dosages higher than 17.2 mg/4.2 mg buprenorphine/naloxone have not been demonstrated to provide any clinical advantage.[5-7]

If the patient is requesting more than the initial quantity limit, then the claim will reject with a message indicating that quantity limits are exceeded.

REFERENCES

1. Bunavail [package insert]. Raleigh, NC: BioDelivery Sciences International, Inc.; October 2019.
2. Buprenorphine and Naloxone tablets [package insert]. Philadelphia, PA: Lannett Company, Inc.; August 2020.
3. Cassipa [package insert]. North Wales, PA: Teva Pharmaceuticals USA, Inc.; October 2019.
4. Suboxone films [package insert]. North Chesterfield, VA: Indivior, Inc.; October 2019.
5. Zubsolv [package insert]. Morristown, NJ: Orexo US, Inc.; April 2019.
6. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. http://online.lexi.com/. Accessed November 2020.
7. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. http://www.micromedexsolutions.com/. Accessed November 2020.
8. American Society of Addiction Medicine National Practice Guideline For the Treatment of Opioid Use Disorder. https://www.asam.org/docs/default-source/quality-science/npg-jam-supplement.pdf?sfvrsn=a00a52c2_2. Accessed November 2020.

Written by:	UM Development (CF/JH)
Date Written:	11/2016
Revised:	(CF/JH) 01/2017 (no clinical changes), 11/2017 (no clinical changes); (DS) 09/2018 (added Cassipa); (CF) 11/2018 (no clinical changes), 11/2019 (opioid dependence updated to opioid use disorder); (DS) 11/2020 (changed from QvT to DD), 11/2021 (no clinical changes)
Reviewed:	Medical Affairs: (DNC) 11/2016, 10/2018; (CHART) 11/27/2019, 12/03/2020, 12/02/2021 External Review: 12/2016, 04/2017, 02/2018, 10/2018, 02/2019, 02/2020, 02/2021, 02/2022

LIMIT CRITERIA

This limit is coded for daily dose. Limits do not accumulate together. Patient is allowed the maximum limit for each drug and strength.

Drug	Daily Limit
Bunavail 2.1 mg/0.3 mg, 4.2 mg/0.7 mg	3 units/day
Bunavail 6.3 mg/1 mg	2 units/day
Cassipa 16 mg/4 mg	1 unit/day
Suboxone 2 mg/0.5 mg, 4 mg/1 mg, 8 mg/2 mg	3 units/day
Suboxone 12 mg/3 mg	2 units/day
Zubsolv 0.7 mg/0.18 mg, 1.4 mg/0.36 mg, 2.9 mg/0.71 mg, 5.7 mg/1.4 mg	3 units/day
Zubsolv 8.6 mg/2.1 mg	2 units/day
Zubsolv 11.4 mg/2.9 mg	1 unit/day

butalbital and acetaminophen	48 units / 25 days	144 units / 75 days
butalbital, acetaminophen, and caffeine	48 units / 25 days	144 units / 75 days
butalbital, acetaminophen, caffeine, and codeine	48 units / 25 days	144 units / 75 days
butalbital, aspirin, and caffeine	48 units/ 25 days	144 units / 75 days
butalbital, aspirin, caffeine, and codeine	48 units / 25 days	144 units / 75 days
**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.* **The limit criteria apply to both brand and generic, if available.*		

RATIONALE

Butalbital containing products are indicated for the relief of the symptom complex of tension (or muscle contraction) headache. Evidence supporting the efficacy and safety of these combination products in the treatment of multiple recurrent headaches is unavailable. Caution in this regard is required because butalbital is habit-forming and potentially abusable.[1-9]

To decrease the risk of medication-overuse headache many experts limit acute therapy to two headache days per week on a regular basis. Drug treatment of acute headache should generally not exceed more than two days per week on a regular basis. More frequent treatment other than this may result in medication-overuse chronic daily headaches. [10,11]

The recommended dosage of butalbital 25 mg and acetaminophen 325 mg tablets is two tablets every four hours. The total daily dose should not exceed 12 tablets. The recommended dosage of all other butalbital combination products is one or two tablets/capsules/tablespoonfuls every four hours as needed. The total daily dose should not exceed 6 tablets/capsules/tablespoonfuls. Extended and repeated use of these products is not recommended because of the potential for physical dependence.[1-9]

The limit is set to 6 doses per day at the maximum daily dose for acute treatment of 8 headaches per month. If the patient is requesting more than the initial quantity limit, then the claim will reject with a message indicating that quantity limits are exceeded.

REFERENCES

1. Allzital [package insert]. Canton, MS: Larken Laboratories, Inc.; September 2020.
2. Butalbital, Aspirin, and Caffeine [package insert]. Kansas City, MO: Nostrum Laboratories, Inc.; October 2021.
3. Butalbital, Aspirin, Caffeine, and Codeine Phosphate [package insert]. Parsippany, NJ: Actavis Pharma, Inc.; April 2021.
4. Esgic [package insert]. Greenville, NC: Mayne Pharma; May 2019.
5. Fioricet [package insert]. Parsippany, NJ: Teva Pharmaceuticals USA, Inc.; January 2021.
6. Fioricet with Codeine [package insert]. Parsippany, NJ: Teva Pharmaceuticals USA, Inc.; March 2021.
7. VTOL LQ [package insert]. Atlanta, GA: Mikart, LLC; August 2019.
8. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2022; Accessed May 13, 2022.
9. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed May 13, 2022.
10. Marmura M, Silberstein S, Schwedt T. The Acute Treatment of Migraine in Adults: The American Headache Society Evidence Assessment of Migraine Pharmacotherapies. *Headache* 2015;55:3-20.
11. American Headache Society. The American Headache Society Consensus Statement: Update on integrating new migraine treatments into clinical practice. *Headache* 2021;61:1021-1039.

Written by:	UM Development (JG)
Date Written:	04/2002
Revised:	(MB) 07/2004; (NB) 08/2005, 09/2006, 12/2006(4), 07/2007; (AM) 07/2008, 07/2009; (CY) 07/2010; (MS) 05/2011, 05/2012; (CT) 05/2013; (RP) 05/2014; (MS) 05/2015, 03/2016 (added Allzital), (TM) 05/2016 (no clinical changes); (CF) 06/2017 (no clinical changes, 06/2018 (no clinical changes), 06/2019 (no clinical changes), (SF) 06/2020 (no clinical changes); (DS) 06/2021 (no clinical changes); (MRS) 06/2022 (no clinical changes)
Reviewed:	Medical Affairs (MM) 08/2004, 08/2005, 09/2006, 12/2006, 07/2007; (WF) 07/2008, 07/2009; (KP) 07/2010, 05/2011, 05/2012; (DHR) 05/2013; (DNC) 05/2014, 05/2015, (CHART) 06/25/2020, 07/01/2021, 06/30/2022 External Review: 12/2004, 12/2005, 02/2006, 04/2007, 12/2007, 12/2008, 12/2009, 10/2010, 10/2011, 10/2012, 10/2013, 10/2014, 10/2015, 10/2016, 10/2017, 10/2018, 10/2019, 10/2020, 10/2021, 10/2022

QUANTITY LIMIT CRITERIA

DRUG CLASS	**BUTALBITAL CONTAINING ANALGESICS (BRAND AND GENERIC)**
BRAND NAME (generic)	
	(butalbital and acetaminophen)
	(butalbital, acetaminophen, and caffeine)
	(butalbital, acetaminophen, caffeine, and codeine)
	(butalbital, aspirin, and caffeine)
	(butalbital, aspirin, caffeine, and codeine)

Status: CVS Caremark® Criteria
Type: Quantity Limit

POLICY

FDA-APPROVED INDICATIONS
Butalbital containing products are indicated for the relief of the symptom complex of tension (or muscle contraction) headache.

Evidence supporting the efficacy and safety of these combination products in the treatment of multiple recurrent headaches is unavailable. Caution in this regard is required because butalbital is habit-forming and potentially abusable.

Butalbital with codeine containing products are indicated for the management of the symptom complex of tension (or muscle contraction) headache when non-opioid analgesic and alternative treatments are inadequate.

Limitations of Use
Because of the risks of addiction, abuse, and misuse with opioids and butalbital, even at recommended doses, reserve butalbital with codeine containing products for use in patients for whom alternative treatment options (e.g., non-opioid, non-barbiturate analgesics) have not been tolerated or are not expected to be tolerated, or have not provided adequate analgesia or are not expected to provide adequate analgesia.

INITIAL LIMIT QUANTITY

This quantity limit should accumulate across all drugs and strengths up to highest quantity listed depending on the order the claims are processed.

Drug	1 Month Limit*	3 Month Limit*
butalbital, acetaminophen, and caffeine syrup	720 mL / 25 days	2,160 mL / 75 days
butalbital 25 mg and acetaminophen 325 mg	96 units / 25 days	288 units / 75 days
butalbital and acetaminophen	48 units / 25 days	144 units / 75 days

butalbital, acetaminophen, and caffeine	48 units / 25 days	144 units / 75 days
butalbital, acetaminophen, caffeine, and codeine	48 units / 25 days	144 units / 75 days
butalbital, aspirin, and caffeine	48 units/ 25 days	144 units / 75 days
butalbital, aspirin, caffeine, and codeine	48 units / 25 days	144 units / 75 days
**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.* **The limit criteria apply to both brand and generic, if available.*		

REFERENCES

1. Allzital [package insert]. Canton, MS: Larken Laboratories, Inc.; June 2022.
2. Ascomp with Codeine [package insert]. Berlin, CT: Breckenridge Pharmaceutical, Inc.; April 2021.
3. Butalbital, Aspirin, and Caffeine [package insert]. Congers, NY: Chartwell RX, LLC; December 2022.
4. Esgic [package insert]. Greenville, NC: Mayne Pharma; May 2019.
5. Fioricet [package insert]. Parsippany, NJ: Teva Pharmaceuticals USA, Inc.; January 2021.
6. Fioricet with Codeine [package insert]. Parsippany, NJ: Teva Pharmaceuticals USA, Inc.; March 2021.
7. VTOL LQ [package insert]. Atlanta, GA: Monarch PCM, LLC; August 2019.
8. Lexicomp Online, Lexi-Drugs Online. Waltham, MA: UpToDate, Inc.; 2023. https://online.lexi.com. Accessed April 21, 2023.
9. Micromedex (electronic version). Merative, Ann Arbor, Michigan, USA. Available at: https://www.micromedexsolutions.com/ (cited: 04/21/2023).
10. Ailani J, Burch RC, Robbins MS, et al. The American Headache Society Consensus Statement: Update on integrating new migraine treatments into clinical practice. *Headache*. 2021;61:1021-1039.

QUANTITY LIMIT CRITERIA

BRAND NAME*
(generic)
(butorphanol tartrate nasal spray)

Status: CVS Caremark Criteria
Type: Quantity Limit ***Ref # 212-H***

** Drugs that are listed in the target drug box include both brand and generic and all dosages forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS
Butorphanol tartrate nasal spray is indicated for the management of pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate.

Limitations of Use
Because of the risks of addiction, abuse, and misuse, with opioids, even at recommended doses, reserve butorphanol tartrate nasal spray for use in patients for whom alternative treatment options [e.g., non-opioid analgesics]

- Have not been tolerated, or are not expected to be tolerated,
- Have not provided adequate analgesia, or are not expected to provide adequate analgesia.

LIMIT CRITERIA

Drug	1 Month Limit*	3 Month Limit*
butorphanol nasal spray	2 bottles / 25 days	6 bottles / 75 days

**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*

RATIONALE
Butorphanol tartrate nasal spray is indicated for the management of pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate. Because of the risks of addiction, abuse, and misuse, with opioids, even at recommended doses, reserve butorphanol tartrate nasal spray for use in patients for whom alternative treatment options [e.g., non-opioid analgesics]: have not been tolerated, or are not expected to be tolerated; or, have not provided adequate analgesia, or are not expected to provide adequate analgesia.[1-3]

In clinical trials, butorphanol was evaluated for several types of pain, including postoperative pain and migraine headache pain. Some experts state that butorphanol tartrate nasal spray may be considered when other antimigraine drugs cannot be used or as rescue therapy when sedative effects will not place the patient at risk.[2] Butorphanol tartrate, by all routes of administration, has been associated with episodes of abuse. Of the cases received, there were more reports of abuse with the nasal spray formulation than with the injectable formulation. Proper assessment of the patient, proper prescribing practices, periodic re-evaluation of therapy, and proper dispensing and storage are appropriate measures that help to limit abuse of opioid drugs. Strategies to reduce these risks include prescribing the drug in the smallest appropriate quantity and advising the patient on the proper disposal of unused drug.[1-3]

The usual recommended dose for initial nasal administration of butorphanol tartrate nasal solution is 1 mg (1 spray in one nostril). If adequate pain relief is not achieved within 60 to 90 minutes, an additional 1 mg dose may be given. The 1 mg dose may be repeated in 3 to 4 hours as required after the second dose of the sequence. Depending on the severity of the pain, an initial dose of 2 mg (1 spray in each nostril) may be used in patients who will be able to remain recumbent in

the event drowsiness or dizziness occurs. In such patients, single additional 2 mg doses should not be given for 3 to 4 hours. Individually titrate butorphanol tartrate nasal spray to a dose that provides adequate analgesia and minimizes adverse reactions.[1-3]

The initial limit criteria are intended to meet the immediate need of a patient being discharged from the hospital with postoperative pain or of a migraine patient in acute need of rescue therapy.

Butorphanol Tartrate Nasal Spray 10 mg/mL is supplied in a 2.5 mL bottle of nasal spray solution with a metered-dose spray pump. On average, one bottle will deliver 14 to 15 doses if no repriming is necessary.[1-3] The initial quantity limit is set at 2 bottles (28-30 doses) per month to allow for up to 5 days of treatment for post-operative pain or for approximately 4 migraine headaches per month.

If the patient is requesting more than the initial quantity limit, then the claim will reject with a message indicating that a prior authorization is required.

REFERENCES

1. Butorphanol Tartrate Nasal Spray [package insert]. Weston, FL: Apotex Corp.; January 2021.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2022; Accessed May 19, 2022.
3. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed May 19, 2022.

Written by:	UM Development (DP)
Date Written:	03/1998
Revised:	(AD) 12/2002; (MG) 01/2004; (JG) 06/2005; (CT) 05/2006(2); (NB) 07/2007, 07/2008, 07/2009; (MS) 06/2010, 05/2011, 05/2012, 05/2013, (TM) 05/2014 (SF) 05/2015, (TM) 05/2016 (no clinical changes); (KM) 06/2017 (no clinical changes); (CF) 06/2018 (no clinical changes); (CF) 06/2019 (no clinical changes), (SF) 06/2020 (no clinical changes); (DS) 06/2021 (no clinical changes); (MRS) 06/2022 (no clinical changes)
Reviewed:	Medical Affairs (MM) 03/1998, 12/2002, 01/2004, 05/2006; (WF) 07/2007, 07/2008, 07/2009; (KP) 06/2010, 05/2011, 05/2012; (DC) 05/2013, (LS) 05/2014 (KJC) 05/2015, (CHART) 06/25/2020, 07/01/2021, 06/30/2022 External Review: 02/2003, 04/2004, 10/2006, 12/2007, 12/2008, 12/2009, 10/2010, 10/2011, 10/2012, 10/2013, 10/2014, 10/2015, 10/2016, 10/2017, 10/2018, 10/2019, 10/2020, 10/2021, 10/2022

1. Member has a confirmed molecular diagnosis of PFIC type 1, 2, or 3
2. Member does not have any other concomitant liver disease (e.g., biliary atresia, liver cancer, alternate non-PFIC related etiology of cholestasis)
3. Member has not received a liver transplant
4. Member is 3 months of age or older.

B. Cholestatic pruritis in Alagille syndrome (ALGS)

Authorization of 6 months may be granted for treatment of cholestatic pruritis in Alagille syndrome (ALGS) when all of the following criteria are met:

1. Member has a diagnosis of ALGS established by one of the following (see Appendix for major clinical features of ALGS):
   i. Genetic testing (e.g., mutations in *JAG1, NOTCH2*)
   ii. Family history of ALGS in a first degree relative, bile duct paucity, and one or more major clinical features of ALGS
   iii. Family history of ALGS in a first degree relative and two or more major clinical features of ALGS
   iv. Bile duct paucity and three or more major clinical features of ALGS
   v. Four or more major clinical features of ALGS
2. Member has evidence of cholestasis (e.g., elevated serum bile acid level)
3. Member does not have a history or presence of other concomitant liver disease (e.g., biliary atresia, PFIC, liver cancer)
4. Member has not received a liver transplant
5. Member is 12 months of age or older.

VI. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for all members (including new members) requesting continuation of therapy when the member is experiencing benefit from therapy (e.g., improvement in pruritis).

VII. APPENDIX

Major clinical features of ALGS

1. Hepatic abnormality (e.g., cholestasis)
2. Cardiac abnormality (e.g., stenosis of the peripheral pulmonary artery and its branches)
3. Skeletal abnormality (e.g., butterfly vertebrae)
4. Ophthalmologic abnormality (e.g., posterior embryotoxon)
5. Characteristic facial features (e.g., triangular-shaped face with a broad forehead and a pointed chin, bulbous tip of the nose, deeply set eyes, and hypertelorism)
6. Central nervous system abnormality (e.g., stroke, intracranial bleeding)
7. Renal structural or functional abnormality (e.g., abnormally small size, cysts)

VIII. REFERENCES

1. Bylvay [package insert]. Boston, MA: Albireo Pharma, Inc.; June 2023.
2. Spinner NB, Gilbert MA, Loomes KM, Krantz ID. Alagille syndrome. GeneReviews® [Internet]. Published May 19, 2020. Last updated December 12, 2019. Accessed June 20, 2023.
3. Genetic and Rare Diseases Information Center. Alagille syndrome. Rare Disease Database. https://rarediseases.info.nih.gov. Last updated February 2023. Accessed June 20, 2023.
4. National Organization for Rare Disorders (NORD). Alagille syndrome. Rare Disease Database. https://rarediseases.org. Published 2020. Last updated May 25, 2023. Accessed June 20, 2023.

5. The Childhood Liver Disease Research Network. Alagille syndrome. https://childrennetwork.org/For-Physicians/Alagille-Syndrome-Information-for-Physicians. Accessed June 22, 2023.

QUANTITY LIMIT CRITERIA

BRAND NAME
(generic)

(butorphanol tartrate nasal spray)

Status: CVS Caremark® Criteria
Type: Quantity Limit

POLICY

FDA-APPROVED INDICATIONS
Butorphanol tartrate nasal spray is indicated for the management of pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate.

Limitations of Use
Because of the risks of addiction, abuse, and misuse, with opioids, even at recommended doses, reserve butorphanol tartrate nasal spray for use in patients for whom alternative treatment options [e.g., non-opioid analgesics]

- Have not been tolerated, or are not expected to be tolerated,
- Have not provided adequate analgesia, or are not expected to provide adequate analgesia.

INITIAL LIMIT QUANTITY

Drug	1 Month Limit*	3 Month Limit*
butorphanol nasal spray	2 bottles / 25 days	6 bottles / 75 days

**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*

REFERENCES

1. Butorphanol Tartrate Nasal Spray [package insert]. Weston, FL: Apotex Corp.; January 2021.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Waltham, MA: UpToDate, Inc.; 2023. https://online.lexi.com. Accessed April 21, 2023.
3. Micromedex (electronic version). Merative, Ann Arbor, Michigan, USA. Available at: https://www.micromedexsolutions.com/ (cited: 04/21/2023).

Reference number(s)
2212-A

SPECIALTY GUIDELINE MANAGEMENT

CABOMETYX (cabozantinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
Cabometyx is indicated for the treatment of patients with:
1. Advanced renal cell carcinoma (RCC)
2. Advanced renal cell carcinoma (RCC), as a first-line treatment in combination with nivolumab
3. Hepatocellular carcinoma (HCC) who have been previously treated with sorafenib
4. Locally advanced or metastatic differentiated thyroid cancer (DTC) that has progressed following prior VEGFR-targeted therapy and who are radioactive iodine-refractory or ineligible (adult and pediatric patients 12 years of age and older)

B. Compendial Uses
1. Relapsed or stage IV renal cell carcinoma
2. Non-small cell lung cancer with RET (rearranged during transfection) gene rearrangement
3. Hepatocellular carcinoma as subsequent treatment
4. Ewing Sarcoma
5. Osteosarcoma
6. Gastrointestinal Stromal Tumor (GIST)
7. Endometrial carcinoma

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of RET gene rearrangement documentation is necessary to initiate the prior authorization review for the indication of non-small cell lung cancer.

III. CRITERIA FOR INITIAL APPROVAL

A. Renal Cell Carcinoma
Authorization of 12 months may be granted for treatment of advanced, relapsed, or stage IV renal cell carcinoma when used in either of the following settings:
1. As a single agent.
2. In combination with nivolumab.

B. Hepatocellular Carcinoma

Authorization of 12 months may be granted as a single agent for subsequent treatment of hepatocellular carcinoma.

C. Non-small Cell Lung Cancer
Authorization of 12 months may be granted as a single agent for treatment of recurrent, advanced, or metastatic non-small cell lung cancer with RET gene rearrangement.

D. Ewing Sarcoma
Authorization of 12 months may be granted for treatment of Ewing sarcoma as a single agent for subsequent therapy.

E. Osteosarcoma
Authorization of 12 months may be granted for treatment of osteosarcoma as a single agent for subsequent therapy.

F. Gastrointestinal Stromal Tumor (GIST)
Authorization of 12 months may be granted for treatment of GIST when either of the following criteria are met:
1. The member meets all of the following criteria:
   i. Member has unresectable, recurrent/progressive or metastatic disease
   ii. Member has failed at least four FDA-approved therapies (e.g., imatininb, sunitinib, regorafenib, ripretinib)
   iii. The requested medication will be used as a single agent
2. The requested medication will be used for palliation of symptoms if previously tolerated and effective.

G. Thyroid Carcinoma
Authorization of 12 months may be granted for treatment of follicular, Hürthle cell, or papillary thyroid carcinoma when all of the following criteria are met:
1. Member has locally advanced or metastatic disease
2. Disease has progressed after VEGFR-targeted therapy (e.g., lenvatinib and sorafenib)
3. Disease is not amenable to radioactive iodine therapy (RAI)
4. Member is at least 12 years old

H. Endometrial Carcinoma
Authorization of 12 months may be granted for treatment of recurrent or metastatic endometrial carcinoma as a single agent for subsequent therapy.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

V. REFERENCES

1. Cabometyx [package insert]. Alameda, CA: Exelixis, Inc.; September 2021.

2. The NCCN Drugs & Biologics Compendium® © 2022 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed May 3, 2022.

Reference number(s)
2397-A

SPECIALTY GUIDELINE MANAGEMENT

CALQUENCE (acalabrutinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. Mantle Cell Lymphoma
      Calquence is indicated for the treatment of adult patients with mantle cell lymphoma (MCL) who have received at least one prior therapy.
   2. Chronic Lymphocytic Leukemia or Small Lymphocytic Lymphoma
      Calquence is indicated for the treatment of adult patients with chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL).

B. Compendial Use
   1. Waldenström Macroglobulinemia/Lymphoplasmacytic Lymphoma
   2. Gastric MALT Lymphoma (Extranodal Marginal Zone Lymphoma of the Stomach)/Non-gastric MALT Lymphoma (Extranodal Marginal Zone Lymphoma of Nongastric Sites)
   3. Nodal Marginal Zone Lymphoma
   4. Splenic Marginal Zone Lymphoma

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Mantle cell lymphoma
Authorization of 12 months may be granted for treatment of mantle cell lymphoma as a single agent when the member has received at least one prior therapy.

B. Chronic Lymphocytic Leukemia (CLL)/Small Lymphocytic Lymphoma (SLL)
Authorization of 12 months may be granted for treatment of CLL/SLL as a single agent or in combination with obinutuzumab.

C. Waldenström Macroglobulinemia/Lymphoplasmacytic Lymphoma
Authorization of 12 months may be granted for subsequent treatment of Waldenström Macroglobulinemia /Lymphoplasmacytic Lymphoma as a single agent.

D. Gastric MALT Lymphoma (Extranodal Marginal Zone Lymphoma of the Stomach)/Non-gastric MALT Lymphoma (Extranodal Marginal Zone Lymphoma of Nongastric Sites)/Nodal Marginal Zone Lymphoma/Splenic Marginal Zone Lymphoma

Authorization of 12 months may be granted for treatment of gastric MALT lymphoma (extranodal marginal zone lymphoma of the stomach), non-gastric MALT lymphoma (extranodal marginal zone lymphoma of nongastric sites), nodal marginal zone lymphoma and splenic marginal zone lymphoma when used as subsequent therapy.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

IV. REFERENCES

1. Calquence [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; August 2022.
2. The NCCN Drugs & Biologics Compendium® © 2023 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed June 2, 2023.

Reference number
1783-A

SPECIALTY GUIDELINE MANAGEMENT

CAPRELSA (vandetanib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication
Treatment of symptomatic or progressive medullary thyroid cancer in patients with unresectable locally advanced or metastatic disease

Use Caprelsa in patients with indolent, asymptomatic or slowly progressing disease only after careful consideration of the treatment related risks of Caprelsa.

B. Compendial Uses
Follicular, Hürthle cell, and papillary thyroid carcinoma

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Thyroid carcinoma
Authorization of 12 months may be granted for treatment of thyroid carcinoma when any of the following criteria are met:
A. Member has follicular, Hürthle cell, or papillary thyroid carcinoma that is not amenable to radioactive iodine (RAI) therapy.
B. Member has medullary thyroid carcinoma.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting authorization for an indication listed in Section II when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

IV. REFERENCES

1. Caprelsa [package insert]. Cambridge, MA: Genzyme Corporation; June 2020.
2. The NCCN Drugs & Biologics Compendium™ © 2021 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed November 4, 2021.

Reference number(s)
2122-A

SPECIALTY GUIDELINE MANAGEMENT

CARBAGLU (carglumic acid)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Acute hyperammonemia in patients with NAGS deficiency
   Carbaglu is indicated as an adjunctive therapy in pediatric and adult patients for the treatment of acute hyperammonemia due to the deficiency of the hepatic enzyme N-acetylglutamate synthase (NAGS). During acute hyperammonemic episodes, concomitant administration of Carbaglu with other ammonia lowering therapies such as alternate pathway medications, hemodialysis, and dietary protein restriction is recommended.

2. Chronic hyperammonemia in patients with NAGS deficiency
   Carbaglu is indicated for maintenance therapy in pediatric and adult patients for the treatment of chronic hyperammonemia due to the deficiency of the hepatic enzyme NAGS. During maintenance therapy, the concomitant use of other ammonia lowering therapies and protein restriction may be needed based on plasma ammonia levels.

3. Acute Hyperammonemia due to Propionic Acidemia (PA) or Methylmalonic Acidemia (MMA)
   Carbaglu is indicated in pediatric and adult patients as adjunctive therapy to standard of care for the treatment of acute hyperammonemia due to PA or MMA.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review for NAGS deficiency:

A. Initial requests:
   1. Enzyme assay, biochemical or genetic testing results supporting diagnosis of NAGS deficiency; and
   2. Lab results documenting baseline plasma ammonia levels.

B. Continuation of therapy requests: lab results documenting a reduction in plasma ammonia levels from baseline.

III. CRITERIA FOR INITIAL APPROVAL

A. N-acetylglutamate synthase (NAGS) Deficiency

Authorization of 12 months may be granted for members with diagnosis of NAGS deficiency when both of the following criteria are met:
1. The diagnosis is confirmed by enzymatic, biochemical, or genetic testing.
2. The member has elevated plasma ammonia levels at baseline.

B. Methylmalonic Acidemia
Authorization of 12 months may be granted for members who have a diagnosis of methylmalonic acidemia.

C. Propionic Acidemia
Authorization of 12 months may be granted for members who have a diagnosis of propionic acidemia.

IV. CONTINUATION OF THERAPY

A. N-acetylglutamate synthase (NAGS) Deficiency
Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for NAGS deficiency who are experiencing benefit from therapy as evidenced by a decrease in ammonia levels from baseline.

B. Methylmalonic Acidemia or Propionic Acidemia
Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for methylmalonic acidemia or propionic academia who are experiencing benefit from therapy as evidenced by disease stability or disease improvement.

V. REFERENCES

1. Carbaglu [package insert]. Lebanon, NJ: Recordati Rare Diseases, Inc.; August 2021.
2. Filippi L, Gozzini E, Fiorini P, et al. N-carbamylglutamate in emergency management of hyperammonemia in neonatal acute onset propionic and methylmalonic aciduria. *Neonatology*. 2010;97(3):286-290.
3. Levrat V, Forest I, Fouilhoux A, et al. Carglumic acid: an additional therapy in the treatment of organic acidurias with hyperammonemia. *Orphanet J Rare Dis*. 2008;3:2.
4. Gebhardt B, Vlaho S, Fischer D, et al. N-carbamylglutamate enhances ammonia detoxification in a patient with decompensated methylmalonic aciduria. *Mol Genet Metab*. 2003:79(4):303-304.
5. Gebhardt B, Dittrich S, Parbel S, et al. N-carbamylglutamate protects patients with decompensated propionic aciduria from hyperammonaemia. *J Interit Metab Dis*. 2005;28(2):241-244.
6. Schwahn BC, Pleterse L, Bisset WM, et al. Biochemical efficacy of N-carbamylglutamate in neonatal severe hyperammonaemia due to propionic acidaemia. *Eur J Pediatr*. 2010;169(1):133-134.
7. Valayannopoulos V, Baruteau J, Delgado MB, et. al. Carglumic acid enhances rapid ammonia detoxification in classical organic acidurias with a favourable risk-benefit profile: a retrospective observational study. *Orphanet J Rare Dis*. 2016;11:32.
8. Baumgartner MR, Hörster F, Dionisi-Vici C, et. al. Proposed guidelines for the diagnosis and management of methylmalonic and propionic acidemia. *Orphanet J Rare Dis*. 2014; 9:130.

Reference number(s)
1880-A

SPECIALTY GUIDELINE MANAGEMENT

CAYSTON (aztreonam for inhalation solution)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Cayston is indicated to improve respiratory symptoms in cystic fibrosis patients with *Pseudomonas aeruginosa*.

All other indications are considered experimental/investigational and are not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Cystic Fibrosis
Authorization of 12 months may be granted for members 2 years of age and older with cystic fibrosis when *Pseudomonas aeruginosa* is present in airway cultures OR the member has a history of *Pseudomonas aeruginosa* infection or colonization in the airways.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II who are experiencing benefit from therapy as evidenced by disease stability or disease improvement.

IV. REFERENCES

1. Cayston [package insert]. Foster City, CA: Gilead Sciences, Inc.; November 2019.
2. Mogayzel PJ, Naureckas ET, Robinson KA, et al. Cystic fibrosis pulmonary guidelines. Chronic medications for maintenance of lung health. *Am J Respir Crit Care Med*. 2013; 187:680-689.
3. Lahiri T, Hempstead SE, Brady C, et al. Clinical practice guidelines from the Cystic Fibrosis Foundation for preschoolers with cystic fibrosis. *Pediatrics*. 2016;137(4):e20151784.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME*
(generic)

CEQUA
(cyclosporine ophthalmic solution)

RESTASIS
(cyclosporine ophthalmic emulsion)

Status: CVS Caremark Criteria ***Ref# 1955-C***
Type: Initial Prior Authorization with Quantity Limit ***Ref# BOG 5484-C***

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATION

Cequa
Cequa ophthalmic solution is a calcineurin inhibitor immunosuppressant indicated to increase tear production in patients with keratoconjunctivitis sicca (dry eye).

Restasis
Restasis ophthalmic emulsion is indicated to increase tear production in patients whose tear production is presumed to be suppressed due to ocular inflammation associated with keratoconjunctivitis sicca. Increased tear production was not seen in patients currently taking topical anti-inflammatory drugs or using punctal plugs.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for dry eye disease

Quantity Limits apply.

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Cequa ophthalmic solution is a calcineurin inhibitor immunosuppressant indicated to increase tear production in patients with keratoconjunctivitis sicca (dry eye). Restasis ophthalmic emulsion is indicated to increase tear production in patients whose tear production is presumed to be suppressed due to ocular inflammation associated with keratoconjunctivitis sicca. Increased tear production was not seen in patients currently taking topical anti-inflammatory drugs or using punctal plugs.[1-5]

Dosage for Cequa and Restasis is one drop in each eye twice a day, 4 drops per day total. Cequa and Restasis are available as single-use vials. Each vial contains enough solution or emulsion to deliver one drop in each eye.[1,2] Therefore, the limit for Cequa and Restasis vials will be set at 60 vials per month.

Restasis is also available as a 5.5 mL multi-dose bottle.[3] According to the Centers for Medicare and Medicaid Services, it is appropriate to use a conversion factor of 20 drops per mL to calculate a days' supply.[6] Using this conversion, there are 110 drops per multi-dose bottle of Restasis. After priming the bottle for first time use by squeezing out 2 drops, 108 drops remain, and at 4 drops per day, this equates to a 27 day supply. Therefore, the limit for Restasis multi-dose bottle will be set at 1 bottle per month.

REFERENCES

1. Cequa [package insert]. Cranbury, NJ: Sun Pharmaceutical Industries, Inc.; January 2021.
2. Restasis [package insert]. Irvine, CA: Allergan, Inc; July 2017.
3. Restasis Multidose [package insert]. Irvine, CA: Allergan, Inc; October 2016.
4. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2021; Accessed Month Day, Year.
5. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed Month Day, Year.
6. Pharmacy Auditing and Dispensing Job Aid: Billing Other Dosage Forms. Centers for Medicare and Medicaid Services. December 2015.

Written by:	UM Development (CT)
Date Written:	02/2010 (client requested)
Revised:	(SE) 09/2011 (MDC-1 standard document); (PL) 02/2012; (CT) 09/2012 (CMS requested changes); (MS) 02/2013; (CF) 11/2013, (SE/WW) 11/2014, (LN) 04/2015 (added denial reasons); (KM) 11/2015 (removed punctal plug question); (MS) 11/2016 ; (KM) 05/2017 (created new for regulatory); (DS) 11/2017, 08/2018 (added Cequa/renamed criteria), 10/2018 (no clinical changes), 10/2019 (removed MDC designation; no clinical changes), 03/2020 (added QLs), 10/2020 (no clinical changes; updated document title), 08/2021 (updated document title), 10/2021 (no clinical changes), (TM) 06/2022 (new BOG)
Reviewed:	Medical Affairs (KP) 02/2010, (WF) 09/2011, (KP) 02/2012, 10/2012; (DC) 02/2013; (LCB) 11/2013; (LMS) 02/2014, (DNC) 11/2014, (LCB) 11/2015; (AA) 01/2017; (DNC) 05/2017; (ME) 11/2017; (EPA) 08/2018; (CHART) 10/31/2019, 04/02/2020, 10/29/2020, 10/28/2021, 06/09/2022 External Review: 03/2010, 10/2011, 06/2012, 10/2012, 04/2013, 02/2014, 02/2015, 02/2016, 02/2017, 06/2017, 12/2017, 10/2018, 02/2019, 02/2020, 06/2020 (FYI), 12/2020, 12/2021, 08/2022 (FYI)

CRITERIA FOR APPROVAL

1	Is the requested drug being prescribed for dry eye disease? [If no, then no further questions.]	Yes	No
2	Does the patient require more than the plan allowance of 4 drops per day of the requested drug? [RPh Note: If yes, then deny and enter a partial approval per Quantity Limit Chart.]	Yes	No

Mapping Instructions			
	Yes	**No**	**DENIAL REASONS – DO NOT USE FOR MEDICARE PART D**
1.	Go to 2	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have dry eye disease. Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]
2.	Deny RPh Note: For the denial verbiage, only include the requested drug. Remove all the other drugs from the verbiage.	Approve, 12 months, (Note for Ref # BOG 5484-C only: If the request is for Restasis approve Brand name Restasis) See Quantity Limit Chart	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to: - 60 vials per month of Cequa - 60 vials per month of Restasis - 1 multi-dose bottle per month of Restasis Your request has been partially approved. You have been approved for the maximum quantity that your plan covers for a

			duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity]

QUANTITY LIMIT		
Drug	**1 Month Limit***	**3 Month Limit***
Cequa vials	60 vials / 25 days	180 vials / 75 days
Restasis vials	60 vials / 25 days	180 vials / 75 days
Restasis multi-dose bottle	1 bottle / 21 days	3 bottles / 63 days
**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.* **The duration of 21 days is used for a 28-day fill period and 63 days is used for a 84-day fill period to allow time for refill processing.*		

Reference number
2050-A

SPECIALTY GUIDELINE MANAGEMENT

CERDELGA (eliglustat)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Cerdelga is indicated for the long-term treatment of adult patients with Gaucher disease type 1 who are CYP2D6 extensive metabolizers (EMs), intermediate metabolizers (IMs), or poor metabolizers (PMs) as detected by an FDA-cleared test.

Limitations of use:
Patients who are CYP2D6 ultra-rapid metabolizers (URMs) may not achieve adequate concentrations of Cerdelga to achieve a therapeutic effect. A specific dosage cannot be recommended for those patients whose CYP2D6 genotype cannot be determined (indeterminate metabolizers).

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
A. Beta-glucocerebrosidase enzyme assay or genetic testing results supporting diagnosis, and
B. The results of the CYP2D6 test

III. CRITERIA FOR INITIAL APPROVAL

Gaucher disease type 1
Authorization of 12 months may be granted for treatment of Gaucher disease type 1 when all of the following criteria are met:
1. Diagnosis of Gaucher disease was confirmed by enzyme assay demonstrating a deficiency of beta-glucocerebrosidase (glucosidase) enzyme activity or by genetic testing
2. Member is a CYP2D6 extensive metabolizer, an intermediate metabolizer, or a poor metabolizer as detected by an FDA-cleared test

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment of an indication listed in Section III when the member is not experiencing an inadequate response or any intolerable adverse events from therapy.

V. REFERENCES

1. Cerdelga [package insert]. Cambridge, MA: Genzyme Corporation; July 2021.

Reference number(s)
1912-A, 1913-A

SPECIALTY GUIDELINE MANAGEMENT

CETROTIDE (cetrorelix acetate)
FYREMADEL (ganirelix acetate)
ganirelix acetate

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Cetrotide, Fyremadel, and ganirelix are indicated for the inhibition of premature luteinizing hormone (LH) surges in women undergoing controlled ovarian stimulation.

All other indications are considered experimental/investigational and not medically necessary.

II. MEDICAL BENEFIT ALIGNMENT

Specialty Guideline Management coverage review will be bypassed for drug(s) being requested for a procedure that has been approved under a member's medical benefit plan. Such members will be exempt from the requirements in Sections III and IV. A medical authorization number and confirmation of the approved procedure(s) will be required.

NOTE: Some plans may opt-out of medical benefit alignment. Members receiving coverage under such plans must meet the requirements in Sections III and IV.

III. CRITERIA FOR INITIAL APPROVAL

Inhibition of premature LH surges
Authorization of 12 months may be granted for the inhibition of premature LH surges in members undergoing ovulation induction or assisted reproductive technology (ART).

IV. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

V. REFERENCES

1. Cetrotide [package insert]. Rockland, MA: EMD Serono; May 2018.
2. Fyremadel [package insert]. Parsippany, NJ: Ferring Pharmaceuticals Inc.; January 2022.
3. Ganirelix [package insert]. Whitehouse Station, NJ: Merck & Co., Inc.; October 2020.

4. Bakas P, Konidaris S, Liapis A, et al. Role of gonadotropin-releasing hormone antagonist in the management of subfertile couples with intrauterine insemination and controlled ovarian stimulation. *Fertil Steril*. 2011;95:2024-2028.

STEP THERAPY CRITERIA

DRUG CLASS	**ORAL, NASAL CALCITONIN GENE-RELATED PEPTIDE (CGRP) RECEPTOR ANTAGONISTS**
BRAND NAME (generic)	**NURTEC ODT (rimegepant)** **QULIPTA (atogepant)** **UBRELVY (ubrogepant)** **ZAVZPRET (zavegepant)**

Status: CVS Caremark® Criteria
Type: Initial Step Therapy with Quantity Limit;
Post Step Therapy Prior Authorization with Quantity Limit

POLICY

FDA-APPROVED INDICATIONS
Nurtec ODT
Acute Treatment of Migraine
Nurtec ODT is indicated for the acute treatment of migraine with or without aura in adults.
Preventive Treatment of Episodic Migraine
Nurtec ODT is indicated for the preventive treatment of episodic migraine in adults.

Qulipta
Qulipta is indicated for the preventive treatment of migraine in adults.

Ubrelvy
Ubrelvy is indicated for the acute treatment of migraine with or without aura in adults.
Limitations of Use
Ubrelvy is not indicated for the preventive treatment of migraine.

Zavzpret
Zavzpret is indicated for the acute treatment of migraine with or without aura in adults.
Limitations of Use
Zavzpret is not indicated for the preventive treatment of migraine.

INITIAL STEP THERAPY with QUANTITY LIMIT* For Ubrelvy and Zavzpret
Include Rx and OTC products unless otherwise stated.

If the patient has filled a prescription for at least a 30 day supply of two triptan 5-HT1 receptor agonists (include combinations) within the past 180 days under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit.**** If the patient does not meet the initial step therapy criteria, then the claim will reject with a message indicating that a prior authorization (PA) is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

**If the patient meets the initial step therapy criteria, then the initial limit criteria will apply. If the patient is requesting more than the initial quantity limit, the claim will reject with a message indicating that a PA is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

INITIAL STEP THERAPY with QUANTITY LIMIT* For Nurtec ODT

***Include Rx and OTC products unless otherwise stated.*

If the patient has filled a prescription for at least a 30 day supply of two triptan 5-HT1 receptor agonists (include combinations) within the past 180 days OR at least a 56 day supply of divalproex sodium, topiramate, valproate sodium, metoprolol, propranolol, timolol, atenolol, nadolol, amitriptyline, or venlafaxine within the past 730 days under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit.** If the patient does not meet the initial step therapy criteria, then the claim will reject with a message indicating that a prior authorization (PA) is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

**If the patient meets the initial step therapy criteria, then the initial limit criteria will apply. If the patient is requesting more than the initial quantity limit, the claim will reject with a message indicating that a PA is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

INITIAL STEP THERAPY with QUANTITY LIMIT* For Qulipta

***Include Rx and OTC products unless otherwise stated.*

If the patient has filled a prescription for at least a 56 day supply of divalproex sodium, topiramate, valproate sodium, metoprolol, propranolol, timolol, atenolol, nadolol, amitriptyline, or venlafaxine within the past 730 days under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit.** If the patient does not meet the initial step therapy criteria, then the claim will reject with a message indicating that a prior authorization (PA) is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

**If the patient meets the initial step therapy criteria, then the initial limit criteria will apply. If the patient is requesting more than the initial quantity limit, the claim will reject with a message indicating that a PA is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

****INITIAL LIMIT CRITERIA**

Limits do not accumulate together; patient is allowed the maximum limit for each drug and strength.

PLEASE NOTE: Since manufacturer package sizes may vary, it is the discretion of the dispensing pharmacy to fill quantities per package size up to these quantity limits. In such cases, the filling limit and day supply may be less than what is indicated.

Drug	1 Month Limit*	3 Month Limit*
Nurtec ODT (rimegepant)	16 orally disintegrating tablets / 25 days	48 orally disintegrating tablets / 75 days
Qulipta 10mg, 30mg, 60mg (atogepant)	30 tablets / 25 days	90 tablets / 75 days

Ubrelvy 50mg, 100mg (ubrogepant)	16 tablets / 25 days	48 tablets / 75 days
Zavzpret (zavegepant)	6 nasal spray units / 18 days	24 nasal spray units / 75 days

**The duration of 18 days is used for a 21-day fill period, 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The request is for Nurtec ODT, Ubrelvy, or Zavzpret being prescribed for the acute treatment of migraine in an adult patient

  AND
  - The patient experienced an inadequate response or an intolerance to two triptan 5-HT1 receptor agonists

    OR
  - The patient has a contraindication that would prohibit a trial of triptan 5-HT1 receptor agonists

  AND
- The requested drug will not be used concurrently with another CGRP receptor antagonist

OR

- The request is for Nurtec ODT being prescribed for the preventive treatment of episodic migraine in an adult patient

OR

- The request is for Qulipta being prescribed for the preventive treatment of migraine in an adult patient

AND

- The requested drug will not be used concurrently with another CGRP receptor antagonist

AND

  - The patient received at least 3 months of treatment with the requested drug and had a reduction in migraine days per month from baseline

    OR
  - The patient experienced an inadequate treatment response with an 8-week trial of any of the following: A) Antiepileptic drugs (AEDs) (e.g., divalproex sodium, topiramate, valproate sodium), B) Beta-adrenergic blocking agents (e.g., metoprolol, propranolol, timolol, atenolol, nadolol), C) Antidepressants (e.g., amitriptyline, venlafaxine)

    OR
  - The patient experienced an intolerance or has a contraindication that would prohibit an 8-week trial of any of the following: A) Antiepileptic drugs (AEDs) (e.g., divalproex sodium, topiramate, valproate sodium), B) Beta-adrenergic blocking agents (e.g., metoprolol, propranolol, timolol, atenolol, nadolol), C) Antidepressants (e.g., amitriptyline, venlafaxine)

Quantity Limits apply.
Ubrelvy: 16 tablets per month, 48 tablets per 3 months
Nurtec ODT: 16 tablets per month, 48 tablets per 3 months
Qulipta: 30 tablets per month, 90 tablets per 3 months
Zavzpret: 6 nasal spray units per 3 weeks, 24 nasal spray units per 3 months

**The duration of 18 days is used for a 21-day fill period, 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*

REFERENCES

1. Nurtec ODT [package insert]. New Haven, CT: Biohaven Pharmaceuticals, Inc; April 2022.
2. Qulipta [package insert]. Madison, NJ: Allergan USA, Inc.; April 2023.
3. Ubrelvy [package insert]. Madison, NJ: Allergan USA, Inc.; March 2021.

4. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. http://online.lexi.com/. Accessed June 8, 2022.
5. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed June 8, 2022
6. American Headache Society. The American Headache Society Position Statement on Integrating New Migraine Treatments into Clinical Practice. Headache 2019; 59:1-18.
7. Marmura M, Silberstein S, Schwedt T. The Acute Treatment of Migraine in Adults: The American Headache Society Evidence Assessment of Migraine Pharmacotherapies. Headache 2015;55:3-20.
8. Ailani J, Burch RC, Robbins MS et al. The American Headache Society Consensus Statement: Update on integrating new migraine treatments into clinical practice. Headache. 2021; 61:1021-1039.
9. Silberstein S, Holland S, Freitag F, et al. Evidence-Based Guideline Update: Pharmacologic Treatment for Episodic Migraine Prevention in Adults: Report of the Quality and the American Headache Society Standards Subcommittee of the American Academy of Neurology. Neurology 2012;78;1337-1346.
10. Silberstein S, Holland S, Freitag F, et al. Evidence-Based Guideline Update: Pharmacologic Treatment for Episodic Migraine Prevention in Adults: Report of the Quality and the American Headache Society Standards Subcommittee of the American Academy of Neurology. Neurology 2013;80;871
11. American Academy of Neurology. Update: Pharmacologic Treatments for Episodic Migraine Prevention in Adults. Available at: https://www.aan.com/Guidelines/Home/GetGuidelineContent/545. Accessed June 2022.
12. Zavzpret [package insert]. New York, NY: Pfizer Las Division of Pfizer Inc.; March 2023.

STEP THERAPY CRITERIA

DRUG CLASS **CALCITONIN GENE-RELATED PEPTIDE (CGRP) RECEPTOR ANTAGONISTS INJECTABLE, INTRAVENOUS INFUSION**

BRAND NAME (generic)

AIMOVIG
(erenumab-aooe injection)

AJOVY
(fremanezumab-vfrm injection)

EMGALITY
(galcanezumab-gnlm injection)

VYEPTI
(eptinezumab-jjmr injection, for intravenous use)

Status: CVS Caremark® Criteria
Type: Initial Step Therapy with Quantity Limit;
Post Step Therapy Prior Authorization with Quantity Limit

POLICY

FDA-APPROVED INDICATIONS

Aimovig
Aimovig is indicated for the preventive treatment of migraine in adults.

Ajovy
Ajovy is indicated for the preventive treatment of migraine in adults.

Emgality
Migraine
Emgality is indicated for the preventive treatment of migraine in adults
Cluster Headache
Emgality is indicated for the treatment of episodic cluster headache in adults

Vyepti
Vyepti is indicated for the preventive treatment of migraine in adults.

INITIAL STEP THERAPY with QUANTITY LIMIT* For AIMOVIG, AJOVY, EMGALITY (except 100mg), VYEPTI
Include Rx and OTC products unless otherwise stated.

If the patient has filled a prescription for at least a 56 day supply of divalproex sodium, topiramate, valproate sodium, metoprolol, propranolol, timolol, atenolol, nadolol, amitriptyline, or venlafaxine within the past 730 days under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit.**

If the patient does not meet the initial step therapy criteria, then the claim will reject with a message indicating that a prior authorization (PA) is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

**If the patient meets the initial step therapy criteria, then the initial limit criteria will apply. If the patient is requesting more than the initial quantity limit the claim will reject with a message indicating that a PA is required.

INITIAL STEP THERAPY* with QUANTITY LIMIT For EMGALITY 100mg
Include Rx and OTC products unless otherwise stated.

If the patient has filled a prescription for at least a 1 day supply of sumatriptan (nasal or subcutaneous) or zolmitriptan (nasal or oral) within the past 730 days under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit.** If the patient does not meet the initial step therapy criteria, then the claim will reject with a message indicating that a prior authorization (PA) is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

**If the patient meets the initial step therapy criteria, then the initial limit criteria will apply. If the patient is requesting more than the initial quantity limit the claim will reject with a message indicating that a PA is required.

****INITIAL LIMIT QUANTITY**
Limits do not accumulate together; patient is allowed the maximum limit for each drug and strength.

Migraine:

Drug	**1 Month Limit***	**3 Month Limit***
Aimovig 70 mg, 140 mg (erenumab-aooe injection)	1 mL (1 autoinjector x 1 mL each) / 25 days	3 mL (3 autoinjectors x 1 mL each) / 75 days
Ajovy 225 mg (fremanezumab-vfrm injection)	4.5 mL (3 autoinjectors or syringes x 1.5 mL each) / 75 days	4.5 mL (3 autoinjectors or syringes x 1.5 mL each) / 75 days
Emgality 120 mg (galcanezumab-gnlm injection):		
LOADING DOSE Loading dose quantity applies to new starts of therapy (i.e. patient has not filled a prescription for Emgality in the past 180 days).	2 mL (2 syringes or pens x 1 mL each) / 25 days	4 mL (4 syringes or pens x 1 mL each) / 75 days
MAINTENANCE DOSE Maintenance dose applies to those not new to therapy (i.e., patient has filled a prescription for Emgality in the past 180 days).	1 mL (1 syringe or pen x 1 mL each) / 25 days	3 mL (3 syringes or pens x 1 mL each) / 75 days
Vyepti 100 mg (eptinezumab-jjmr injection, for intravenous use)	3 mL (3 single dose vials x 1 mL each) / 75 days	3 mL (3 single dose vials x 1 mL each) / 75 days
Cluster Headache:		
Drug	**1 Month Limit***	**3 Month Limit***
Emgality 100 mg (galcanezumab-gnlm injection)	3 mL (3 syringes x 1 mL each) / 25 days	9 mL (9 syringes x 1 mL each) / 75 days

**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for the preventive treatment of migraine in an adult patient
  AND
  - The request is for Aimovig, Ajovy, Emgality 120 mg, or Vyepti.
  AND
  - The requested drug will not be used concurrently with another CGRP receptor antagonist
    AND
    - The patient has NOT received at least 3 months of treatment with the requested drug
      AND
      - The patient experienced an inadequate treatment response with an 8-week trial of any of the following: A) Antiepileptic drugs (AEDs) (e.g., divalproex sodium, topiramate, valproate sodium), B) Beta-adrenergic blocking agents (e.g., metoprolol, propranolol, timolol, atenolol, nadolol), C) Antidepressants (e.g., amitriptyline, venlafaxine)

      OR
      - The patient experienced an intolerance to, or the patient has a contraindication that would prohibit an 8-week trial of any of the following: A) Antiepileptic drugs (AEDs) (e.g., divalproex sodium, topiramate, valproate sodium), B) Beta-adrenergic blocking agents (e.g., metoprolol, propranolol, timolol, atenolol, nadolol), C) Antidepressants (e.g., amitriptyline, venlafaxine)

    OR
    - The patient has received at least 3 months of treatment with the requested drug
      AND
      - The patient had a reduction in migraine days per month from baseline

OR

- The request is for Emgality 100 mg for the treatment of episodic cluster headaches in an adult patient
  AND
  - The requested drug will not be used concurrently with another CGRP receptor antagonist
    AND
    - The patient has NOT received at least 3 weeks treatment with the requested drug
      AND
      - The patient experienced an inadequate treatment response to any of the following: A) sumatriptan (nasal or subcutaneous), B) zolmitriptan (nasal or oral)

      OR
      - The patient experienced an intolerance to, or the patient has a contraindication to any of the following: A) sumatriptan (nasal or subcutaneous), B) zolmitriptan (nasal or oral)

    OR
    - The patient received at least 3 weeks treatment with the requested drug
      AND
      - The patient had a reduction in weekly cluster headache attack frequency from baseline

Quantity limits apply.

POST LIMIT QUANTITY

Migraine:

Drug	1 Month Limit*	3 Month Limit*
Aimovig 70 mg, 140 mg (erenumab-aooe injection)	1 mL (1 autoinjector) / 25 days	3 mL (3 autoinjectors x 1 mL each) / 75 days

Ajovy 225 mg (fremanezumab-vfrm injection)	4.5 mL (3 autoinjectors or syringes x 1.5 mL each) / 75 days	4.5 mL (3 autoinjectors or syringes x 1.5 mL each) / 75 days
Emgality 120 mg (galcanezumab-gnlm injection)	1 mL (1 syringe or pen x 1 mL each) / 25 days	3 mL (3 syringes or pens x 1 mL each) / 75 days
Vyepti 100 mg (eptinezumab-jjmr injection, for intravenous use)	3 mL (3 single dose vials x 1 mL each) / 75 days	3 mL (3 single dose vials x 1 mL each) / 75 days
**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*		

Duration of Approval (DOA):

- 2761-E:
  - Aimovig, Ajovy, Emgality 120 mg, Vyepti (Migraine Prevention): Initial therapy DOA: 3 months; Continuation of therapy DOA: 12 months
  - Emgality 100 mg (Cluster Headache): Initial therapy DOA: 1 month; Continuation of therapy DOA: 12 months
- REG 3155-E:
  - Aimovig, Ajovy, Emgality 120 mg, Vyepti (Migraine Prevention): Initial therapy DOA: 12 months; Continuation of therapy DOA: 12 months
  - Emgality 100 mg (Cluster Headache): Initial therapy DOA: 1 month; Continuation of therapy DOA: 12 months

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4. Vyepti [package insert]. Bothell, WA: Lundbeck Seattle Bio Pharmaceuticals, Inc; October 2022.
5. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Waltham, MA: UpToDate, Inc.; 2023. https://online.lexi.com. Accessed April 3, 2023.
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STEP THERAPY CRITERIA

DRUG CLASS	**ORAL, NASAL CALCITONIN GENE-RELATED PEPTIDE (CGRP) RECEPTOR ANTAGONISTS**
BRAND NAME (generic)	**NURTEC ODT (rimegepant)** **QULIPTA (atogepant)** **UBRELVY (ubrogepant)** **ZAVZPRET (zavegepant)**

Status: CVS Caremark® Criteria
Type: Initial Step Therapy with Quantity Limit;
Post Step Therapy Prior Authorization with Quantity Limit

POLICY

FDA-APPROVED INDICATIONS

Nurtec ODT

Acute Treatment of Migraine

Nurtec ODT is indicated for the acute treatment of migraine with or without aura in adults.

Preventive Treatment of Episodic Migraine

Nurtec ODT is indicated for the preventive treatment of episodic migraine in adults.

Qulipta

Qulipta is indicated for the preventive treatment of migraine in adults.

Ubrelvy

Ubrelvy is indicated for the acute treatment of migraine with or without aura in adults.

Limitations of Use

Ubrelvy is not indicated for the preventive treatment of migraine.

Zavzpret

Zavzpret is indicated for the acute treatment of migraine with or without aura in adults.

Limitations of Use

Zavzpret is not indicated for the preventive treatment of migraine.

INITIAL STEP THERAPY with QUANTITY LIMIT* For Ubrelvy and Zavzpret
***Include Rx and OTC products unless otherwise stated.*

If the patient has filled a prescription for at least a 30 day supply of two triptan 5-HT1 receptor agonists (include combinations) within the past 180 days under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit.** If the patient does not meet the initial step therapy criteria, then the claim will reject with a message indicating that a prior authorization (PA) is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

**If the patient meets the initial step therapy criteria, then the initial limit criteria will apply. If the patient is requesting more than the initial quantity limit, the claim will reject with a message indicating that a PA is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

INITIAL STEP THERAPY with QUANTITY LIMIT* For Nurtec ODT
***Include Rx and OTC products unless otherwise stated.*

If the patient has filled a prescription for at least a 30 day supply of two triptan 5-HT1 receptor agonists (include combinations) within the past 180 days OR at least a 56 day supply of divalproex sodium, topiramate, valproate sodium, metoprolol, propranolol, timolol, atenolol, nadolol, amitriptyline, or venlafaxine within the past 730 days under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit.** If the patient does not meet the initial step therapy criteria, then the claim will reject with a message indicating that a prior authorization (PA) is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

**If the patient meets the initial step therapy criteria, then the initial limit criteria will apply. If the patient is requesting more than the initial quantity limit, the claim will reject with a message indicating that a PA is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

INITIAL STEP THERAPY with QUANTITY LIMIT* For Qulipta
***Include Rx and OTC products unless otherwise stated.*

If the patient has filled a prescription for at least a 56 day supply of divalproex sodium, topiramate, valproate sodium, metoprolol, propranolol, timolol, atenolol, nadolol, amitriptyline, or venlafaxine within the past 730 days under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit.** If the patient does not meet the initial step therapy criteria, then the claim will reject with a message indicating that a prior authorization (PA) is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

**If the patient meets the initial step therapy criteria, then the initial limit criteria will apply. If the patient is requesting more than the initial quantity limit, the claim will reject with a message indicating that a PA is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

****INITIAL LIMIT QUANTITY**

Limits do not accumulate together; patient is allowed the maximum limit for each drug and strength.

PLEASE NOTE: Since manufacturer package sizes may vary, it is the discretion of the dispensing pharmacy to fill quantities per package size up to these quantity limits. In such cases, the filling limit and day supply may be less than what is indicated.

Drug	1 Month Limit*	3 Month Limit*
Nurtec ODT (rimegepant)	16 orally disintegrating tablets / 25 days	48 orally disintegrating tablets / 75 days
Qulipta 10 mg, 30 mg, 60 mg (atogepant)	30 tablets / 25 days	90 tablets / 75 days
Ubrelvy 50 mg, 100 mg (ubrogepant)	16 tablets / 25 days	48 tablets / 75 days
Zavzpret (zavegepant)	6 nasal spray units / 18 days	24 nasal spray units / 75 days
**The duration of 18 days is used for a 21-day fill period, 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*		

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The request is for Nurtec ODT, Ubrelvy, or Zavzpret being prescribed for the acute treatment of migraine in an adult patient
  AND
  - The requested drug will not be used concurrently with another CGRP receptor antagonist
    AND
    - The patient experienced an inadequate treatment response or an intolerance to two triptan 5-HT1 receptor agonists
    OR
    - The patient has a contraindication that would prohibit a trial of triptan 5-HT1 receptor agonists

OR

- The request is for Nurtec ODT being prescribed for the preventive treatment of episodic migraine in an adult patient

OR

- The request is for Qulipta being prescribed for the preventive treatment of migraine in an adult patient
  AND
  - The requested drug will not be used concurrently with another CGRP receptor antagonist
    AND
    - The patient has NOT received at least 3 months of treatment with the requested drug
      AND
      - The patient experienced an inadequate treatment response with an 8-week trial of any of the following: A) Antiepileptic drugs (AEDs) (e.g., divalproex sodium, topiramate, valproate sodium), B) Beta-adrenergic blocking agents (e.g., metoprolol, propranolol, timolol, atenolol, nadolol), C) Antidepressants (e.g., amitriptyline, venlafaxine)
      OR
      - The patient experienced an intolerance to, or the patient has a contraindication that would prohibit an 8-week trial of any of the following: A) Antiepileptic drugs (AEDs) (e.g., divalproex sodium, topiramate, valproate sodium), B) Beta-adrenergic blocking agents (e.g., metoprolol, propranolol, timolol, atenolol, nadolol), C) Antidepressants (e.g., amitriptyline, venlafaxine)

    OR

    - The patient has received at least 3 months of treatment with the requested drug
      AND
      - The patient had a reduction in migraine days per month from baseline

Quantity Limits apply.
Ubrelvy: 16 tablets per month, 48 tablets per 3 months
Nurtec ODT: 16 tablets per month, 48 tablets per 3 months
Qulipta: 30 tablets per month, 90 tablets per 3 months
Zavzpret: 6 nasal spray units per 3 weeks, 24 nasal spray units per 3 months

**The duration of 18 days is used for a 21-day fill period, 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*

Duration of Approval (DOA):

- 3481-E:
  - Nurtec ODT, Ubrelvy, Zavzpret (Acute Treatment): DOA: 12 months
  - Nurtec ODT, Qulipta (Preventive Treatment): Initial therapy DOA: 3 months; Continuation of therapy DOA: 12 months

REFERENCES

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2. Qulipta [package insert]. Madison, NJ: Allergan USA, Inc.; April 2023.
3. Ubrelvy [package insert]. Madison, NJ: Allergan USA, Inc.; February 2023.
4. Zavzpret [package insert]. New York, NY: Pfizer Las Division of Pfizer Inc.; March 2023.
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Reference number(s)
2119-A

SPECIALTY GUIDELINE MANAGEMENT

CHOLBAM (cholic acid)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Cholbam is indicated for:
1. Treatment of bile acid synthesis disorders due to single enzyme defects (SEDs)
2. Adjunctive treatment of peroxisomal disorders (PDs) including Zellweger spectrum disorders in patients who exhibit manifestations of liver disease, steatorrhea or complications from decreased fat soluble vitamin absorption

Limitation of use: The safety and effectiveness of Cholbam on extrahepatic manifestations of bile acid synthesis disorders due to SEDs or PDs including Zellweger spectrum disorders have not been established.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
A. Initial requests:
   1. Mass spectrometry, enzyme assay, biochemical testing results, or genetic testing results confirming diagnosis; and
   2. Lab test results documenting baseline liver function (i.e., transaminases, bilirubin, presence of cholestasis).
B. Continuation of therapy requests: lab results documenting an improvement in liver function (i.e., reduced transaminases, reduced bilirubin, no evidence of cholestasis on liver biopsy).

III. CRITERIA FOR INITIAL APPROVAL

A. Bile acid synthesis disorders due to single enzyme defects (SEDs)
Authorization of 6 months may be granted for treatment of bile acid synthesis disorders due to single enzyme defects when both of the following criteria are met:
1. The diagnosis is confirmed by mass spectrometry or other biochemical testing, genetic testing, or enzyme assay.
2. The member has liver dysfunction (i.e., elevated transminases, bilirubin, presence of cholestasis) at baseline.

B. Peroxisomal disorders (PDs) including Zellweger spectrum disorders

Authorization of 6 months may be granted for adjunctive treatment of peroxisomal disorders when the diagnosis is confirmed by mass spectrometry or other biochemical testing or genetic testing, and the member exhibits manifestations of liver disease.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted to members with an indication listed in Section III who are currently receiving the requested medication through a paid pharmacy or medical benefit, and who are experiencing benefit from therapy as evidenced by improvement from baseline as documented per clinical chart notes.

A. Bile acid synthesis disorders due to single enzyme defects (SEDs)

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for bile acid synthesis disorders due to single enzyme defects who have achieved and maintained improvement in liver function (i.e., reduced transaminases, reduced bilirubin, no evidence of cholestasis on liver biopsy).

B. Peroxisomal disorders (PDs) including Zellweger spectrum disorders

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for adjunctive treatment of peroxisomal disorders with Cholbam who have achieved and maintained improvement in liver function (i.e. reduced transaminases, reduced bilirubin, no evidence of cholestasis on liver biopsy).

IV. REFERENCES

1. Cholbam [package insert]. San Diego, CA: Retrophin, Inc.; October 2020.
2. Gonzales E, Gerhardt MF, Fabre M et al. Oral cholic acid for hereditary defects of primary bile acid synthesis: a safe and effective long-term therapy. *Gastroenterology.* 2009;137:1310-1320.
3. Heubi J, Setchell KDR, Bove KE. Inborn errors of bile acid metabolism. *Seminars Liver Dis*. 2007;27:282-294.
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Reference number(s)
2005-A

SPECIALTY GUIDELINE MANAGEMENT

CIMZIA (certolizumab pegol)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

A. Reducing signs and symptoms of Crohn's disease and maintaining clinical response in adult patients with moderately to severely active disease who have had an inadequate response to conventional therapy.
B. Treatment of adults with moderately to severely active rheumatoid arthritis.
C. Treatment of adult patients with active psoriatic arthritis.
D. Treatment of adults with active ankylosing spondylitis.
E. Treatment of adults with active non-radiographic axial spondyloarthritis with objective signs of inflammation.
F. Treatment of adults with moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

A. Rheumatoid arthritis (RA)
   1. For initial requests:
      i. Chart notes, medical record documentation, or claims history supporting previous medications tried (if applicable), including response to therapy. If therapy is not advisable, documentation of clinical reason to avoid therapy.
      ii. Laboratory results, chart notes, or medical record documentation of biomarker testing (i.e., rheumatoid factor [RF], anti-cyclic citrullinated peptide [anti-CCP], and C-reactive protein [CRP] and/or erythrocyte sedimentation rate [ESR]) (if applicable).
   2. For continuation requests: Chart notes or medical record documentation supporting positive clinical response.

B. Ankylosing spondylitis (AS), non-radiographic axial spondyloarthritis (nr-axSpA), and psoriatic arthritis (PsA)
   1. Initial requests: Chart notes, medical record documentation, or claims history supporting previous medications tried (if applicable), including response to therapy. If therapy is not advisable, documentation of clinical reason to avoid therapy.
   2. Continuation requests: Chart notes or medical record documentation supporting positive clinical response.

C. Crohn's disease (CD)

Continuation requests: Chart notes or medical record documentation supporting positive clinical response to therapy or remission.

D. Plaque psoriasis (PsO)
   1. Initial requests:
      i. Chart notes or medical record documentation of affected area(s) and body surface area (BSA) affected (if applicable).
      ii. Chart notes, medical record documentation, or claims history supporting previous medications tried (if applicable), including response to therapy. If therapy is not advisable, documentation of clinical reason to avoid therapy.
   2. Continuation requests: Chart notes or medical record documentation of decreased body surface area (BSA) affected and/or improvement in signs and symptoms.

III. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with one of the following:
A. Rheumatoid arthritis, ankylosing spondylitis, or non-radiographic axial spondyloarthritis: rheumatologist
B. Psoriatic arthritis: rheumatologist or dermatologist
C. Crohn's disease: gastroenterologist
D. Plaque psoriasis: dermatologist

IV. CRITERIA FOR INITIAL APPROVAL

B. Rheumatoid arthritis (RA)
1. Authorization of 12 months may be granted for adult members who have previously received a biologic or targeted synthetic drug (e.g., Rinvoq, Xeljanz) indicated for moderately to severely active rheumatoid arthritis.

2. Authorization of 12 months may be granted for adult members for treatment of moderately to severely active RA when all of the following criteria are met:
   i. Member meets either of the following criteria:
      a. Member has been tested for either of the following biomarkers and the test was positive:
         1. Rheumatoid Factor (RF)
         2. Anti-cyclic citrullinated peptide (anti-CCP)
      b. Member has been tested for ALL of the following biomarkers:
         1. RF
         2. Anti-CCP
         3. C-reactive protein (CRP) and/or erythrocyte sedimentation rate (ESR)
   ii. Member meets either of the following criteria:
      a. Member has experienced an inadequate response to at least a 3-month trial of methotrexate despite adequate dosing (i.e., titrated to at least 15 mg/week).
      b. Member has an intolerance or contraindication to methotrexate (see Appendix).

C. Psoriatic arthritis (PsA)
1. Authorization of 12 months may be granted for adult members who have previously received a biologic or targeted synthetic drug (e.g., Rinvoq, Otezla) indicated for active psoriatic arthritis.

2. Authorization of 12 months may be granted for adult members for treatment of active psoriatic arthritis when either of the following criteria is met:
   i. Member has mild to moderate disease and meets one of the following criteria:

a. Member has had an inadequate response to methotrexate, leflunomide, or another conventional synthetic drug (e.g., sulfasalazine) administered at an adequate dose and duration.
b. Member has an intolerance or contraindication to methotrexate or leflunomide (see Appendix), or another conventional synthetic drug (e.g., sulfasalazine).
c. Member has enthesitis or predominantly axial disease.

ii. Member has severe disease.

D. Ankylosing spondylitis (AS) and non-radiographic axial spondyloarthritis (nr-axSpA)

1. Authorization of 12 months may be granted for adult members who have previously received a biologic or targeted synthetic drug (e.g., Rinvoq, Xeljanz) indicated for active ankylosing spondylitis or active non-radiographic axial spondyloarthritis.

2. Authorization of 12 months may be granted for adult members for treatment of active ankylosing spondylitis or active non-radiographic axial spondyloarthritis when either of the following criteria is met:
   i. Member has experienced an inadequate response to at least two non-steroidal anti-inflammatory drugs (NSAIDs).
   ii. Member has an intolerance or contraindication to two or more NSAIDs.

E. Crohn's disease (CD)

Authorization of 12 months may be granted for adult members for treatment of moderately to severely active Crohn's disease.

F. Plaque psoriasis (PsO)

1. Authorization of 12 months may be granted for adult members who have previously received a biologic or targeted synthetic drug (e.g., Sotyktu, Otezla) indicated for the treatment of moderate to severe plaque psoriasis.

2. Authorization of 12 months may be granted for adult members for treatment of moderate to severe plaque psoriasis when any of the following criteria is met:
   i. Crucial body areas (e.g., hands, feet, face, neck, scalp, genitals/groin, intertriginous areas) are affected.
   ii. At least 10% of body surface area (BSA) is affected.
   iii. At least 3% of body surface area (BSA) is affected and the member meets either of the following criteria:
      a. Member has had an inadequate response or intolerance to either phototherapy (e.g., UVB, PUVA) or pharmacologic treatment with methotrexate, cyclosporine, or acitretin.
      b. Member has a clinical reason to avoid pharmacologic treatment with methotrexate, cyclosporine, and acitretin (see Appendix).

V. CONTINUATION OF THERAPY

A. Rheumatoid arthritis (RA)

Authorization of 12 months may be granted for all adult members (including new members) who are using the requested medication for moderately to severely active rheumatoid arthritis and who achieve or maintain a positive clinical response as evidenced by disease activity improvement of at least 20% from baseline in tender joint count, swollen joint count, pain, or disability.

B. Psoriatic arthritis (PsA)

Authorization of 12 months may be granted for all adult members (including new members) who are using the requested medication for psoriatic arthritis and who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition when there is improvement in any of the following from baseline:

1. Number of swollen joints
2. Number of tender joints
3. Dactylitis
4. Enthesitis
5. Axial disease
6. Skin and/or nail involvement

C. Ankylosing spondylitis (AS) and non-radiographic axial spondyloarthritis (nr-axSpA)

Authorization of 12 months may be granted for all adult members (including new members) who are using the requested medication for active ankylosing spondylitis or active non-radiographic axial spondyloarthritis and who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition when there is improvement in any of the following from baseline:

1. Functional status
2. Total spinal pain
3. Inflammation (e.g., morning stiffness)

D. Crohn's disease (CD)

1. Authorization of 12 months may be granted for all adult members (including new members) who are using the requested medication for moderately to severely active Crohn's disease and who achieve or maintain remission.

2. Authorization of 12 months may be granted for all adult members (including new members) who are using the requested medication for moderately to severely active Crohn's disease and who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition when there is improvement in any of the following from baseline:
   i. Abdominal pain or tenderness
   ii. Diarrhea
   iii. Body weight
   iv. Abdominal mass
   v. Hematocrit
   vi. Appearance of the mucosa on endoscopy, computed tomography enterography (CTE), magnetic resonance enterography (MRE), or intestinal ultrasound
   vii. Improvement on a disease activity scoring tool (e.g., Crohn's Disease Activity Index [CDAI] score)

E. Plaque psoriasis (PsO)

Authorization of 12 months may be granted for all adult members (including new members) who are using the requested medication for moderate to severe plaque psoriasis and who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition when either of the following is met:

1. Reduction in body surface area (BSA) affected from baseline
2. Improvement in signs and symptoms from baseline (e.g., itching, redness, flaking, scaling, burning, cracking, pain)

VI. OTHER

For all indications: Member has had a documented negative tuberculosis (TB) test (which can include a tuberculosis skin test [PPD], an interferon-release assay [IGRA], or a chest x-ray)* within 6 months of initiating therapy for persons who are naïve to biologic drugs or targeted synthetic drugs associated with an increased risk of TB.

* If the screening testing for TB is positive, there must be further testing to confirm there is no active disease. Do not administer the requested medication to members with active TB infection. If there is latent disease, TB treatment must be started before initiation of the requested medication.

For all indications: Member cannot use the requested medication concomitantly with any other biologic drug or targeted synthetic drug.

VII. DOSAGE AND ADMINISTRATION

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

VIII. APPENDIX

Examples of Clinical Reasons to Avoid Pharmacologic Treatment with Methotrexate, Cyclosporine, Acitretin, or Leflunomide

1. Clinical diagnosis of alcohol use disorder, alcoholic liver disease, or other chronic liver disease
2. Drug interaction
3. Risk of treatment-related toxicity
4. Pregnancy or currently planning pregnancy
5. Breastfeeding
6. Significant comorbidity prohibits use of systemic agents (e.g., liver or kidney disease, blood dyscrasias, uncontrolled hypertension)
7. Hypersensitivity
8. History of intolerance or adverse event

IX. REFERENCES

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Reference number(s)
1624-A

SPECIALTY GUIDELINE MANAGEMENT

SENSIPAR (cinacalcet)
cinacalcet (generic)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
1. Secondary hyperparathyroidism (HPT) in adult patients with chronic kidney disease (CKD) on dialysis
2. Hypercalcemia in adult patients with parathyroid carcinoma
3. Hypercalcemia in adult patients with primary HPT for whom parathyroidectomy would be indicated on the basis of serum calcium levels, but who are unable to undergo parathyroidectomy

B. Compendial Use
Tertiary hyperparathyroidism in post-kidney transplant patients not receiving dialysis

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Secondary Hyperparathyroidism with CKD on Dialysis
Authorization of 12 months may be granted for treatment of secondary hyperparathyroidism in a member with chronic kidney disease on dialysis who has a serum calcium level (corrected for albumin) greater than or equal to 8.4 mg/dL (see Appendix).

B. Primary Hyperparathyroidism
Authorization of 12 months may be granted for treatment of primary hyperparathyroidism in a member who is not able to undergo parathyroidectomy and has a serum calcium level (corrected for albumin) greater than or equal to 8.4 mg/dL (see Appendix).

C. Tertiary Hyperparathyroidism in Post-Kidney Transplant Patients Not Receiving Dialysis
Authorization of 12 months may be granted for treatment of tertiary hyperparathyroidism in a member who has had a kidney transplant, is not receiving dialysis, and has a serum calcium level (corrected for albumin) greater than or equal to 8.4 mg/dL (see Appendix).

D. Parathyroid Carcinoma
Authorization of 12 months may be granted for the treatment of parathyroid carcinoma in a member who has a serum calcium level (corrected for albumin) greater than or equal to 8.4 mg/dL (see Appendix).

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II when the following criteria are met:

A. Secondary Hyperparathyroidism with CKD on Dialysis
Member is experiencing benefit from therapy as evidenced by a decrease in intact parathyroid hormone (iPTH) levels from pretreatment baseline.

B. All other indications
Member is experiencing benefit from therapy (e.g., decreased or normalized corrected serum calcium levels since starting therapy).

IV. APPENDIX

Corrected calcium = measured total calcium + 0.8(4.0 – serum albumin)

V. REFERENCES

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Reference number(s)
1604-A

SPECIALTY GUIDELINE MANAGEMENT

CINRYZE (C1 esterase inhibitor [human])

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Cinryze is indicated for routine prophylaxis against angioedema attacks in adults, adolescents and pediatric patients (6 years of age or older) with hereditary angioedema (HAE).

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
A. For initial authorization, the following should be documented:
   1. C1 inhibitor functional and antigenic protein levels
   2. F12, angiopoietin-1, plasminogen, kininogen-1 (KNG1), heparan sulfate-glucosamine 3-O-sulfotransferase 6 (HS3ST6), or myoferlin (MYOF) gene mutation testing, if applicable
   3. Chart notes confirming family history of angioedema and the angioedema was refractory to a trial of high-dose antihistamine therapy, if applicable
B. For continuation of therapy, chart notes demonstrating a reduction in frequency of attacks

III. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with a prescriber who specializes in the management of HAE.

IV. CRITERIA FOR INITIAL APPROVAL

Hereditary angioedema (HAE)
Authorization of 6 months may be granted for prevention of HAE attacks when the requested medication will not be used in combination with any other medication used for the prophylaxis of HAE attacks and either of the following criteria is met at the time of diagnosis:
A. Member has C1 inhibitor deficiency or dysfunction as confirmed by laboratory testing and meets one of the following criteria:
   1. C1 inhibitor (C1-INH) antigenic level below the lower limit of normal as defined by the laboratory performing the test, or
   2. Normal C1-INH antigenic level and a low C1-INH functional level (functional C1-INH less than 50% or C1-INH functional level below the lower limit of normal as defined by the laboratory performing the test).

B. Member has normal C1 inhibitor as confirmed by laboratory testing and meets one of the following criteria:
   1. Member has an F12, angiopoietin-1, plasminogen, kininogen-1 (KNG1), heparan sulfate-glucosamine 3-O-sulfotransferase 6 (HS3ST6), or myoferlin (MYOF) gene mutation as confirmed by genetic testing, or
   2. Member has a documented family history of angioedema and the angioedema was refractory to a trial of high-dose antihistamine therapy (i.e., cetirizine at 40 mg per day or the equivalent) for at least one month.

V. CONTINUATION OF THERAPY

Authorization of 6 months may be granted for continuation of therapy when all of the following criteria are met:
A. Member meets the criteria for initial approval.
B. Member has experienced a significant reduction in frequency of attacks (e.g., ≥ 50%) since starting treatment.
C. Member has reduced the use of medications to treat acute attacks since starting treatment.

VI. REFERENCES

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QUANTITY LIMIT PRIOR AUTHORIZATION CRITERIA

DRUG CLASS	**TOPICAL CLINDAMYCIN AND ERYTHROMYCIN**
BRAND NAME (generic)	**CLINDAGEL (clindamycin gel)** **CLEOCIN-T (clindamycin gel, lotion, solution)** **ERYGEL (erythromycin gel)** **(erythromycin solution)**

Status: CVS Caremark® Criteria
Type: Quantity Limit; Post Limit Prior Authorization

POLICY

FDA-APPROVED INDICATIONS

Clindagel
Clindagel is indicated for topical application in the treatment of acne vulgaris. In view of the potential for diarrhea, bloody diarrhea, and pseudomembranous colitis, the physician should consider whether other agents are more appropriate.

Cleocin-T Gel, Lotion, Solution
Cleocin-T Topical Solution, Cleocin-T Topical Gel and Cleocin-T Topical Lotion are indicated in the treatment of acne vulgaris. In view of the potential for diarrhea, bloody diarrhea and pseudomembranous colitis, the physician should consider whether other agents are more appropriate

Erygel
Erygel Topical Gel is indicated for the topical treatment of acne vulgaris.

Erythromycin Topical Solution
Erythromycin Topical Solution USP, 2% is indicated for the topical treatment of acne vulgaris.

INITIAL QUANTITY LIMIT**

INITIAL LIMIT QUANTITY
Limits should accumulate across same chemical entity up to highest quantity listed depending on the order the claims are processed. Accumulation does not apply if limit is coded for daily dose.

PLEASE NOTE: Since manufacturer package sizes may vary, it is the discretion of the dispensing pharmacy to fill quantities per package size up to these quantity limits. In such cases the filling limit and day supply may be less than what is indicated.

Drug	1 Month Limit*	3 Month Limit*
Clindagel (clindamycin gel)	75 mL / 25 days	225 mL / 75 days
Cleocin-T gel (clindamycin gel)	75 gm / 25 days	225 gm / 75 days
Cleocin-T lotion (clindamycin lotion)	60 mL / 25 days	180 mL / 75 days
Cleocin-T solution (clindamycin topical solution)	60 mL / 25 days	180 mL / 75 days
Erygel (erythromycin gel)	60 gm / 25 days	180 gm / 75 days
erythromycin topical solution	60 mL / 25 days	180 mL / 75 days

**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*

**If the patient is requesting more than the initial quantity limit, the claim will reject with a message indicating that a prior authorization is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for the topical treatment of acne vulgaris

AND

- The requested drug is not being used in a footbath

Quantity Limits apply.

POST LIMIT QUANTITY

PLEASE NOTE: Since manufacturer package sizes may vary, it is the discretion of the dispensing pharmacy to fill quantities per package size up to these quantity limits. In such cases the filling limit and day supply may be less than what is indicated.

Drug	1 Month Limit*	3 Month Limit*
Clindagel (clindamycin gel)	150 mL / 25 days	450 mL / 75 days
Cleocin-T gel (clindamycin gel)	150 gm / 25 days	450 gm / 75 days
Cleocin-T lotion (clindamycin lotion)	120 mL / 25 days	360 mL / 75 days
Cleocin-T solution (clindamycin topical solution)	120 mL / 25 days	360 mL / 75 days
Erygel (erythromycin gel)	120 gm / 25 days	360 gm / 75 days
erythromycin topical solution	120 mL / 25 days	360 mL / 75 days

** The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*

REFERENCES

1. Clindagel [package insert]. Bridgewater, NJ: Bausch Health US, LLC. January 2020.
2. Cleocin-T Gel, Lotion, Solution [package insert]. New York, NY: Pfizer; December 2019.
3. Erygel [package insert]. Morgantown, WV: Mylan Pharmaceuticals Inc.; June 2018.
4. Erythromycin Topical Solution [package insert]. Allegan, MI: Perrigo; August 2022.
5. Lexicomp Online, Lexi-Drugs Online, Hudson, OH: UpToDate, Inc.; 2023; Accessed March 9, 2023.
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9. Burn Triage and Treatment - Thermal Injuries. Available at: https://chemm.hhs.gov/burns.htm. Accessed February 25, 2022.

QUANTITY LIMIT PRIOR AUTHORIZATION CRITERIA

BRAND NAME
(generic)

(clotrimazole troches/lozenges)

Status: CVS Caremark Criteria
Type: Quantity Limit; Post Limit Prior Authorization

POLICY

FDA-APPROVED INDICATIONS

Clotrimazole lozenges are indicated for the local treatment of oropharyngeal candidiasis. The diagnosis should be confirmed by a KOH smear and/or culture prior to treatment.

Clotrimazole lozenges are also indicated prophylactically to reduce the incidence of oropharyngeal candidiasis in patients immunocompromised by conditions that include chemotherapy, radiotherapy, or steroid therapy utilized in the treatment of leukemia, solid tumors, or renal transplantation. There are no data from adequate and well-controlled trials to establish the safety and efficacy of this product for prophylactic use in patients immunocompromised by etiologies other than those listed in the previous sentence.

INITIAL QUANTITY LIMIT**

LIMIT CRITERIA

PLEASE NOTE: Since manufacturer package sizes may vary, it is the discretion of the dispensing pharmacy to fill quantities per package size up to these quantity limits. In such cases the filling limit and day supply may be less than what is indicated.

Drug	1 Month Limit*	3 Month Limit*
Clotrimazole Lozenges (Troches)	90 lozenges / 25 days	270 lozenges / 75 days

**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*

**If the patient is requesting more than the initial quantity limit, the claim will reject with a message indicating that a prior authorization is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being used for the treatment of oropharyngeal candidiasis

AND

- The requested drug is not being used in a footbath

Quantity Limits apply.

** The duration of 21 days is used for a 28-day fill period to allow time for refill processing.*
*** These drugs are for short-term acute use; therefore, the mail limit will be the same as the retail limit. The intent is for prescriptions of the requested drug to be filled one month at a time, even if filled at mail order; there should be no 3-month supplies filled.*

REFERENCES

1. Clotrimazole Lozenges (clotrimazole troche) [package insert]. Minneapolis, MN: Perrigo; December 2021.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2023; Accessed February 2, 2023.

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Reference number
1854-A

SPECIALTY GUIDELINE MANAGEMENT

COMETRIQ (cabozantinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication
Treatment of progressive, metastatic medullary thyroid cancer (MTC).

B. Compendial Uses
1. Follicular, Hürthle cell, and papillary thyroid carcinoma
2. Non-small cell lung cancer with RET gene arrangements

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of RET gene rearrangement documentation is necessary to initiate the prior authorization review for the indication of non-small cell lung cancer.

III. CRITERIA FOR INITIAL APPROVAL

A. Follicular, Hurthle Cell, and Papillary Thyroid carcinoma
Authorization of 12 months may be granted for treatment of follicular, Hürthle cell, or papillary thyroid carcinoma when all of the following criteria are met:
1. The disease is not amenable to radioactive iodine (RAI) therapy.
2. The disease has progressed after treatment with lenvatinib or sorafenib.

B. Medullary Thyroid Carcinoma
Authorization of 12 months may be granted for treatment of medullary thyroid carcinoma.

C. Non-small cell lung cancer (NSCLC)
Authorization of 12 months may be granted for treatment of recurrent, advanced, or metastatic NSCLC with RET gene rearrangements when used as a single agent.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

V. REFERENCES

1. Cometriq [package insert]. South San Francisco, CA: Exelixis; October 2020.
2. The NCCN Drugs & Biologics Compendium® © 2021 National Comprehensive Cancer Network, Inc. Available at: https://www.nccn.org. Accessed November 4, 2021.

PRIOR AUTHORIZATION CRITERIA

DRUG CLASS **COMPOUNDED DRUG PRODUCTS**

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

POLICY

COVERAGE CRITERIA

Compounded drug products will be covered with prior authorization when the following criteria are met:

- The request is for any of the following: intraveneous (IV) injection or infusion, anti-infective for injectable use (e.g., antibacterials, antivirals, antifungals), total parenteral nutrition (TPN), leuprolide acetate for infertility in a patient unable to utilize the FDA-approved commercially available product (1mg per 0.2mL kit), pyrimethamine, hydroxyprogesterone, sirolimus for tuberous sclerosis where other dermatological treatments (e.g., laser therapy, surgery, dermabrasion) are inappropriate

OR

- The request is for tacrolimus (Prograf) or everolimus (Zortress) for a patient receiving a transplant

OR

- Each of the active ingredients in the compound are FDA-approved drugs
- Each of the active ingredients in the compound are FDA-approved for the indication for which the compound is being prescribed
- The compound route of administration (ROA) is the same as the FDA-approved route of administration for each active ingredient
- The dosage or concentration of each active ingredient in the compound is equal to or below the FDA-approved dosage or concentration
- The request is not for a topical compound or a topical compound kit for use on skin (e.g., cream, gel, lotion, ointment)
- The compound is not intended for anti-aging or cosmetic use, or is not a compound kit, or does not contain a bulk powder or dietary supplement
- The request is not for a hormone therapy compound for menopause or for androgen decline due to aging, (e.g., testosterone, estrogen, progestin, bioidentical hormone)
- Coverage is provided for additional fills of the compounded drug if patient needs more than 1 fill per month (necessity may include continuation of antibiotic therapy, stability is less than a month, dose adjustment)
  AND
  - There is a current supply shortage of the commercially manufactured product
    OR
  - The patient has a medical need for a dosage form or dosage strength that is not available commercially or manufactured
    OR
  - The patient had an intolerance or contraindication to the commercially manufactured product (e.g., allergen or adverse effects due to inactive ingredients)
    OR
  - The commercial product has been discontinued by the pharmaceutical manufacturer for reasons other than lack of safety or effectiveness

REFERENCES

1. 21 USC 353a: Pharmacy compounding From Title 21-FOOD AND DRUGS CHAPTER 9-FEDERAL FOOD, DRUG, AND COSMETIC ACT SUBCHAPTER V-DRUGS AND DEVICES Part A-Drugs and Devices. Available at: https://uscode.house.gov/view.xhtml?hl=false&edition=prelim&req=granuleid%3AUSC-prelim-title21-section353a&num=0&saved=%7CKGNvbXBvdW5kIGRydWdzKQ%3D%3D%7CdHJlZXNvcnQ%3D%7CdHJ1ZQ%3D%3D%7C15%7Ctrue%7Cprelim. Accessed February 2023.
2. Compounding Quality Act. U.S. Food and Drug Administration. Pharmacy Compounding. Available at: https://www.govinfo.gov/app/details/BILLS-113hr3204enr. Accessed February 2023.
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QUANTITY LIMIT CRITERIA

DRUG CLASS	**DIABETIC CONTINUOUS GLUCOSE MONITOR SENSORS**
BRAND NAME* (generic)	
	DEXCOM (ALL PRODUCTS)
	EVERSENSE (ALL PRODUCTS)
	FREESTYLE LIBRE (ALL PRODUCTS)
	GUARDIAN (ALL PRODUCTS)

Status: CVS Caremark® Criteria
Type: Quantity Limit ***Ref # 5282-H***

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

INITIAL LIMIT QUANTITY
Limits do not accumulate together; patient is allowed the maximum limit for each drug and strength

Drug	1 Month Limit*	3 Month Limit*
Dexcom G6	3 sensors / 25 days	9 sensors / 75 days
Dexcom G7	3 sensors / 25 days	9 sensors / 75 days
Freestyle Libre 10-Day	3 sensors / 25 days	9 sensors / 75 days
Enlite	5 sensors / 25 days	15 sensors / 75 days

**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*

Drug	4 Week Limit**	12 Week Limit**
Freestyle Libre 2	2 sensors / 21 days	6 sensors / 63 days
Freestyle Libre 3	2 sensors / 21 days	6 sensors / 63 days
Freestyle Libre 14-Day	2 sensors / 21 days	6 sensors / 63 days
Guardian 3	5 sensors / 21 days	15 sensors / 63 days
Guardian 4	5 sensors / 21 days	15 sensors / 63 days

***The duration of 21 days is used for a 28-day fill period and 63 days is used for an 84-day fill period to allow time for refill processing.*

Drug	Limit***

Eversense	1 sensor / 75 days
Eversense E3 (XL)	1 sensor / 150 days

****The duration of 75 days is used for a 90-day fill period and 150 days is used for a 180-day fill period to allow time for refill processing.*

RATIONALE

The limit allows a quantity sufficient for each product based on the individual sensor lifespan. If the patient is requesting more than the initial quantity limit, the claim will reject with a message indicating that quantity limits are exceeded.

REFERENCES

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Written by:	UM Development (RZ)
Date Written:	03/2022
Revised:	(ASA) 09/2022 (updated QL for Guardian 3, added Freestyle Libre 3), 12/2022 (added Dexcom G7), 05/2023 (added Guardian 4)
Reviewed:	Medical Affairs (CHART) 03/31/2022, 09/22/2022, 12/22/2022, 06/01/2023 MD Committee: 09/2022 External Review: 06/2022 (MD Subcommittee); 12/2022 (MD Subcommittee), 06/2023 (MD Subcommittee)

PRIOR AUTHORIZATION CRITERIA

DRUG CLASS	**WEIGHT LOSS MANAGEMENT**
BRAND NAME (generic)	**CONTRAVE (naltrexone HCl and bupropion HCl extended release)**

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

POLICY

FDA-APPROVED INDICATIONS

Contrave is indicated as an adjunct to a reduced-calorie diet and increased physical activity for chronic weight management in adult patients with an initial body mass index (BMI) of:

- 30 kg/m^2 or greater (obese), or
- 27 kg/m^2 or greater (overweight) in the presence of at least one weight related comorbid condition (e.g., hypertension, type 2 diabetes mellitus or dyslipidemia)

Limitations of Use

- The effect of Contrave on cardiovascular morbidity and mortality has not been established.
- The safety and effectiveness of Contrave in combination with other products intended for weight loss, including prescription drugs, over-the-counter drugs, and herbal preparations, have not been established.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has completed at least 4 months of therapy with the requested drug
  AND
  - The patient lost at least 5 percent of baseline body weight OR the patient has continued to maintain their initial 5 percent weight loss. [Documentation is required for approval.]

OR

- The requested drug will be used with a reduced calorie diet and increased physical activity for chronic weight management in an adult
  AND
- The patient has participated in a comprehensive weight management program that encourages behavioral modification, reduced calorie diet and increased physical activity with continuing follow-up for at least 6 months prior to using drug therapy
  AND
  - The patient has a body mass index (BMI) greater than or equal to 30 kilogram per square meter
    OR
  - The patient has a body mass index (BMI) greater than or equal to 27 kilogram per square meter AND has at least one weight related comorbid condition (e.g., hypertension, type 2 diabetes mellitus or dyslipidemia)

REFERENCES

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Reference number(s)
2754-A

SPECIALTY GUIDELINE MANAGEMENT

COPIKTRA (duvelisib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
Chronic Lymphocytic Leukemia (CLL)/Small Lymphocytic Lymphoma (SLL)
Copiktra is indicated for the treatment of adult patients with relapsed or refractory CLL or SLL after at least two prior therapies.

B. Compendial Use
1. Chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL)
2. T-Cell lymphomas
   a. Breast implant associated anaplastic large cell lymphoma (ALCL)
   b. Hepatosplenic T-Cell lymphoma
   c. Peripheral T-cell lymphomas (PTCL)

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Chronic Lymphocytic Leukemia (CLL)/Small Lymphocytic Lymphoma (SLL)
Authorization of 12 months may be granted for treatment of relapsed or refractory CLL/SLL when the requested medication is used as single agent.

B. T-Cell Lymphomas
Authorization of 12 months may be granted for treatment of T-cell lymphomas with any of the following subtypes:
1. Breast implant-associated anaplastic large cell lymphoma (ALCL) when all of the following are met:
   i. The requested drug is used as subsequent therapy for relapsed or refractory disease.
   ii. The requested drug is used as a single agent
2. Hepatosplenic T-Cell lymphoma when all of the following criteria are met:
   i. The requested drug is used for refractory disease after 2 first-line therapy regimens
   ii. The requested drug is used as a single agent
3. Peripheral T-cell lymphoma (PTCL) [including the following subtypes: peripheral T-cell lymphoma not otherwise specified, enteropathy-associated T-cell lymphoma (EATL), monomorphic epitheliotropic intestinal T-cell lymphoma (MEITL), angioimmunoblastic T-cell lymphoma (AITL), nodal peripheral T-cell lymphoma with TFH phenotype (PTCL, TFH), follicular T-cell lymphoma (FTCL), or anaplastic large cell lymphoma (ALCL) when all of the following criteria are met:
   i. The requested drug is used as palliative or subsequent therapy for relapsed or refractory disease
   ii. The requested drug is used as a single agent

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

IV. REFERENCES

1. Copiktra [package insert]. Las Vegas, NV: Secura Bio, Inc.; December 2021.
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PRIOR AUTHORIZATION CRITERIA

BRAND NAME
(generic)

CORLANOR
(ivabradine)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

POLICY

FDA-APPROVED INDICATIONS

Heart Failure in Adult Patients

Corlanor is indicated to reduce the risk of hospitalization for worsening heart failure in adult patients with stable, symptomatic chronic heart failure with left ventricular ejection fraction ≤ 35%, who are in sinus rhythm with resting heart rate ≥ 70 beats per minute and either are on maximally tolerated doses of beta-blockers or have a contraindication to beta-blocker use.

Heart Failure in Pediatric Patients

Corlanor is indicated for the treatment of stable symptomatic heart failure due to dilated cardiomyopathy (DCM) in pediatric patients aged 6 months and older, who are in sinus rhythm with an elevated heart rate.

Compendial Uses

Inappropriate Sinus Tachycardia, adults[3]

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for an adult patient

AND

- The requested drug is being prescribed to reduce the risk of hospitalization for worsening heart failure in a patient with stable, symptomatic chronic heart failure

AND

- The patient has a left ventricular ejection fraction (LVEF) less than or equal to 35 percent. Documentation is required for approval.

AND

- The patient is currently receiving optimal therapy for heart failure management (e.g., angiotensin-converting enzyme inhibitor [ACEI], angiotensin II receptor blocker [ARB], angiotensin receptor-neprilysin inhibitor [ARNI], beta-blocker, sodium-glucose co-transporter-2 inhibitor [SGLT2I], mineralocorticoid receptor antagonist [MRA])

AND

- The patient is receiving treatment with a maximally tolerated dose of a beta-blocker OR the patient has an intolerance or contraindication to beta-blocker use

AND

- The patient is in sinus rhythm

AND

- If the request is not for continuation of therapy, the patient has a resting heart rate greater than or equal to 70 beats per minute [BPM]

OR

- The requested drug is being prescribed for the management of symptomatic inappropriate sinus tachycardia (IST)

OR

- The requested drug is being prescribed for a pediatric patient 6 months of age or older

AND

- The requested drug is being prescribed for the treatment of stable, symptomatic heart failure due to dilated cardiomyopathy (DCM)

  AND

- The patient is in sinus rhythm

  AND

- If the request is not for continuation of therapy, the patient has an elevated heart rate

REFERENCES

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5. Page PL, Joglar JA, Caldwell MA et al. 2015 ACC/AHA/HRS Guideline for the Management of Adult Patients with Supraventricular Tachycardia: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society. *Circulation*. 2016;133;e506-e574.

QUANTITY LIMIT CRITERIA

DRUG CLASS	**CORTICOSTEROID ORAL INHALATION**
BRAND NAME (generic)	
	ALVESCO (ciclesonide)
	ARMONAIR DIGIHALER (fluticasone propionate)
	ARNUITY ELLIPTA (fluticasone furoate)
	ASMANEX HFA (mometasone furoate)
	ASMANEX TWISTHALER (mometasone furoate)
	FLOVENT DISKUS (fluticasone propionate)
	FLOVENT HFA (fluticasone propionate)
	PULMICORT FLEXHALER (budesonide)
	PULMICORT RESPULES (budesonide)
	QVAR REDIHALER (beclomethasone)

Status: CVS Caremark Criteria
Type: Quantity Limit

POLICY

FDA-APPROVED INDICATIONS

Alvesco

Alvesco is indicated for the maintenance treatment of asthma as prophylactic therapy in adult and adolescent patients 12 years of age and older.
Alvesco is NOT indicated for children under 12 years of age.

ArmonAir Digihaler

ArmonAir Digihaler is indicated for the maintenance treatment of asthma as prophylactic therapy in adult and pediatric patients 4 years of age and older.

Arnuity Ellipta
Arnuity Ellipta is indicated for the once-daily maintenance treatment of asthma as prophylactic therapy in patients aged 5 years and older.

Asmanex HFA
Asmanex HFA is indicated for the maintenance treatment of asthma as prophylactic therapy in patients 5 years of age and older.

Asmanex Twisthaler
Asmanex Twisthaler is indicated for the maintenance treatment of asthma as prophylactic therapy in patients 4 years of age and older.
Asmanex Twisthaler is NOT indicated in children less than 4 years of age.

Flovent Diskus
Flovent Diskus is indicated for the maintenance treatment of asthma as prophylactic therapy in patients aged 4 years and older.

Flovent HFA
Flovent HFA is indicated for the maintenance treatment of asthma as prophylactic therapy in patients aged 4 years and older.

Pulmicort Flexhaler
Pulmicort Flexhaler is indicated for the maintenance treatment of asthma as prophylactic therapy in patients six years of age or older.

Pulmicort Respules
Pulmicort Respules is indicated for the maintenance treatment of asthma and as prophylactic therapy in children 12 months to 8 years of age.

QVAR Redihaler
QVAR Redihaler is indicated in the maintenance treatment of asthma as prophylactic therapy in adults and pediatric patients 4 years of age and older.

Important Limitations of Use
Oral inhaled corticosteroids are NOT indicated for the relief of acute bronchospasm.

REFERENCES

1. Alvesco [package insert]. Zug, 6300 Switzerland: Covis Pharma; October 2020.
2. ArmonAir Digihaler [package insert]. Parsippany, NJ: Teva Pharmaceuticals USA, Inc.; April 2022.
3. Arnuity Ellipta [package insert]. Research Triangle Park, NC: GlaxoSmithKline; February 2020.
4. Asmanex HFA [package insert]. Jersey City, NJ: Organon Global Inc.; June 2021.
5. Asmanex Twisthaler [package insert]. Jersey City, NJ: Organon Global Inc.; June 2021.
6. Flovent Diskus [package insert]. Research Triangle Park, NC: GlaxoSmithKline; July 2020.
7. Flovent HFA [package insert]. Research Triangle Park, NC: GlaxoSmithKline; August 2021.
8. Pulmicort Flexhaler [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; October 2019.
9. Pulmicort Respules [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; October 2019.
10. QVAR Redihaler [package insert]. Parsippany, NJ: Teva Pharmaceuticals USA, Inc.; January 2021.

LIMIT CRITERIA
Limits do not accumulate together; patient is allowed the maximum limit for each drug and strength

PLEASE NOTE: Since manufacturer package sizes may vary, it is the discretion of the dispensing pharmacy to fill quantities per package size up to these quantity limits. In such cases the filling limit and day supply may be less than what is indicated.

Medication**	**Starting Dose**	**Maximum** Daily Dose**	**Package Size**	**1 Month Limit* 3 Months Limit***
Alvesco 80mcg** (ciclesonide)	1-3 inhalations twice daily	6 inhalations**	60 inhalations per 6.1gm canister	3 packages (6.1gm each) / 25 days 9 packages (6.1gm each) / 75 days
Alvesco 160mcg (ciclesonide)	1-2 inhalations twice daily	4 inhalations (640mcg)	60 inhalations per 6.1gm canister	2 packages (6.1gm each) / 25 days 6 packages (6.1gm each) / 75 days
ArmonAir Digihaler 30mcg** (fluticasone propionate)	1 inhalation twice daily	2 inhalations**	60 inhalations per inhaler	1 package / 25 days 3 packages / 75 days
ArmonAir Digihaler 55mcg** (fluticasone propionate)	1 inhalation twice daily	2 inhalations**	60 inhalations per inhaler	1 package / 25 days 3 packages / 75 days
ArmonAir Digihaler 113mcg** (fluticasone propionate)	1 inhalation twice daily	2 inhalations**	60 inhalations per inhaler	1 package / 25 days 3 packages / 75 days
ArmonAir Digihaler 232mcg (fluticasone propionate)	1 inhalation twice daily	2 inhalations (464mcg)	60 inhalations per inhaler	1 package / 25 days 3 packages / 75 days
Arnuity Ellipta 50mcg (fluticasone furoate)	1 inhalation once daily	1 inhalation	30 blisters per inhaler	1 package (30 blisters) / 25 days 3 packages (30 blisters each) / 75 days
Arnuity Ellipta 100mcg** (fluticasone furoate)	1 inhalation once daily	1 inhalation**	30 blisters per inhaler	1 package (30 blisters) / 25 days 3 packages (30 blisters each) / 75 days
Arnuity Ellipta 200mcg (fluticasone furoate)	1 inhalation once daily	1 inhalation (200mcg)	30 blisters per inhaler	1 package (30 blisters) / 25 days 3 packages (30 blisters each) / 75 days
Asmanex HFA 50mcg (mometasone furoate)	2 inhalations twice daily	4 inhalations	120 inhalations per 13gm canister	1 package (13gm each) / 25 days 3 packages (13gm each) / 75 days
Asmanex HFA 100mcg** (mometasone furoate)	2 inhalations twice daily	4 inhalations**	120 inhalations per 13gm canister	1 package (13gm each) / 25 days 3 packages (13gm each) / 75 days
Asmanex HFA 200mcg (mometasone furoate)	2 inhalations twice daily	4 inhalations (800mcg)	120 inhalations per 13gm canister	1 package (13gm each) / 25 days 3 packages (13gm each) / 75 days
Asmanex Twisthaler 110mcg** (mometasone furoate)	1 inhalation once daily	2 inhalations**	30 inhalation units per package	2 packages / 25 days 6 packages / 75 days
Asmanex Twisthaler 220mcg (mometasone furoate)	1-2 inhalations once to twice daily	4 inhalations (880mcg)	30 inhalation units per package	4 packages / 25 days 12 packages / 75 days
			60 inhalation units per package	2 packages / 25 days 6 packages / 75 days
			120 inhalation units per package	1 package / 25 days 3 packages / 75 days
Flovent Diskus 50mcg** (fluticasone propionate)	1-3 inhalations twice daily	6 inhalations**	60 blisters per device	3 packages (60 blisters each) / 25 days 9 packages (60 blisters each) / 75 days
Flovent Diskus 100mcg**	1-4 inhalations twice daily	8 inhalations**	60 blisters per device	4 packages (60 blisters each) / 25 days 12 packages (60 blisters each) / 75 days

(fluticasone propionate)				
Flovent Diskus 250mcg (fluticasone propionate)	1-4 inhalations twice daily	8 inhalations (2000mcg)	60 blisters per device	4 packages (60 blisters each) / 25 days 12 packages (60 blisters each) / 75 days
Flovent HFA 44mcg** (fluticasone propionate)	2-4 inhalations twice daily	8 inhalations**	120 inhalations per 10.6gm canister	2 packages (10.6gm each) / 25 days 6 packages (10.6gm each) / 75 days
Flovent HFA 110mcg** (fluticasone propionate)	1-3 inhalations twice daily	6 inhalations**	120 inhalations per 12gm canister	2 packages (12gm each) / 25 days 6 packages (12gm each) / 75 days
Flovent HFA 220mcg (fluticasone propionate)	1-4 inhalations twice daily	8 inhalations (1760mcg)	120 inhalations per 12gm canister	2 packages (12gm each) / 25 days 6 packages (12gm each) / 75 days
Pulmicort Flexhaler 90mcg** (budesonide)	2-3 inhalations twice daily	6 inhalations**	60 inhalations per device	3 packages / 25 days 9 packages / 75 days
Pulmicort Flexhaler 180mcg (budesonide)	1-4 inhalations twice daily	8 inhalations (1440mcg)	120 inhalations per device	2 packages / 25 days 6 packages / 75 days
Pulmicort Respules 0.25mg** (budesonide)	nebulization of 1-2 respules (2-4mL) daily	3 respules**	30 respules (2mL each) per carton	3 packages (90 respules x 2mL) / 25 days 9 packages (270 respules x 2mL) / 75 days
Pulmicort Respules 0.5mg (budesonide)	nebulization of 1-2 respules (2-4mL) daily	2 respules (1mg)	30 respules (2mL each) per carton	2 packages (60 respules x 2mL) / 25 days 6 packages (180 respules x 2mL) / 75 days
Pulmicort Respules 1mg (budesonide)	nebulization of 1 respule (2mL) daily	1 respule (1mg)	30 respules (2mL each) per carton	1 package (30 respules x 2mL) / 25 days 3 packages (90 respules x 2mL) / 75 days
QVAR Redihaler 40mcg** (beclomethasone)	1-3 inhalations twice daily	6 inhalations**	120 inhalations per 10.6gm canister	2 packages (10.6gm each) / 25 days 6 packages (10.6gm each) / 75 days
QVAR Redihaler 80mcg (beclomethasone)	1-4 inhalations twice daily	8 inhalations (640mcg)	120 inhalations per 10.6gm canister	2 packages (10.6gm each) / 25 days 6 packages (10.6gm each) / 75 days
**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.* ***Utilize higher strength available.*				

QUANTITY LIMIT PRIOR AUTHORIZATION CRITERIA

DRUG CLASS	**DERMATOLOGICAL TOPICAL CORTICOSTEROIDS** **BRAND AND GENERIC** **ALL DOSAGE FORMS**
BRAND NAME (generic)	**BRAND AND GENERIC**
	ALCLOMETASONE: **(alclometasone dipropionate)**
	AMCINONIDE: **(amcinonide)**
	BETAMETHASONE: **(betamethasone dipropionate)** **(betamethasone valerate)**
	CLOBETASOL: **(clobetasol propionate)**
	CLOCORTOLONE: **(clocortolone pivalate)**
	DESONIDE: **(desonide)**
	DESOXIMETASONE: **(desoximetasone)**
	DIFLORASONE: **(diflorasone diacetate)**
	FLUOCINOLONE: **(fluocinolone acetonide)**
	FLUOCINONIDE: **(fluocinonide)**
	FLURANDRENOLIDE: **(flurandrenolide, include tape)**
	FLUTICASONE: **(fluticasone propionate)**
	HALCINONIDE:

(halcinonide)

HALOBETASOL:
(halobetasol propionate)

HYDROCORTISONE:
(hydrocortisone)

(hydrocortisone butyrate)

(hydrocortisone probutate)

(hydrocortisone valerate)

MOMETASONE:
(mometasone furoate)

PREDNICARBATE:
(prednicarbate)

TRIAMCINOLONE:
(triamcinolone acetonide)

Status: CVS Caremark® Criteria
Type: Quantity Limit; Post Limit Prior Authorization

POLICY

FDA-APPROVED INDICATIONS
Alclometasone dipropionate, amcinonide, betamethasone dipropionate, betamethasone valerate, clobetasol propionate, clocortolone pivalate, desonide, desoximetasone, diflorasone diacetate, fluocinolone acetonide, fluocinonide, flurandrenolide, fluticasone propionate, halcinonide, halobetasol propionate, hydrocortisone, hydrocortisone butyrate, hydrocortisone probutate, hydrocortisone valerate, mometasone furoate, prednicarbate, and triamcinolone acetonide are indicated for the relief of the inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses.

Bryhali Lotion, Clobetasol Propionate Emollient Base Cream, Clobex Shampoo, Clobex Lotion, Clobex Spray, Derma-Smooth/FS (Scalp) Oil, Impoyz Cream, Lexette Foam, Olux Foam, Sernivo Spray, Topicort Spray, and Ultravate Lotion are indicated for the treatment of psoriasis.

Cutivate Lotion, Derma-Smooth/FS (Body) Oil, desonide gel, Locoid Lipocream, Locoid Lotion, and Verdeso Foam are indicated for the treatment of atopic dermatitis.

Capex Shampoo and hydrocortisone butyrate solution are indicated for the relief of the inflammatory and pruritic manifestations of seborrheic dermatitis.

INITIAL QUANTITY LIMIT

Tape

The initial quantity limit for flurandrenolide 4mcg/cm Tape is set to 1 package of one roll per 25 days*, 3 packages or three rolls per 75 days*. If the patient is requesting more than the initial quantity limit, the claim will reject with a message indicating that a prior authorization is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

All Dosage Forms (except Tape)

The initial quantity limit for topical corticosteroids all dosage forms (except Tape) are set to 120 grams or 120 milliliters per 25 days*, 360 grams or 360 milliliters per 75 days*. If the patient is requesting more than the initial quantity limit, the claim will reject with a message indicating that a prior authorization is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

* Limits do not accumulate together; patient is allowed the maximum limit for each drug and strength
* PLEASE NOTE: Since manufacturer package sizes may vary, it is the discretion of the dispensing pharmacy to fill quantities per package size up to these quantity limits. In such cases the filling limit and day supply may be less than what is indicated.

** The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for a corticosteroid-responsive dermatosis or condition (e.g., atopic dermatitis, eczema, psoriasis, seborrheic dermatitis)

AND

- The requested drug is not being used in a footbath

Quantity limits apply.

POST LIMIT QUANTITY

* PLEASE NOTE: Since manufacturer package sizes may vary, it is the discretion of the dispensing pharmacy to fill quantities per package size up to these quantity limits. In such cases the filling limit and day supply may be less than what is indicated.

Drug	1 Month Limit*	3 Month Limit*
	180gm or 180mL / 25 days	540gm or 540mL / 75 days
flurandrenolide 4mcg/cm (Cordran) Tape	2 packages or two rolls / 25 days	6 packages or six rolls / 75 days
low potency products: Alclometasone, Desonide (DesOwen, Tridesilon, Verdeso), Fluocinolone acetonide 0.01 percent (Synalar solution), Hydrocortisone 1, 2, or 2.5 percent (Ala-Scalp, Texacort)	240gm or 240mL / 25 days	720gm or 720mL / 75 days
oils, shampoos, sprays [Oil examples are fluocinolone acetonide oil (Derma-Smoothe/FS), Shampoo examples are fluocinolone acetonide (Capex), clobetasol propionate (Clobex), Spray examples are clobetasol propionate (Clobex), triamcinolone acetonide (Kenalog), betamethasone dipropionate (Sernivo), desoximetasone (Topicort)]	240gm or 240mL / 25 days	720gm or 720mL / 75 days
Clobetasol propionate 0.025 percent cream (Impoyz), Clobetasol propionate 0.05 percent lotion (Impeklo),	240gm or 240mL / 25 days	540gm or 540mL / 75 days

Fluocinolone acetonide 0.025 percent (Synalar 0.025 percent), Flurandrenolide cream, lotion (Cordran cream, Cordran lotion), Fluticasone lotion (Cutivate lotion), Halcinonide solution (Halog solution)		
Triamcinolone acetonide 0.05 percent ointment	430gm / 25 days	540gm / 75 days
** The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*		

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Reference number
2017-A

SPECIALTY GUIDELINE MANAGEMENT

COSENTYX (secukinumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

A. Moderate to severe plaque psoriasis (PsO) in patients 6 years of age and older who are candidates for systemic therapy or phototherapy
B. Active psoriatic arthritis (PsA) in patients 2 years of age and older
C. Adults with active ankylosing spondylitis (AS)
D. Adults with active non-radiographic axial spondyloarthritis (nr-axSpA) with objective signs of inflammation
E. Active enthesitis-related arthritis (ERA) in patients 4 years of age and older

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

A. Plaque psoriasis (PsO)
    1. Initial requests
        i. Chart notes or medical record documentation of affected area(s) and body surface area (BSA) affected (if applicable).
        ii. Chart notes, medical record documentation, or claims history supporting previous medications tried (if applicable), including response to therapy. If therapy is not advisable, documentation of clinical reason to avoid therapy.
    2. Continuation requests: Chart notes or medical record documentation of decreased body surface area (BSA) affected and/or improvement in signs and symptoms.

B. Psoriatic arthritis (PsA), ankylosing spondylitis (AS), axial spondyloarthritis (axSpA), and enthesitis-related arthritis (ERA)
    1. Initial requests: Chart notes, medical record documentation, or claims history supporting previous medications tried (if applicable), including response to therapy. If therapy is not advisable, documentation of clinical reason to avoid therapy.
    2. Continuation requests: Chart notes or medical record documentation supporting positive clinical response.

III. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with one of the following:
A. Plaque psoriasis: dermatologist
B. Psoriatic arthritis: rheumatologist or dermatologist
C. Ankylosing spondylitis, axial spondyloarthritis, and enthesis-related arthritis: rheumatologist

IV. CRITERIA FOR INITIAL APPROVAL

A. Plaque psoriasis (PsO)

1. Authorization of 12 months may be granted for members 6 years of age or older who have previously received a biologic or targeted synthetic drug (e.g., Sotyktu, Otezla) indicated for the treatment of moderate to severe plaque psoriasis.

2. Authorization of 12 months may be granted for members 6 years of age or older for the treatment of moderate to severe plaque psoriasis when any of the following criteria is met:
   i. Crucial body areas (e.g., hands, feet, face, neck, scalp, genitals/groin, intertriginous areas) are affected.
   ii. At least 10% of body surface area (BSA) is affected.
   iii. At least 3% of body surface area (BSA) is affected and the member meets any of the following criteria:
      a. Member has had an inadequate response or intolerance to either phototherapy (e.g., UVB, PUVA) or pharmacologic treatment with methotrexate, cyclosporine, or acitretin.
      b. Member has a clinical reason to avoid pharmacologic treatment with methotrexate, cyclosporine, and acitretin (see Appendix).

B. Psoriatic arthritis (PsA)

1. Authorization of 12 months may be granted for members 2 years of age or older who have previously received a biologic or targeted synthetic drug (e.g., Rinvoq, Otezla) indicated for active psoriatic arthritis.

2. Authorization of 12 months may be granted for members 2 years of age or older for treatment of active psoriatic arthritis when either of the following criteria is met:
   i. Member has mild to moderate disease and meets one of the following criteria:
      a. Member has had an inadequate response to methotrexate, leflunomide, or another conventional synthetic drug (e.g., sulfasalazine) administered at an adequate dose and duration.
      b. Member has an intolerance or contraindication to methotrexate or leflunomide (see Appendix), or another conventional synthetic drug (e.g., sulfasalazine).
      c. Member has enthesitis or predominantly axial disease.
   ii. Member has severe disease.

C. Ankylosing spondylitis (AS) and axial spondyloarthritis (axSpA)

1. Authorization of 12 months may be granted for adult members who have previously received a biologic or targeted synthetic drug (e.g., Rinvoq, Xeljanz) indicated for active ankylosing spondylitis or active axial spondyloarthritis.

2. Authorization of 12 months may be granted for adult members for treatment of active ankylosing spondylitis or active axial spondyloarthritis when any of the following criteria is met:
   i. Member has had an inadequate response to at least two nonsteroidal anti-inflammatory drugs (NSAIDs).
   ii. Member has an intolerance or contraindication to two or more NSAIDs.

D. Enthesitis-related arthritis (ERA)

1. Authorization of 12 months may be granted for members 4 years of age or older who have previously received a biologic for the treatment of active enthesitis-related arthritis.

2. Authorization of 12 months may be granted for members 4 years of age or older for the treatment of active enthesitis-related arthritis when both of the following criteria are met:
   i. Member has active disease demonstrated by at least three active joints involved and at least one site of active enthesitis at baseline or documented by history.
   ii. Member meets either of the following:
      a. Member has had an inadequate response to nonsteroidal anti-inflammatory drugs (NSAIDs), sulfasalazine, or methotrexate.
      b. Member has an intolerance or contraindication to NSAIDs, sulfasalazine (e.g., porphyria, intestinal or urinary obstruction), and methotrexate (see Appendix).

V. CONTINUATION OF THERAPY

A. Plaque psoriasis (PsO)

Authorization of 12 months may be granted for all members 6 years of age or older (including new members) who are using the requested medication for moderate to severe plaque psoriasis and who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition when either of the following is met:

1. Reduction in body surface area (BSA) affected from baseline
2. Improvement in signs and symptoms from baseline (e.g., itching, redness, flaking, scaling, burning, cracking, pain)

B. Psoriatic arthritis (PsA)

Authorization of 12 months may be granted for all members 2 years of age or older (including new members) who are using the requested medication for psoriatic arthritis and who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition when there is improvement in any of the following from baseline:

1. Number of swollen joints
2. Number of tender joints
3. Dactylitis
4. Enthesitis
5. Axial disease
6. Skin and/or nail involvement

C. Ankylosing spondylitis (AS) and axial spondyloarthritis (axSpA)

Authorization of 12 months may be granted for all adult members (including new members) who are using the requested medication for ankylosing spondylitis or axial spondyloarthritis and who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition when there is improvement in any of the following from baseline:

1. Functional status
2. Total spinal pain
3. Inflammation (e.g., morning stiffness)

D. Enthesitis-related arthritis (ERA)

Authorization of 12 months may be granted for all members 4 years of age or older (including new members) who are using the requested medication for active enthesitis-related arthritis and who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition when there is improvement in any of the following from baseline:

1. Number of flares
2. Number of joints with active arthritis (e.g., swelling, pain)
3. Number of joints with limited movement
4. Dactylitis
5. Enthesitis

VI. OTHER

For all indications: Member has had a documented negative tuberculosis (TB) test (which can include a tuberculosis skin test [PPD], an interferon-release assay [IGRA], or a chest x-ray)* within 6 months of initiating therapy for persons who are naïve to biologic drugs or targeted synthetic drugs associated with an increased risk of TB.

* If the screening testing for TB is positive, there must be further testing to confirm there is no active disease. Do not administer the requested medication to members with active TB infection. If there is latent disease, TB treatment must be started before initiation of the requested medication.

For all indications: Member cannot use the requested medication concomitantly with any other biologic drug or targeted synthetic drug.

VII. DOSAGE AND ADMINISTRATION

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

VIII. APPENDIX

Examples of Clinical Reasons to Avoid Pharmacologic Treatment with Methotrexate, Cyclosporine, Acitretin, or Leflunomide

1. Clinical diagnosis of alcohol use disorder, alcoholic liver disease, or other chronic liver disease
2. Drug interaction
3. Risk of treatment-related toxicity
4. Pregnancy or currently planning pregnancy
5. Breastfeeding
6. Significant comorbidity prohibits use of systemic agents (e.g., liver or kidney disease, blood dyscrasias, uncontrolled hypertension)
7. Hypersensitivity
8. History of intolerance or adverse event

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Reference number
1784-A

SPECIALTY GUIDELINE MANAGEMENT

COTELLIC (cobimetinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met, and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication
1. Cotellic is indicated for the treatment of adult patients with unresectable or metastatic melanoma with a BRAF V600E or V600K mutation, in combination with vemurafenib.
2. Cotellic is indicated as a single agent for the treatment of adult patients with histiocytic neoplasms.

B. Compendial Uses
1. Glioma, BRAF V600 activating mutation-positive
2. Meningioma, BRAF V600 activating mutation-positive
3. Astrocytoma, BRAF V600 activating mutation-positive
4. Cutaneous melanoma

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of BRAF mutation documentation is necessary to initiate the prior authorization review for applicable indications as outlined in section III.

III. CRITERIA FOR INITIAL APPROVAL

A. Cutaneous Melanoma

Authorization of 12 months may be granted for treatment of cutaneous melanoma with a BRAF V600 activating mutation (e.g., V600E or V600K) in any of the following settings:
1. Unresectable or metastatic disease when used in combination with vemurafenib (Zelboraf) with or without atezolizumab (Tecentriq).
2. Adjuvant treatment of resected stage III disease in combination with vemurafenib (Zelboraf) when the member has had an unacceptable toxicity to dabrafenib (Tafinlar) in combination with trametinib (Mekinist) or dabrafenib/trametinib are less desirable based on side-effect profiles.
3. Limited resectable local satellite/in-transit recurrent disease in combination with vemurafenib (Zelboraf) when the member has had an unacceptable toxicity to dabrafenib (Tafinlar) in combination with trametinib (Mekinist) or dabrafenib/trametinib are less desirable based on side-effect profiles.

B. Central Nervous System Cancer

Authorization of 12 months may be granted for treatment of BRAF V600 mutation-positive (e.g., BRAF V600E or V600K mutations) gliomas, meningiomas, or astrocytomas.

C. Histiocytic Neoplasms
Authorization of 12 months may be granted for treatment of histiocytic neoplasms as a single agent.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

V. REFERENCES

1. Cotellic [package insert]. South San Francisco, CA: Genentech USA, Inc.; October 2022.
2. The NCCN Drugs & Biologics Compendium 2022 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed November 14, 2022.
3. Usubalieva A, Pierson CR, Kavran CA, et al. Primary Meningeal Pleomorphic Xanthoastrocytoma With Anaplastic Features: A Report of 2 Cases, One With BRAFV600E Mutation and Clinical Response to the BRAF Inhibitor Dabrafenib. Journal of neuropathology and experimental neurology. 2015;74(10):960-969. doi:10.1097/NEN.0000000000000240.
4. Mordechai O, Postovsky S, Vlodavsky E, et al. Metastatic Rhabdoid Meningioma with BRAF V600E Mutation and Good Response to Personalized Therapy: Case Report and Review of the Literature. Pediatric Hematology and Oncology. 2015; 32:3, 207-211, DOI: 10.3109/08880018.2014.936058
5. Lassaletta, A, Guerreiro Stucklin, A, Ramaswamy, V, et al. Profound clinical and radiological response to BRAF inhibition in a 2-month-old diencephalic child with hypothalamic/chiasmatic glioma. Pediatric Blood and Cancer. 2016; 63: 2038-2041. doi:10.1002/pbc.26086.
6. Meletah SK, Pavlick D, Brennan T, et al. Personalized Treatment for a Patient with a BRAF V600E Mutation using Dabrafenib and a Tumor Treatment Fields Device in a High-Grade Glioma Arising from Ganglioglioma. Journal of the National Comprehensive Cancer Network. 2016; 14(11): 1345-1350.

Reference number(s)
2988-A

SPECIALTY GUIDELINE MANAGEMENT

CYSTADANE (betaine anhydrous)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
Cystadane is indicated for the treatment of homocystinuria to decrease elevated homocysteine blood concentrations in pediatric and adult patients. Included within the category of homocystinuria are:
1. Cystathionine beta-synthase (CBS) deficiency
2. 5,10-methylenetetrahydrofolate reductase (MTHFR) deficiency
3. Cobalamin cofactor metabolism (cbl) defect

B. Compendial Use
1. Methylmalonic acidemia with homocystinuria

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
A. For cystathionine beta-synthase (CBS) deficiency, enzyme analysis of CBS activity or genetic testing results
B. For 5,10-methylenetetrahydrofolate reductase (MTHFR) deficiency, enzyme analysis of MTHFR activity or genetic testing results
C. For cobalamin cofactor metabolism (cbl) defect, genetic testing results

III. CRITERIA FOR INITIAL APPROVAL

A. Homocystinuria
Authorization of 12 months may be granted for treatment of homocystinuria to decrease elevated homocysteine blood levels when all of the following criteria are met:
1. The member has one of the following types of homocystinuria and the diagnosis was confirmed by enzyme assay or genetic testing:
   i. Cystathionine beta-synthase (CBS) deficiency
   ii. 5,10-methylenetetrahydrofolate reductase (MTHFR) deficiency
   iii. Cobalamin cofactor metabolism (cbl) defect
2. If the member has CBS deficiency, plasma methionine concentrations will be monitored and kept below 1,000 micromol/L through dietary modification, and if necessary, a reduction in Cystadane dose.

B. Methylmalonic acidemia with homocystinuria

Authorization of 12 months may be granted for members who have a diagnosis of methylmalonic acidemia with homocystinuria.

IV. CONTINUATION OF THERAPY

A. Homocystinuria

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for homocystinuria when both of the following criteria are met:

1. The total homocysteine level is undetectable or present only in small amounts, OR there is a substantial decrease in homocysteine levels and the dose will be increased until maximum tolerability or plasma total homocysteine is undetectable or present in only small amounts.
2. If the member has CBS deficiency, plasma methionine concentrations will be monitored and kept below 1,000 micromol/L through dietary modification, and if necessary, a reduction in Cystadane dose.

B. Methylmalonic acidemia with homocystinuria

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for methylmalonic acidemia with homocystinuria who are experiencing benefit from therapy as evidenced by disease stability or disease improvement.

V. REFERENCES

1. Cystadane [package insert]. Lebanon, NJ: Recordati Rare Diseases, Inc.; October 2019.
2. Morris AA, Kožich V, Santra S, et al. Guidelines for the diagnosis and management of cystathionine beta-synthase deficiency. *J Inherit Metab Dis*. 2017;40(1):49-74. doi:10.1007/s10545-016-9979-0.
3. Sloan JL, Carrillo N, Adams D, et al. Disorders of Intracellular Cobalamin Metabolism. 2008 Feb 25 [Updated 2021 Dec 16]. In: Adam MP, Ardinger HH, Pagon RA, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2021.
4. Genetic and Rare Diseases Information Center. List of FDA Orphan Drugs. Methylmalonic Acidemia. https://rarediseases.info.nih.gov/diseases/fda-orphan-drugs/M. Accessed December 17, 2021.
5. National Organization for Rare Disorders (2003). *NORD guide to rare disorders.* Philadelphia: Lippincott Williams & Wilkins. Methylmalonic Acidemia. https://rarediseases.org/rare-diseases/acidemia-methylmalonic/. Accessed December 17, 2021.

Reference number
2089-A

SPECIALTY GUIDELINE MANAGEMENT

CYSTAGON (cysteamine bitartrate)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Cystagon is indicated for the management of nephropathic cystinosis in children and adults.

All other indications are considered experimental/investigational and not medically necessary.

II. REQUIRED DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

A. Initial requests: assay detecting increased cystine concentration in leukocytes or genetic testing results supporting diagnosis.
B. Continuation requests: lab results or chart notes documenting a positive response to therapy (e.g., improvement, stabilization, or slowing of disease progression for serum creatinine, calculated creatinine clearance, leukocyte cystine concentration, or maintained growth [height]).

III. CRITERIA FOR INITIAL APPROVAL

Nephropathic cystinosis
Authorization of 12 months may be granted for treatment of nephropathic cystinosis when all of the following criteria are met:

A. Diagnosis of cystinosis was confirmed by the presence of increased cystine concentration in leukocytes or by genetic testing; and
B. Member will not use Cystagon in combination with Procysbi.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for neprhopathic cystinosis who are responding to therapy (e.g., improvement, stabilization, or slowing of disease progression for serum creatinine, calculated creatinine clearance, or leukocyte cystine concentration).

V. REFERENCES

1. Cystagon [package insert]. Morgantown, WV: Mylan Pharmaceuticals Inc.; January 2019.

CVS caremark®

Reference number
2090-A

SPECIALTY GUIDELINE MANAGEMENT

CYSTARAN (cysteamine ophthalmic solution)
CYSTADROPS (cysteamine ophthalmic solution)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Cystaran
Cystaran is indicated for the treatment of corneal cystine crystal accumulation in patients with cystinosis.

Cystadrops
Cystadrops is indicated for the treatment of corneal cystine crystal deposits in adults and children with cystinosis.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: assay detecting increased cystine concentration in leukocytes or genetic testing results supporting the diagnosis.

III. CRITERIA FOR INITIAL APPROVAL

Cystinosis
Authorization of 12 months may be granted for treatment of corneal cystine crystal accumulation when all of the following criteria are met:
A. Diagnosis of cystinosis was confirmed by the presence of increased cystine concentration in leukocytes or by genetic testing; and
B. Member has corneal cystine crystal accumulation.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for corneal cystine crystal accumulation with cystinosis who are responding to therapy met by either of the following criteria:
A. Member has experienced a decrease in corneal cystine crystal accumulation; or
B. Member did not experience an increase in corneal cystine crystal accumulation.

V. REFERENCES

1. Cystaran [package insert]. Gaithersburg, MD: Lediant Biosciences, Inc.; April 2020.

2. Cystadrops [package insert]. Lebanon, NJ: Recordati Rare Diseases Inc.; August 2020.
3. Ivanova E, De Leo MG, De Matteis MA, Levtchenko E. Cystinosis: clinical presentation, pathogenesis, and treatment. *Pediatr Endocrinol Rev.* 2014;12(1):176-184.

Reference number(s)
1836-A

SPECIALTY GUIDELINE MANAGEMENT

AMPYRA (dalfampridine)
dalfampridine

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Indicated as a treatment to improve walking in adult patients with multiple sclerosis. This was demonstrated by an increase in walking speed.

All other indications are considered experimental/investigational and are not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Authorization of 30 days may be granted to members with a diagnosis of multiple sclerosis if the member has sustained walking impairment (prior to initiating therapy with Ampyra).

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted to members with multiple sclerosis if the member has experienced an improvement in walking speed or other objective measure of walking ability since starting Ampyra.

IV. REFERENCES

1. Ampyra [package insert]. Pearl River, NY: Acorda Therapeutics, Inc.; June 2022.
2. Dalfampridine [package insert]. Somerset, NJ: Micro Labs USA, Inc.; December 2021.
3. Goodman AD, Brown TR, Krupp LB, et al. Sustained-release oral fampridine in multiple sclerosis: a randomized, double-blind, controlled trial. Lancet. 2009; 373:732-8.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME*
(generic)

DALIRESP
(roflumilast)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization ***Ref # 646-A***

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Daliresp is indicated as a treatment to reduce the risk of COPD exacerbations in patients with severe COPD associated with chronic bronchitis and a history of exacerbations.
Limitations of Use
Daliresp is not a bronchodilator and is not indicated for the relief of acute bronchospasm.
Daliresp 250 mcg is a starting dose, for the first 4 weeks of treatment only and is not the effective (therapeutic) dose.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed to reduce the risk of chronic obstructive pulmonary disease (COPD) exacerbations in a patient with severe COPD associated with chronic bronchitis and a history of exacerbations

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Daliresp is indicated as a treatment to reduce the risk of COPD exacerbations in patients with severe COPD associated with chronic bronchitis and a history of exacerbations. Daliresp is not a bronchodilator and is not indicated for the relief of acute bronchospasm. Daliresp 250 mcg is a starting dose, for the first 4 weeks of treatment only and is not the effective (therapeutic) dose.

REFERENCES

1. Daliresp [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; March 2019.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2021; Accessed October 4, 2021.
3. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed October 4, 2021.

Written by:	UM Development (RP)
Date Written:	04/2011
Revised:	(RP) 06/2011 (revised question #2, added question #3), 02/2012; 10/2012 (extended duration); (RP) 02/2013, (TM) 11/2013; (RP) 11/2014, 11/2015 (no clinical changes), 11/2016, 11/2017 (no clinical changes); (KC) 11/2018 (no clinical changes), 04/2019 (changed DOA to 12 months); (RP) 03/2020 (no clinical changes), (TM) 11/2020 (no clinical changes); (PM) 10/2021 (no clinical changes)
Reviewed:	Medical Affairs (KP) 04/2011, 06/2011, 02/2012, 10/2012; (LS) 02/2013, (DC) 11/2013; (LMS) 11/2014; (ME) 11/2016; (GAD) 04/2019; (CHART) 03/26/2020, 12/03/2020, 10/14/2021 External Review: 06/2011, 06/2012, 06/2013, 04/2014, 02/2015, 02/2016, 02/2017, 02/2018, 02/2019, 06/2019, 06/2020, 02/2021, 02/2022

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CRITERIA FOR APPROVAL

1	Is the requested drug being prescribed to reduce the risk of chronic obstructive pulmonary disease (COPD) exacerbations in a patient with severe COPD associated with chronic bronchitis and a history of exacerbations?	Yes	No

Mapping Instructions			
	Yes	**No**	**DENIAL REASONS – DO NOT USE FOR MEDICARE PART D**
1.	Approve, 12 months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you meet all of these conditions: - You have severe chronic obstructive pulmonary disease (COPD) - Your condition is associated with chronic bronchitis and a history of exacerbations Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]

PRIOR AUTHORIZATION CRITERIA

BRAND NAME
(generic)

DARAPRIM
(pyrimethamine)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

POLICY

FDA-APPROVED INDICATIONS

Treatment of Toxoplasmosis
Daraprim is indicated for the treatment of toxoplasmosis when used conjointly with a sulfonamide, since synergism exists with this combination.

Compendial Uses
Toxoplasmosis; Prophylaxis[2,3,4,5]
Pneumocystis jirovecii pneumonia; Prophylaxis[2,3,4]
Cystoisosporiasis; Treatment and secondary prophylaxis [2,4,5]

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for the treatment of congenital toxoplasmosis in a pediatric patient

OR

- The requested drug is being prescribed for the treatment of toxoplasmosis

OR

- The requested drug is being prescribed for secondary prophylaxis of toxoplasmosis
  - **AND**
  - The patient has had a CD4 cell count of less than 200 cells/mm3 within the past 6 months

OR

- The patient has experienced an intolerance or has a contraindication to sulfamethoxazole/trimethoprim AND the requested drug is being prescribed for any of the following: A) primary prophylaxis of toxoplasmosis, B) *Pneumocystis jirovecii* pneumonia prophylaxis
  - **AND**
  - The patient has had a CD4 cell count less than 200 cells/mm3 within the past 3 months

OR

- The patient has experienced an intolerance or has a contraindication to sulfamethoxazole/trimethoprim AND the requested drug is being prescribed for the treatment of cystoisosporiasis

OR

- The patient has experienced an intolerance or has a contraindication to sulfamethoxazole/trimethoprim AND the requested drug is being prescribed for secondary prophylaxis of cystoisosporiasis
  - **AND**
  - The patient has had a CD4 cell count less than 200 cells/mm3 within the past 6 months

REFERENCES

1. Daraprim [package insert]. New York, New York: Vyera Pharmaceuticals, LLC; August 2017.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2022; Accessed November 29, 2022.

3. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. https://www.micromedexsolutions.com/. Accessed November 29, 2022.
4. Panel on Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents with HIV. Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents with HIV. National Institutes of Health, Centers for Disease Control and Prevention, HIV Medicine Association, and Infectious Diseases Society of America. Available at https://clinicalinfo.hiv.gov/en/guidelines/adult-and-adolescent-opportunistic-infection. Accessed November 29, 2022.
5. Panel on Opportunistic Infections in HIV-Exposed and HIV-Infected Children. Guidelines for the Prevention and Treatment of Opportunistic Infections in HIV-Exposed and HIV-Infected Children. Department of Health and Human Services. Available at https://clinicalinfo.hiv.gov/en/guidelines/pediatric-opportunistic-infection. Accessed November 29, 2022.
6. Treatment of Malaria: Guidelines for Clinicians (United States). Centers for Disease Control and Prevention. Available at https://www.cdc.gov/malaria/diagnosis_treatment/index.html. Accessed November 29, 2022.
7. Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV. Department of Health and Human Services. Available at https://clinicalinfo.hiv.gov/en/guidelines/adult-and-adolescent-arv. Accessed November 29, 2022.

Reference number(s)
2793-A

SPECIALTY GUIDELINE MANAGEMENT

DAURISMO (glasdegib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
Daurismo is indicated, in combination with low-dose cytarabine, for the treatment of newly diagnosed acute myeloid leukemia (AML) in adult patients who are ≥ 75 years old or who have comorbidities that preclude use of intensive induction chemotherapy.

B. Compendial Uses
1. Post induction therapy following response to previous therapy with the same regimen
2. Relapsed/refractory disease as a component of repeating the initial successful induction regimen

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Acute Myeloid Leukemia (AML)
Authorization of 12 months may be granted for treatment of AML when all of the following criteria is met (A, B, and C):
A. The requested medication is used in combination with low-dose cytarabine
B. One of the following criteria is met:
   1. Member is 75 years of age or older.
   2. Member has comorbidities that preclude treatment with intensive induction chemotherapy.
C. The requested medication will be used as treatment for induction therapy, post-induction therapy, or relapsed/refractory disease.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II when there is no evidence of disease progression or an unacceptable toxicity while on the current regimen.

IV. REFERENCES

1. Daurismo [package insert]. New York, NY: Pfizer, Inc.; March 2020.
2. The NCCN Drugs & Biologics Compendium® © 2023 National Comprehensive Cancer Network, Inc. Available at: https://www.nccn.org Accessed January 7, 2023.

Reference number(s)
1622-A

SPECIALTY GUIDELINE MANAGEMENT

EXJADE (deferasirox)
JADENU (deferasirox)
deferasirox (generic)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. Chronic iron overload due to blood transfusions (transfusional hemosiderosis) in patients 2 years of age and older
   2. Chronic iron overload in patients 10 years of age and older with non-transfusion-dependent thalassemia (NTDT) syndromes and with a liver iron concentration (LIC) of at least 5 milligrams of iron per gram of liver dry weight (mg Fe/g dw) and a serum ferritin greater than 300 mcg/L

B. Compendial Use
   Hereditary hemochromatosis

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
A. Chronic Iron Overload due to Blood Transfusions (transfusional iron overload):
   1. Initial requests: pretreatment serum ferritin level
   2. Continuation requests: current serum ferritin level
B. Chronic Iron Overload in Patients with Non-transfusion Dependent Thalassemia Syndromes:
   1. Initial requests: pretreatment serum ferritin level and liver iron concentration
   2. Continuation requests: current serum ferritin level

III. CRITERIA FOR INITIAL APPROVAL

A. Chronic Iron Overload due to Blood Transfusions (transfusional iron overload)
Authorization of 6 months may be granted for treatment of chronic iron overload due to blood transfusions when all of the following criteria are met:
   1. Pretreatment serum ferritin level is consistently greater than 1000 mcg/L.
   2. Dose of deferasirox tablet for suspension/Exjade will not exceed 40 mg/kg per day, dose of deferasirox/Jadenu will not exceed 28 mg/kg per day.

B. Chronic Iron Overload in Patients with Non-transfusion Dependent Thalassemia Syndromes
Authorization of 6 months may be granted for treatment of chronic iron overload in members with non-transfusion dependent thalassemia syndromes when all of the following criteria are met:

1. Pretreatment serum ferritin level is greater than 300 mcg/L.
2. Pretreatment liver iron concentration (LIC) is at least 5 milligrams of iron per gram of liver dry weight (mg Fe/g dw).
3. Dose of deferasirox tablet for suspension/Exjade will not exceed 20 mg/kg per day, dose of deferasirox/Jadenu will not exceed 14 mg/kg per day.

C. Hereditary Hemochromatosis
Authorization of 6 months may be granted for treatment of hereditary hemochromatosis when phlebotomy is not an option (e.g., poor venous access, poor candidate due to underlying medical disorders) or the member had an unsatisfactory response to phlebotomy.

IV. CONTINUATION OF THERAPY

A. Chronic Iron Overload due to Blood Transfusions (transfusional iron overload)
Authorization of 6 months may be granted for continued treatment in members requesting reauthorization for chronic iron overload due to blood transfusions (transfusional iron overload) when following criteria are met:
1. Member is experiencing benefit from therapy as evidenced by a decrease in serum ferritin levels as compared to pretreatment baseline.
2. Serum ferritin level is not consistently below 500 mcg/L.

B. Chronic Iron Overload in Patients with Non-transfusion Dependent Thalassemia Syndromes
Authorization of 6 months may be granted for continued treatment in members requesting reauthorization for chronic iron overload with non-transfusion dependent thalassemia syndrome when following criteria are met:
1. Member is experiencing benefit from therapy as evidenced by a decrease in serum ferritin levels as compared to pretreatment baseline.
2. Serum ferritin level is not consistently below 300 mcg/L.

C. Hereditary Hemochromatosis
Authorization of 6 months may be granted for continued treatment in members requesting reauthorization for hereditary hemochromatosis when member is experiencing benefit from therapy as evidenced by a decrease in serum ferritin levels as compared to pretreatment baseline.

V. REFERENCES

1. Exjade [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; July 2020.
2. Jadenu [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; July 2020.
3. Deferasirox tablet for suspension [package insert]. North Wales, PA: Actavis Pharma, Inc; August 2021.
4. Deferasirox tablet [package insert]. Princeton, NJ: Dr. Reddy's Laboratories Inc.; January 2021.
5. Deferasirox granule [package insert]. Bridgewater, NJ: Amneal Pharmaceuticals LLC; August 2021
6. Cappellini MD, Cohen A, Porter J, et al. Guidelines for the management of transfusion dependent thalassaemia (TDT) 4th Edition [Internet]. Thalassaemia International Federation 2021;20:1-351.
7. Hoffbrand AV, Taher A, Cappellini MD. How I treat transfusional iron overload. Blood 2012;120(18):3657-69.
8. Taher A, Musallam K, Cappellini M, et al. Guidelines for the management of non-transfusion dependent thalassaemia (NTDT) 2nd Edition. Thalassaemia International Federation 2018;1-117.
9. Phatak P, Brissot P, Bonkovsky H et al. A phase I/II, open-label, dose-escalation trial of once daily oral chelator deferasirox to treat iron overload in HFE-related hereditary hemochromatosis: Final Results of the Core Study. Blood 2009;114: 1514.

10. Adams P, Barton J, et al. How I Treat Hemochromatosis. Blood 2010;(116): 317-325.
11. Kowdley, Kris V. MD, FACG1; Brown, Kyle E. MD, MSc2,3,4; Ahn, Joseph MD, MS, MBA, FACG (GRADE Methodologist)5; Sundaram, Vinay MD, MSc6 ACG Clinical Guideline: Hereditary Hemochromatosis, The American Journal of Gastroenterology: August 2019 - Volume 114 - Issue 8 - p 1202-1218

STEP THERAPY CRITERIA

DRUG CLASS	**ANTIDEPRESSANTS**
BRAND NAME (generic)	**(desvenlafaxine extended-release tablets) (generic Khedezla)** **FETZIMA (levomilnacipran)** **PRISTIQ (desvenlafaxine succinate extended-release tablets)**

Status: CVS Caremark Criteria
Type: Initial Step Therapy with Quantity Limit;
Post Step Therapy Prior Authorization with Quantity Limit

POLICY

FDA-APPROVED INDICATIONS
Desvenlafaxine ER (generic for Khedezla)
Desvenlafaxine is indicated for the treatment of adults with major depressive disorder (MDD).

Fetzima
Fetzima is indicated for the treatment of major depressive disorder (MDD) in adults.

Limitation of Use: Fetzima is not approved for the management of fibromyalgia. The efficacy and safety of Fetzima for the management of fibromyalgia have not been established.

Pristiq
Pristiq is indicated for the treatment of adults with major depressive disorder (MDD).

INITIAL STEP THERAPY with QUANTITY LIMIT*
**Include Rx and OTC products unless otherwise stated.*

If the patient has filled a prescription for at least a 30-day supply of a serotonin and norepinephrine reuptake inhibitor (SNRI), mirtazapine, bupropion (except generic for Zyban), OR a selective serotonin reuptake inhibitor (SSRI) within the past 180 days under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit. If the patient does not meet the initial step therapy criteria, then the claim will reject with a message indicating that a prior authorization (PA) is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

**If the patient meets the initial step therapy criteria, then the initial limit criteria will apply. If the patient is requesting more than the initial quantity limit the claim will reject with a message indicating that a PA is required.

****INITIAL LIMIT CRITERIA**

Limits do not accumulate together, patient is allowed the maximum limit for each drug and strength

Drug	1 Month Limit*	3 Month Limit*
Desvenlafaxine (all brand/generic products)	30 tablets / 25 days	90 tablets / 75 days
Fetzima	30 capsules / 25 days	90 capsules / 75 days

** The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for the treatment of an adult patient with major depressive disorder (MDD)

AND

- The patient has experienced an inadequate treatment response, intolerance or the patient has a contraindication to ANY of the following: A) a serotonin and norepinephrine reuptake inhibitor (SNRI), B) a selective serotonin reuptake inhibitor (SSRI), C) mirtazapine, D) bupropion

Quantity Limits apply.
Desvenlafaxine (all brand/generic products): 30 tablets / 25 days*
Fetzima: 30 capsules / 25 days*
**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing*

REFERENCES

1. Fetzima [package insert]. Madison, NJ: Allergan USA, Inc.; September 2021.
2. Desvenlafaxine Extended Release [package insert]. Cranbury, NJ: Sun Pharmaceutical Industries, Inc.; September 2021.
3. Pristiq [package insert]. Philadelphia, PA: Wyeth Pharmaceuticals LLC; November 2021.
4. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2023; Accessed January 12, 2023.
5. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed January 12, 2023.
6. Gelenberg AJ, Freeman MP, Markowitz JC, et al. American Psychiatric Association (APA) Practice Guideline for the Treatment of Patients with Major Depressive Disorder, Third Edition. October 2010. Available at: https://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/mdd.pdf. Accessed January 12, 2023.

STEP THERAPY CRITERIA

DRUG CLASS	**ANTIDEPRESSANTS**
BRAND NAME* **(generic)**	**FETZIMA** **(levomilnacipran)**
	KHEDEZLA **(desvenlafaxine extended release tablets)**
	PRISTIQ **(desvenlafaxine succinate extended release tablets)**

Status: CVS Caremark Criteria
Type: Initial Step Therapy with Quantity Limit;
Post Step Therapy Prior Authorization with Quantity Limit ***Ref # 1888-E***

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Fetzima
Fetzima is indicated for the treatment of major depressive disorder (MDD) in adults.

Limitation of Use: Fetzima is not approved for the management of fibromyalgia. The efficacy and safety of Fetzima for the management of fibromyalgia have not been established.

Khedezla
Khedezla is indicated for the treatment of adults with major depressive disorder (MDD).

Pristiq
Pristiq is indicated for the treatment of adults with major depressive disorder (MDD).

INITIAL STEP THERAPY with QUANTITY LIMIT*
**Include Rx and OTC products unless otherwise stated.*

If the patient has filled a prescription for at least a 30 day supply of a serotonin and norepinephrine reuptake inhibitor (SNRI), mirtazapine, bupropion (Wellbutrin IR, SR/XL), OR a selective serotonin reuptake inhibitor (SSRI) within the past 180 days under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit. If the patient does not meet the initial step therapy criteria, then the claim will reject with a message indicating that a prior authorization (PA) is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

**If the patient meets the initial step therapy criteria, then the initial limit criteria will apply. If the patient is requesting more than the initial quantity limit the claim will reject with a message indicating that a PA is required.

****INITIAL LIMIT CRITERIA**

Limits do not accumulate together, patient is allowed the maximum limit for each drug and strength

Drug	1 Month Limit*	3 Month Limit*
Desvenlafaxine (Khedezla, Pristiq)	30 tablets / 25 days	90 tablets / 75 days
Fetzima	30 capsules / 25 days	90 capsules / 75 days

** The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for the treatment of an adult patient with major depressive disorder

AND

- The patient has experienced an inadequate treatment response, intolerance or the patient has a contraindication to any of the following: A) a serotonin and norepinephrine reuptake inhibitor (SNRI), B) a selective serotonin reuptake inhibitor (SSRI), C) mirtazapine, D) bupropion

Quantity Limits apply.

RATIONALE

If the patient has filled a prescription for at least a 30 day supply of a serotonin and norepinephrine reuptake inhibitor (SNRI), mirtazapine, bupropion (Wellbutrin IR, SR/XL), or a selective serotonin reuptake inhibitor (SSRI) within the past 180 days under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit. If the patient meets the initial step therapy criteria, then the initial limit criteria will apply.

If the patient does not meet the initial step therapy criteria, then prior authorization is required. If the patient is requesting more than the initial quantity limit the claim will reject with a message indicating that a PA is required.

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Khedezla, Pristiq and Fetzima are indicated for the treatment of major depressive disorder (MDD) in adult patients.[1-5]

The American Psychiatric Association recommends an antidepressant medication as an initial treatment choice for patients with mild to moderate major depressive disorder and for patients with severe major depressive disorder unless electroconvulsive therapy (ECT) is planned. Because the effectiveness of antidepressant medications is generally comparable between drug classes and within classes of medications, the initial selection of an antidepressant medication is largely based on the anticipated side effects, the safety or tolerability of these side effects for the individual patient, pharmacological properties of the medication (e.g., half-life, actions on cytochrome P450 enzymes, other drug interactions), and additional factors such as medication response in prior episodes, cost, and patient preference. For most patients, a selective serotonin reuptake inhibitor (SSRI), serotonin norepinephrine reuptake inhibitor (SNRI), mirtazapine or bupropion is optimal.[6] Since antidepressant medications are comparable between and within drug classes, if the patient has had an inadequate treatment response, intolerance, or the patient has a contraindication to any of the following alternatives, then the requested drug will be covered: a serotonin and norepinephrine reuptake inhibitor (SNRI), a selective serotonin reuptake inhibitor (SSRI), mirtazapine, or bupropion.

The recommended dose for desvenlafaxine (Khedezla and Pristiq) is 50 mg once daily, with or without food. The 50 mg dose is both a starting dose and the therapeutic dose. In clinical studies, doses of 50 mg to 400 mg per day were shown to be effective, although no additional benefit was demonstrated at doses greater than 50 mg per day and adverse

reactions and discontinuations were more frequent at higher doses. The recommended dose range for Fetzima is 40 mg to 120 mg once daily, with or without food. Fetzima should be initiated at 20 mg once daily for 2 days and then increased to 40 mg once daily. Based on efficacy and tolerability, Fetzima may then be increased in increments of 40 mg at intervals of 2 or more days. The maximum recommended dose is 120 mg once daily.[1-3] Therefore, the quantity limit will be set at 1 unit per day or 30 units per month (e.g., 30 tablets of desvenlafaxine per month or 30 capsules of Fetzima per month).

REFERENCES

1. Fetzima [package insert]. Madison, NJ: Allergan USA, Inc.; September 2021.
2. Khedezla [package insert]. Marietta, GA: Osmotica Pharmaceutical US LLC; August 2021.
3. Pristiq [package insert]. Philadelphia, PA: Wyeth Pharmaceuticals LLC; November 2021.
4. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2021; Accessed January 2022.
5. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed January 2022.
6. Gelenberg A, Freeman M, Markowitz J, et al. American Psychiatric Association (APA). Practice Guideline for the Treatment of Patients with Major Depressive Disorder, Third Edition. October 2010. Available at: https://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/mdd.pdf. Accessed January 2022.

Written by	UM Development (TM)
Date Written:	05/2017
Revised:	(TM) 08/2017 (clarify pre-req bup), (ME) 05/2018 (added Fetzima), 03/2019, (DFW) 03/2020; (CJH) 02/2021 (no clinical changes); (DS) 02/2022 (no clinical changes)
Reviewed:	Medical Affairs (LS) 06/2017; (DNC) 05/2018, 03/2019; (CHART) 03/26/20, 02/25/21, 02/24/22 External Review: 07/2017, 08/2018, 08/2019, 08/2020, 06/2021, 06/2022

CRITERIA FOR APPROVAL

1	Is the requested drug being prescribed for the treatment of an adult patient with major depressive disorder? [If no, then no further questions.]	Yes	No
2	Has the patient experienced an inadequate treatment response, intolerance or does the patient have a contraindication to any of the following: A) a serotonin and norepinephrine reuptake inhibitor (SNRI), B) a selective serotonin reuptake inhibitor (SSRI), C) mirtazapine, D) bupropion? [If no, then no further questions.]	Yes	No
3	Does the patient require more than the plan allowance of 30 units per month? [RPh Note: If yes, then deny and enter a partial approval for 30 tablets / 25 days or 90 tablets / 75 days of Desvenlafaxine or 30 capsules / 25 days or 90 capsules / 75 days of Fetzima.]	Yes	No

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Mapping Instructions			
	Yes	**No**	**DENIAL REASONS – DO NOT USE FOR MEDICARE PART D**
1.	Go to 2	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you meet all of these conditions: - You are an adult - You have major depressive disorder (MDD) Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]
2.	Go to 3	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have tried any of these drugs, which did not work for you or you cannot take them: - Bupropion - Mirtazapine - A serotonin and norepinephrine reuptake inhibitor (SNRI) - A selective serotonin reuptake inhibitor (SSRI) Your request has been denied based on the information we have. [Short Description: No inadequate response, intolerance or contraindication to bupropion, mirtazapine, SNRI or SSRI]
3.	Deny For the denial verbiage, only include the requested drug. Remove all the other drugs from the verbiage.	Approve, 12 months, 30 tabs/25 days* or 90 tabs/75 days* of Desvenlafaxine or 30 caps/25 days* or 90 caps/75 days* of Fetzima	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to: - 30 tablets per month of Desvenlafaxine - 30 capsules per month of Fetzima Your request has been partially approved. You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity]

**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing*

QUANTITY LIMIT CRITERIA

DRUG CLASS **DIABETIC TEST STRIPS**

Status: CVS Caremark Criteria
Type: Quantity Limit

POLICY

FDA-APPROVED INDICATIONS
N/A

INITIAL LIMIT QUANTITY
Limits should accumulate across all products up to highest quantity listed.
PLEASE NOTE: Since manufacturer package sizes may vary, it is the discretion of the dispensing pharmacy to fill quantities per package size up to these quantity limits. In such cases, the filling limit and day supply may be less than what is indicated.

Product	1 Month Limit*	3 Month Limit*
Diabetic Test Strips	150 test strips / 25 days	450 test strips / 75 days

**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*

REFERENCES

1. American Diabetes Association. Standards of Medical Care in Diabetes—2022: *Diabetes Care* 2022;45(Suppl 1):S1-S264.
2. Weinstock RS, Aleppo G, Bailey TS, et al. *The Role of Blood Glucose Monitoring in Diabetes Management*. Arlington (VA): American Diabetes Association; October 2020.

PRIOR AUTHORIZATION CRITERIA

DRUG CLASS **DIABETIC TEST STRIPS**

Status: CVS Caremark Criteria
Type: Post Limit Prior Authorization ***Ref # 1373-J***

FDA-APPROVED INDICATIONS
N/A

COVERAGE CRITERIA
The requested product will be covered with prior authorization when the following criteria are met:

- The patient is on an intensive insulin regimen (multiple-dose insulin or insulin pump therapy)

Quantity Limits apply.
** The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*
*** Since manufacturer package sizes may vary, it is the discretion of the dispensing pharmacy to fill quantities per package size up to these quantity limits. In such cases the filling limit and day supply may be less than what is indicated.*

RATIONALE
The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines.

According to the American Diabetes Association (ADA) Standards of Medical Care in Diabetes—2022, blood glucose monitoring (BGM) is an integral component of effective diabetes management. Glucose monitoring allows patients to evaluate their individual response to therapy and assess whether glycemic targets are being achieved. Integrating results into diabetes management can be a useful tool for guiding medical nutrition therapy and physical activity, preventing hypoglycemia, and adjusting medications (particularly prandial insulin doses). Among patients with type 1 diabetes, there is a correlation between greater BGM frequency and lower hemoglobin A1c (A1C). The patient's specific needs and goals should dictate BGM frequency and timing.[1]

Most patients using intensive insulin regimens (multiple-dose insulin or insulin pump therapy) should be encouraged to assess glucose levels using BGM prior to meals and snacks, at bedtime, occasionally postprandially, prior to exercise, when they suspect low blood glucose, after treating low blood glucose until they are normoglycemic, and prior to critical tasks such as driving. For many patients, this will require testing 6 to 10 times daily, although individual needs may vary. A database study of almost 27,000 children and adolescents with type 1 diabetes showed that, after adjustment for multiple confounders, increased daily frequency of BGM was significantly associated with lower A1C (-0.2% per additional test per day) and with fewer acute complications.[1]

The evidence is insufficient regarding when to prescribe BGM and how often monitoring is needed for insulin-treated patients who do not use intensive insulin regimens, such as those with type 2 diabetes using basal insulin with or without oral agents. However, for patients using basal insulin, assessing fasting glucose with BGM to inform them of dose adjustments to achieve blood glucose targets results in lower A1C. In people with type 2 diabetes not using insulin, routine glucose monitoring may be of limited additional clinical benefit. By itself, even when combined with education, it has showed limited improvement in outcomes. However, for some individuals, glucose monitoring can provide insight into the impact of diet, physical activity, and medication management on glucose levels. Glucose monitoring may also be useful in assessing hypoglycemia, glucose levels during intercurrent illness, or discrepancies between measured A1C and glucose levels when there is concern an A1C result may not be reliable in specific individuals. Meta-analyses have suggested that SMBG can reduce A1C by 0.25%-0.3% at 6 months, but the effect was attenuated at 12 months in one analysis. A key consideration is that performing BGM alone does not lower blood glucose levels. To be useful, the information must be integrated into clinical and self-management plans.[1]

Reference number(s)
5545-A

SPECIALTY GUIDELINE MANAGEMENT

DIACOMIT (stiripentol)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Diacomit is indicated for the treatment of seizures associated with Dravet syndrome (DS) in patients taking clobazam who are 6 months of age and older and weighing 7 kg or more. There are no clinical data to support the use of Diacomit as monotherapy in Dravet syndrome.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Seizures associated with Dravet syndrome
Authorization of 12 months may be granted for treatment of seizures associated with Dravet syndrome in members 6 months of age and older.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continuation of treatment in members (including new members) 6 months of age or older requesting reauthorization for seizures associated with Dravet syndrome when the member has achieved or maintained a positive clinical response as evidenced by reduction in frequency or duration of seizures compared with seizure activity prior to initiating Diacomit.

IV. OTHER

Member must be taking clobazam concurrently with another anti-seizure medication and cannot use the requested medication as monotherapy in Dravet syndrome.

V. REFERENCE

1. Diacomit [package insert]. San Mateo, CA: Biocodex, Inc.; July 2022.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME
(generic)

DIBENZYLINE
(phenoxybenzamine)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization with Quantity Limit

POLICY

FDA-APPROVED INDICATIONS

Dibenzyline is indicated in the treatment of pheochromocytoma, to control episodes of hypertension and sweating. If tachycardia is excessive, it may be necessary to use a beta-blocking agent concomitantly.

Compendial Uses
Paraganglioma[5,6]

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for the treatment of pheochromocytoma or paraganglioma to control episodes of hypertension and sweating
  AND
  - The patient has experienced an inadequate treatment response to an alpha 1 selective adrenergic receptor blocker (e.g., doxazosin, prazosin, terazosin)
  OR
  - The patient has experienced an intolerance to an alpha 1 selective adrenergic receptor blocker (e.g., doxazosin, prazosin, terazosin)
  OR
  - The patient has a contraindication that would prohibit a trial of an alpha 1 selective adrenergic receptor blocker (e.g., doxazosin, prazosin, terazosin)

Quantity Limits apply.
360 capsules/25 days* or 1080 capsules/75 days*
**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*

REFERENCES

1. Dibenzyline [package insert]. Dublin 9, Ireland: Amdipharm Limited; April 2020.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2023; Accessed February 15, 2023.
3. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed February 15, 2023.
4. Neumann HPH, Young WF, Eng C. Pheochromocytoma and Paraganglioma. *The New England Journal of Medicine* 2019;381:552-65.
5. Lenders JWM, Duh QY, Eisenhofer G, et al. Pheochromocytoma and Paraganglioma: An Endocrine Society Clinical Practice Guideline. *Journal of Clinical Endocrinology and Metabolism* 2014;99(6):1915-1942.

6. Neuroendocrine and Adrenal Tumors. NCCN Guidelines version 2.2022. Available at: https://www.nccn.org/professionals/physician_gls/pdf/neuroendocrine.pdf. Accessed February 15, 2023.

Post limit quantities are limited to 300 test strips per month to allow for patients that require blood glucose testing up to 10 times per day. Since manufacturer package sizes may vary, it is the discretion of the dispensing pharmacy to fill quantities per package size up to these quantity limits. In such cases the filling limit and day supply may be less than what is indicated.

REFERENCES

1. American Diabetes Association. Standards of Medical Care in Diabetes—2022: Diabetes Care 2022;45(Suppl 1):S1-S264.

Written by:	UM Development (MS)
Date Written:	06/2016
Revised:	(KM) 07/017 (increased limit), (DS) 07/2018 (no clinical changes), (ME) 10/2020 (no clinical changes); (ASA) 08/2022 (updated quantity limit due available package sizes)
Reviewed:	Medical Affairs (ME) 06/2016; (SD) 07/2017; (EPA) 08/2018, (CHART) 10/29/20, (CHART) 09/30/21, 08/25/2022 MD Committee: 08/2018, 10/2020, 11/2021, 08/2022 External Review: 12/2022 (MD Subcommittee)

CRITERIA FOR APPROVAL

1	Is the patient on an intensive insulin regimen (multiple-dose insulin or insulin pump therapy)? [If yes, go to 2. If no, then no further questions.]	Yes	No
2	Does the patient require blood glucose testing MORE than 10 times daily? [No further questions] [RPh Note: If yes, then deny and enter a partial approval for 300 test strips per month.]	Yes	No

Mapping Instructions			
	Yes	**No**	**DENIAL REASONS**
1.	Go to 2	Deny	You do not meet the requirements of your plan. Your plan covers additional quantities of this product when you are on an intensive insulin regimen. Your request has been denied based on the information we have. [Short Description: Not on an intensive insulin regimen]
2.	Deny	Approve, 12 Months, 300 test strips / 25 days or 900 test strips / 75 days	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 300 test strips per month. Your request has been partially approved. You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of test strips has been denied. [Short Description: Over max quantity]

PRIOR AUTHORIZATION CRITERIA

BRAND NAME*
(generic) (diclofenac sodium gel 3%)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization ***Ref # 621-C***

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Diclofenac sodium gel 3% is indicated for the topical treatment of actinic keratoses (AK). Sun avoidance is indicated during therapy.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug [diclofenac sodium gel 3 percent (generic Solaraze)] is being prescribed for the treatment of actinic keratoses (AK)

AND

- The patient experienced an inadequate treatment response, intolerance, or has a contraindication to ONE of the following: A) imiquimod 5 percent cream, B) fluorouracil cream or solution

Quantity limits apply.

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Diclofenac sodium gel 3% is indicated for the topical treatment of actinic keratoses (AK).[1]

Diclofenac sodium gel 3% is applied to lesion areas twice daily. Normally 0.5 grams of gel is used on each 5 cm x 5 cm lesion site. Up to three major body areas were studied in any patient. A major body area was defined as one of five 5 cm x 5 cm regions: scalp, forehead, face, forearm and hand.[1]

Per National Comprehensive Cancer Care Network (NCCN) guidelines, actinic keratoses (AKs) are a premalignant skin condition that should be treated at first development, particularly in patients with diffuse AKs and/or field cancerization, as these patients are at high risk of developing multiple primary cutaneous squamous cell carcinomas (CSCCs). In more recent years, large prospective randomized trials in patients with AKs have shown that each of the following therapies provides better complete clearance rates compared with placebo: topical fluorouracil (5-FU) with or without calcipotriol, topical Imiquimod, topical tirbanibulin, and photodynamic therapy (PDT). The NCCN panel currently assigns a preference for 5-FU based on data from a randomized trial which reported the cumulative probability of remaining free from treatment failure was significantly higher for 5-FU (74.7%) than imiquimod (53.9%), methyl aminolevulinate plus photodynamic therapy (MAL-PDT) (37.7%), or ingenol mebutate (28.9%). Topical tirbanibulin was added to the list of recommended treatment for AK based on results from two identically designed double-blind phase III trials in which patients received either tirbanibulin or vehicle ointment for the treatment of AKs on the face or scalp. In both trials, complete clearance by day 57 occurred in significantly more patients in the tirbanibulin group compared to the vehicle group. The utility of topical diclofenac is less clear, as efficacy results vary across large, randomized trials, with some studies reporting no significant difference between diclofenac/hyaluronan and hyaluronan alone. Diclofenac/hyaluronan has also been shown to be inferior to MAL-PDT and to 5-FU for the treatment of AKs. The panel therefore assigns category 2b for diclofenac in this setting.[4]

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Per the American Academy of Dermatology Guidelines of care for the management of actinic keratosis, the literature on AK treatment supports a strong recommendation for field treatment with either 5-fluorouracil (5-FU) or imiquimod. Due to the various commercial preparations of these drugs, the treatment regimens studied often vary in terms of the concentration, dosing interval, and duration. The Work Group conditionally recommends the use of diclofenac, based on lower quality of evidence than that of the evidence supporting strong recommendations for the use of 5-FU or imiquimod.[5]

Diclofenac sodium gel 3% is available in tubes of 100 grams.[1] 100 grams should be sufficient to adequately cover three areas at a size of 5 cm x 5 cm for 30 days. The recommended duration of therapy is from 60 days to 90 days.[1]

REFERENCES

1. Diclofenac Gel 3% [package insert]. Parsippany, NJ: Activis Pharma, Inc.; Octoberl 2021.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2022; Accessed May 20, 2022.
3. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed May 20, 2022.
4. National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology. Squamous Cell Skin Cancer. Version 2.2022. May 2, 2022. NCCN.org. Accessed May 20, 2022.
5. Eisen DB, Asgari MM, Bennett DD, et al. Guidelines of care for the management of actinic keratosis. *J Am Acad Dermatol.* 2021;85:e209-e233.

Written by:	UM Development (CT)
Date Written:	01/2010
Revised:	(MS) 02/2011 (new MDC-1 created from Silverscript), 09/2011; (CT) 08/2012; (MS) 06/2013, 06/2014; (RP) 06/2015; (MS) 06/2016, (TM) 06/2017 (add limit, revise duration), (SF) 06/2018 (no clinical changes); (DFW) 06/2019 (removed MDC designation from title/document), (ME) 06/2020 (no clinical changes); (RP) 05/2021 (added t/f question), (VLS) 05/2022 (no clinical changes)
Reviewed:	Medical Affairs (KP) 01/2010, 02/2011, 09/2011, 08/2012; (LS) 06/2013; (DC) 06/2014, 06/2015; (ME) 06/2016, (AN) 06/2017, (AN) 06/2019, (CHART) 06/25/20, 07/01/2021, (CHART) 06/30/2022 External Review: 03/2010, 05/2011, 02/2012, 12/2012, 10/2013, 10/2014, 10/2015, 10/2016, 10/2017, 10/2018, 08/2019, 08/2020, 08/2021, 08/2022

CRITERIA FOR APPROVAL

1	Is the requested drug [diclofenac sodium gel 3 percent (generic Solaraze)] being prescribed for the treatment of actinic keratoses (AK)? [If yes, go to 2. If no, then no further questions.]	Yes	No
2	Has the patient experienced an inadequate treatment response, intolerance, or does the patient have a contraindication to ONE of the following: A) imiquimod 5 percent cream, B) fluorouracil cream or solution? [If yes, go to 3. If no, then no further questions.]	Yes	No
3	Does the patient require more than the plan allowance of 100 grams per month? [No further questions] [RPh Note: If yes, then deny and enter a partial approval for 100 grams / 25 days or 300 grams / 75 days of diclofenac sodium gel 3 percent.]	Yes	No

Mapping Instructions			
	Yes	**No**	**DENIAL REASONS**
1.	Go to 2	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have actinic keratoses (AK). Your request has been denied based on the information we have.

			[Short Description: No approvable diagnosis]
2.	Go to 3	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have tried imiquimod 5 percent cream or fluorouracil cream/solution and it did not work for you, or you cannot use it. Your request has been denied based on the information we have. [Short Description: No inadequate response, intolerance or contraindication to imiquimod 5 percent cream, topical fluorouracil cream/solution]
3.	Deny	Approve, 3 Months, PA approved for 3 month(s).100 grams/25 days	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 100 grams/month of diclofenac sodium gel 3 percent. You have been approved for the maximum quantity that your plan covers for a duration of 3 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity]

PRIOR AUTHORIZATION CRITERIA

BRAND NAME*
(generic)

DIFICID
(fidaxomicin)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization ***Ref # 662-A***

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA APPROVED INDICATIONS

Dificid is indicated in adult and pediatric patients aged 6 months and older for the treatment of C. difficile-associated diarrhea (CDAD).

Usage

To reduce the development of drug-resistant bacteria and maintain the effectiveness of Dificid and other antibacterial drugs, Dificid should be used only to treat infections that are proven or strongly suspected to be caused by *C. difficile*. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has the diagnosis of *C. difficile*-associated diarrhea (CDAD) confirmed by a positive stool assay

AND

- The patient requires additional medication to complete a 10 day course of the requested drug for therapy that was initiated in the hospital
  OR
- The patient has experienced an inadequate treatment response to oral vancomycin
  OR
- The patient has experienced an intolerance to vancomycin
  OR
- The patient has a contraindication that would prohibit a trial of vancomycin
  OR
- The requested drug is being prescribed for a pediatric patient **AND**
  - The patient has experienced an inadequate treatment response to oral metronidazole
    OR
  - The patient has experienced an intolerance to metronidazole
    OR
  - The patient has a contraindication that would prohibit a trial of metronidazole

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Dificid is indicated in adult and pediatric patients aged 6 months and older for the treatment of C. difficile-associated diarrhea (CDAD).[1]

The recommended dose for adults is 200 mg orally twice daily for 10 days. The recommended dosing for pediatric patients, who weigh at least 12.5 kg and are able to swallow tablets, is 200 mg orally twice daily for 10 days. If unable to

swallow tablets or weigh less than 12.5 kg, Dificid oral suspension is available for use. The recommended dosing for pediatric patients is based on body weight and administered via oral syringe twice daily for 10 days.[1]

C*lostridium difficile* infection (CDI) is defined by the presence of symptoms (usually diarrhea) and either a stool test positive for *C. difficile* toxins or detection of toxigenic *C. difficile,* or colonoscopic or histopathologic findings revealing pseudomembranous colitis.[4]

The Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA) 2021 Focused Update Guideline of the Management of Clostridioides difficile infection in adults suggests using fidaxomicin rather than a standard course of oral vancomycin for an initial CDI episode. This is a conditional recommendation; therefore, providers should be prepared to help patients make a decision that is consistent with their own values/decision aids and shared decision making. Additional, well-designed, independent, cost-effectiveness studies for patients with CDI are needed to improve the strength of this recommendation given that cost is a substantial barrier to fidaxomicin use. In patients with recurrent CDI episodes, the IDSA guideline suggests fidaxomicin rather than a standard course of oral vancomycin, also as a conditional recommendation. Oral vancomycin as a standard course or as a tapered and pulsed regimen is an acceptable alternative. The IDSA guideline recommends oral vancomycin rather than fidaxomicin for the treatment of fulminant CDI.[5] The American College of Gastroenterology (ACG) Clinical Guideline: Prevention, Diagnosis and Treatment of Clostridioides difficile Infections recommends either oral vancomycin or fidaxomicin in adult patients with non-severe CDI, stating oral vancomycin or fidaxomicin are appropriate initial treatments for most patients. For lower-risk patients (younger outpatients with minimal comorbidities), particularly in cost-sensitive environments, metronidazole is an appropriate alternative. As initial therapy for severe CDI in adults, the ACG guideline also recommends either oral vancomycin or fidaxomicin. For fulminant CDI, oral vancomycin is recommended. For the treatment of recurrent CDI, the guideline states that the choice of treatment is dependent on what was used to treat the initial episode. Vancomycin is recommended for patients experiencing a first recurrence after an initial course of fidaxomicin, vancomycin or metronidazole. Fidaxomicin is recommended for patients experiencing a first recurrence after an initial course of vancomycin or metronidazole.[6] Due to the conditional status of the IDSA recommendations that favor fidaxomicin over vancomycin and the ACG recommendations for use of either vancomycin or fidaxomicin, an inadequate treatment response to oral vancomycin or an intolerance or contraindication to vancomycin will be required prior to approval of Dificid in adult patients with C. Difficile associated diarrhea.

For pediatric patients, the 2017 Update to the Infectious Disease Society of America (IDSA) Clinical Practice Guidelines for Clostridium difficile Infection recommends oral metronidazole or oral vancomycin for initial episodes or first recurrence of nonsevere CDI. For children with an initial episode of severe CDI, oral vancomycin is recommended with or without metronidazole IV. For children with a second or greater episode of recurrent CDI, oral vancomycin is recommended. Use of Dificid in pediatric patients is not yet addressed in treatment guidelines. Therefore, an inadequate treatment response to oral vancomycin or oral metronidazole or an intolerance or contraindication to vancomycin or metronidazole will be required for pediatric patients with CDAD.

Dificid will be approved for completion of the 10-day course of therapy for patients started on the drug for the treatment of CDAD while in the hospital without a trial of vancomycin for adult patients or vancomycin or metronidazole for pediatric patients.

Since the recommended duration of treatment with Dificid for C. difficile-associated diarrhea is 10 days, the duration of approval will be 10 days if coverage criteria are met.

REFERENCES

1. Dificid [package insert]. Whitehouse Station, NJ: Merck & Co., Inc.; February 2021.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2021; Accessed November 9, 2021.
3. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Accessed November 9, 2021.
4. McDonald L, Gerding D, Johnson S, et al. Clinical Practice Guidelines for *Clostridium difficile* Infection in Adults and Children: 2017 Update by the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA). *Clinical Infectious Diseases* 2018:66 (7): e1-e48. https://doi.org/10.1093/cid/cix1085. Accessed November 9, 2021.

5. Johnson S, Lavergne V, Skinner A et al. Clinical Practice Guideline by the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA): 2021 Focused Update Guidelines on Management of Clostridioides difficile Infection in Adults, *Clinical Infectious Diseases* 2021;73 (5): e1029–e1044. https://doi.org/10.1093/cid/ciab549. Accessed November 9, 2021.
6. Kelly CR, Fischer M, Allegretti JR, LaPlante K, et al. ACG Clinical Guidelines: Prevention, Diagnosis, and Treatment of Clostridioides difficile Infections. *Am J Gastroenterol.* 2021 Jun 1;116(6):1124-1147.

Written by:	UM Development (RP)
Date Written:	02/2012
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Reviewed:	Medical Affairs (DR) 03/2012; (WF) 06/2012; (DC) 07/2012; (LMS) 03/2013; (KP) 02/2014; (LCB) 12/2014; (KRU) 04/2015; (ME) 03/2018, (CHART) 01/02/20, (CHART) 12/03/20, (CHART) 12/02/2021 External Review: 05/2012, 06/2012, 06/2013, 04/2014, 04/2015, 04/2016, 04/2017, 04/2018, 04/2019, 04/2020, 04/2021, 02/2022

CRITERIA FOR APPROVAL

1	Does the patient have the diagnosis of *C. difficile*-associated diarrhea (CDAD) confirmed by a positive stool assay? [If no, then no further questions.]	Yes	No
2	Does the patient require additional medication to complete a 10 day course of the requested drug for therapy that was initiated in the hospital? [If yes, then no further questions.]	Yes	No
3	Has the patient experienced an inadequate treatment response to oral vancomycin? [If yes, then no further questions.]	Yes	No
4	Has the patient experienced an intolerance to vancomycin? [If yes, then no further questions.]	Yes	No
5	Does the patient have a contraindication that would prohibit a trial of vancomycin? [If yes, then no further questions.]	Yes	No
6	Is the requested drug being prescribed for a pediatric patient? [If no, then no further questions.]	Yes	No
7	Has the patient experienced an inadequate treatment response to oral metronidazole? [If yes, then no further questions.]	Yes	No
8	Has the patient experienced an intolerance to metronidazole? [If yes, then no further questions.]	Yes	No
9	Does the patient have a contraindication that would prohibit a trial of metronidazole?	Yes	No

Mapping Instructions			
	Yes	**No**	**DENIAL REASONS – DO NOT USE FOR MEDICARE PART D**
1.	Go to 2	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have these conditions: -You have a certain type of bacterial infection that is causing diarrhea

			-The type of bacteria has been confirmed by a stool test Your request has been denied based on the information we have. [Short Description: No approvable diagnosis, no confirmation of diagnosis]
2.	Approve, 10 days	Go to 3	
3.	Approve, 10 days	Go to 4	
4.	Approve, 10 days	Go to 5	
5.	Approve, 10 days	Go to 6	
6.	Go to 7	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you are an adult and you have tried oral vancomycin and it did not work for you or you cannot use it. Your request has been denied based on the information we have. [Short Description: No inadequate response, intolerance, or contraindication to vancomycin for adult patient]
7.	Approve, 10 days	Go to 8	
8.	Approve, 10 days	Go to 9	
9.	Approve, 10 days	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you meet any of these conditions: -You have tried oral vancomycin and it did not work for you, or you cannot use it -You are a pediatric patient and you have tried oral metronidazole and it did not work for you or you cannot use it Your request has been denied based on the information we have. [Short Description: No inadequate response, intolerance, or contraindication to vancomycin or metronidazole for pediatric patient]

QUANTITY LIMIT CRITERIA

DRUG CLASS	**ERGOT DERIVATIVES**
BRAND NAME (generic)	**MIGRANAL NASAL SPRAY (dihydroergotamine mesylate)** **TRUDHESA NASAL SPRAY (dihydroergotamine mesylate)**

Status: CVS Caremark® Criteria
Type: Quantity Limit

POLICY

FDA-APPROVED INDICATIONS

Migranal

Migranal (dihydroergotamine mesylate) Nasal Spray is indicated for the acute treatment of migraine headaches with or without aura.

Migranal (dihydroergotamine mesylate) Nasal Spray is not intended for the prophylactic therapy of migraine or for the management of hemiplegic or basilar migraine.

Trudhesa

Trudhesa is indicated for the acute treatment of migraine with or without aura in adults.

Limitations of Use

Trudhesa is not indicated for the preventive treatment of migraine.

Trudhesa is not indicated for the management of hemiplegic or basilar migraine.

INITIAL LIMIT QUANTITY

Limits should accumulate across all drugs and strengths up to highest quantity listed depending on the order the claims are processed.

Drug	1 Month Limit*	3 Month Limit*
Migranal (dihydroergotamine mesylate)	8 nasal units / 25 days	24 nasal units / 75 days
Trudhesa (dihydroergotamine mesylate)	12 units (3 packages) / 25 days	36 units (9 packages) / 75 days

**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*

REFERENCES

1. Migranal Nasal Spray [package insert]. Bridgewater, NJ: Bausch Health US, LLC; September 2022.
2. Trudhesa [package insert]. Seattle, WA: Impel NeuroPharma Inc; September 2021.
3. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Waltham, MA: UpToDate, Inc.; 2023. https://online.lexi.com. Accessed April 21, 2023.

4. Lexicomp Online, Lexi-Drugs Online. Walham, MA: UpToDate, Inc.; 2023. https://online.lexi.com. Accessed May 1, 2023.
5. Micromedex (electronic version). Merative, Ann Arbor, Michigan, USA. Available at: https://www.micromedexsolutions.com/ (cited: 04/21/2023).

Reference number(s)
1845-A

SPECIALTY GUIDELINE MANAGEMENT

TECFIDERA (dimethyl fumarate)
dimethyl fumarate

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Tecfidera is indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.

All other indications are considered experimental/investigational and not medically necessary.

II. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with a neurologist.

III. CRITERIA FOR INITIAL APPROVAL

A. Relapsing forms of multiple sclerosis
Authorization of 12 months may be granted to members who have been diagnosed with a relapsing form of multiple sclerosis (including relapsing-remitting and secondary progressive disease for those who continue to experience relapse).

B. Clinically isolated syndrome
Authorization of 12 months may be granted to members for the treatment of clinically isolated syndrome.

IV. CONTINUATION OF THERAPY

For all indications: Authorization of 12 months may be granted for members who are experiencing disease stability or improvement while receiving the requested medication.

V. OTHER

Members will not use the requested medication concomitantly with other disease modifying multiple sclerosis agents (Note: Ampyra and Nuedexta are not disease modifying).

VI. REFERENCES

1. Tecfidera [package insert]. Cambridge, MA: Biogen Inc.; February 2023.
2. dimethyl fumarate [package insert]. East Windsor, NJ: Aurobindo Pharma USA, Inc.; February 2023.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME
(generic)

DIPENTUM
(olsalazine)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

POLICY

FDA-APPROVED INDICATIONS
Dipentum is indicated for the maintenance of remission of ulcerative colitis in adult patients who are intolerant of sulfasalazine.

COVERAGE CRITERIA
The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for the maintenance of remission of ulcerative colitis in a patient who is intolerant of sulfasalazine

REFERENCES

1. Dipentum [package insert]. Somerset, New Jersey: Meda Pharmaceuticals Inc.; December 2022.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, Ohio: UpToDate, Inc.; 2023; Accessed January 5, 2023.
3. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed January 5, 2023.

Reference number(s)
1873-A

SPECIALTY GUIDELINE MANAGEMENT

TIKOSYN (dofetilide)
dofetilide (generic)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. Maintenance of normal sinus rhythm (delay in time to recurrence of atrial fibrillation/atrial flutter [AF/AFI]) in patients with AF/AFl of greater than one week duration who have been converted to normal sinus rhythm
   2. Conversion of AF/AFI to normal sinus rhythm

B. Compendial Uses
   1. Supraventricular tachycardia
   2. Ventricular tachyarrhythmia

All other indications are considered experimental/investigational and not medically necessary.

II. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with a cardiologist.

III. CRITERIA FOR APPROVAL

A. Atrial Flutter/Atrial fibrillation
Authorization of 12 months may be granted for the maintenance of, or conversion to, normal sinus rhythm after atrial flutter or atrial fibrillation.

B. Supraventricular tachycardia
Authorization of 12 months may be granted for treatment and prevention of supraventricular tachycardia.

C. Ventricular tachyarrhythmia
Authorization of 12 months may be granted for treatment and prevention of ventricular tachyarrhythmia.

IV. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

V. REFERENCES

1. Tikosyn [package insert]. New York, NY: Pfizer Inc.; July 2021.
2. Dofetilide [package insert]. East Windsor, NJ: Aurobindo Pharma USA, Inc.; April 2021.
3. Micromedex® [electronic version]. Merative, Ann Arbor, Michigan, USA. Available at: https://www.micromedexsolutions.com/. Accessed April 5, 2023.
4. Page RL, Joglar JA, Caldwell MA, et al. 2015 ACC/AHA/HRS Guideline for the Management of adult patients with supraventricular tachycardia. A report of the American College of Cardiology/American Heart Association Task Force on clinical practice guidelines and the Heart Rhythm Society. *J Am Coll Cardiol*. 2016;67(13).
5. Fuster V, Ryden LE, Asinger RW, et al. ACC/AHA/ESC guidelines for the management of patients with atrial fibrillation: Executive summary. A report of the American College of Cardiology/American Heart Association Task Force on practice guidelines and the European Society of Cardiology committee for practice guidelines and policy conferences (Committee to develop guidelines for the management of patients with atrial fibrillation) developed in collaboration with the North American Society of Pacing and Electrophysiology. *Circulation.* 2001;104(17):2118-50.

Reference number(s)
3081-A

SPECIALTY GUIDELINE MANAGEMENT

DOPTELET (avatrombopag)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

1. Treatment of Thrombocytopenia in Patients with Chronic Liver Disease (CLD)
   Doptelet is indicated for the treatment of thrombocytopenia in adult patients with chronic liver disease who are scheduled to undergo a procedure.

2. Treatment of Thrombocytopenia in Patients with Chronic Immune Thrombocytopenia (ITP)
   Doptelet is indicated for the treatment of thrombocytopenia in adult patients with chronic immune thrombocytopenia who have had an insufficient response to a previous treatment.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
A. Thrombocytopenia in chronic liver disease: pretreatment platelet count
B. Immune thrombocytopenia: pretreatment and current platelet counts

III. EXCLUSIONS

Coverage will not be provided for members with the following exclusion: concomitant use of Doptelet with other thrombopoietin receptor agonists (e.g., Mulpleta, Promacta, Nplate) or with spleen tyrosine kinase inhibitors (e.g., Tavalisse)

IV. PRESCRIBER SPECIALTIES

A. For diagnosis of chronic immune thrombocytopenia, this medication must be prescribed by or in consultation with a hematologist.
B. For diagnosis of thrombocytopenia in patients with chronic liver disease, this medication must be prescribed by or in consultation with a hematologist, hepatologist or gastroenterologist.

V. CRITERIA FOR INITIAL APPROVAL

A. Thrombocytopenia in chronic liver disease

Authorization of 30 days may be granted for treatment of thrombocytopenia in members with chronic liver disease when both of the following criteria are met:
1. Member has an untransfused platelet count of less than $50x10^9$/L taken within 14 days of the request.
2. Member is scheduled to undergo a procedure.

B. Chronic immune thrombocytopenia (ITP)
Authorization of 6 months may be granted for treatment of chronic ITP when both of the following criteria are met:
1. Inadequate response or intolerance to prior therapy (for example, corticosteroids or immunoglobulins).
2. Untransfused platelet count at any point prior to the initiation of the requested medication is less than $30x10^9$/L OR $30x10^9$/L to $50x10^9$/L with symptomatic bleeding (e.g., significant mucous membrane bleeding, gastrointestinal bleeding or trauma) or risk factors for bleeding (see Section VII).

VI. CONTINUATION OF THERAPY

A. Thrombocytopenia in chronic liver disease
Continuation of therapy, defined as use beyond the initial approval for same procedure, is not approvable. All members (including new members) requesting authorization due to newly scheduled procedure must meet all initial authorization criteria.

B. Chronic ITP
1. Authorization of 3 months may be granted to members with current platelet count less than $50x10^9$/L for whom the platelet count is not sufficient to prevent clinically important bleeding and who have not received a maximal Doptelet dose for at least 4 weeks.
2. Authorization of 12 months may be granted to members with current platelet count less than $50x10^9$/L for whom the current platelet count is sufficient to prevent clinically important bleeding.
3. Authorization of 12 months may be granted to members with current platelet count of $50x10^9$/L to $200x10^9$/L.
4. Authorization of 12 months may be granted to members with current platelet count greater than $200x10^9$/L to less than or equal to $400x10^9$/L for whom Doptelet dosing will be adjusted to achieve a platelet count sufficient to avoid clinically important bleeding.

VII. APPENDIX

Examples of risk factors for bleeding (not all inclusive)
- Undergoing a medical or dental procedure where blood loss is anticipated
- Comorbidity (e.g., peptic ulcer disease, hypertension)
- Mandated anticoagulation therapy
- Profession (e.g., construction worker) or lifestyle (e.g., plays contact sports) that predisposes patient to trauma

VIII. REFERENCES
1. Doptelet [package insert]. Durham, NC: AkaRx, Inc.; July 2021.
2. Jurczak W, Chojnowski K, et al. Phase 3 randomised study of avatrombopag, a novel thrombopoietin receptor agonist for the treatment of chronic immune thrombocytopenia. *Br J Haematol.* 2018;183(3):479-490.
3. Nuenert C, Terrel DR, Arnold DM, et al. American Society of Hematology 2019 guidelines for immune thrombocytopenia. *Blood Adv* 2019;3(23):3829–3866.

4. Provan D, Arnold DM, Bussel JB, et al. Updated international consensus report on the investigation and management of primary immune thrombocytopenia. *Blood Adv* 2019;3(22): 3780–3817.
5. Rodeghiero F, Stasi R, Gernsheimer T, et al. Standardization of terminology, definitions and outcome criteria in immune thrombocytopenic purpura of adults and children: report from an international working group. *Blood*. 2009;113(11):2386-2393.

PRIOR AUTHORIZATION CRITERIA

DRUG CLASS	**DIPEPTIDYL PEPTIDASE-4 (DPP-4) INHIBITORS**
BRAND NAME (generic)	**JANUMET (sitagliptin/metformin)** **JANUMET XR (sitagliptin/metformin extended-release)** **JANUVIA (sitagliptin)** **JENTADUETO (linagliptin/metformin)** **JENTADUETO XR (linagliptin/metformin extended-release)** **KAZANO (alogliptin/metformin)** **KOMBIGLYZE XR (saxagliptin/metformin extended-release)** **NESINA (alogliptin)** **ONGLYZA (saxagliptin)** **OSENI (alogliptin/pioglitazone)** **TRADJENTA (linagliptin)**

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

POLICY

FDA-APPROVED INDICATIONS
Janumet/Janumet XR

Janumet/Janumet XR are indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.
Limitations of Use
- Janumet/Janumet XR should not be used in patients with type 1 diabetes mellitus.
- Janumet/Janumet XR have not been studied in patients with a history of pancreatitis. It is unknown whether patients with a history of pancreatitis are at increased risk for the development of pancreatitis while using Janumet/Janumet XR.

Januvia
Januvia is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.
Limitations of Use:
- Januvia should not be used in patients with type 1 diabetes.
- Januvia has not been studied in patients with a history of pancreatitis. It is unknown whether patients with a history of pancreatitis are at increased risk for the development of pancreatitis while using Januvia.

Jentadueto/Jentadueto XR
Jentadueto/Jentadueto XR are indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.
Limitations of Use:
- Jentadueto/Jentadueto XR should not be used in patients with type 1 diabetes.
- Jentadueto/Jentadueto XR have not been studied in patients with a history of pancreatitis. It is unknown whether patients with a history of pancreatitis are at increased risk for the development of pancreatitis while using Jentadueto/Jentadueto XR.

Kazano
Kazano is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.
Limitations of Use:
- Kazano should not be used in patients with type 1 diabetes mellitus.

Kombiglyze XR
Kombiglyze XR is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus when treatment with both saxagliptin and metformin is appropriate.
Limitations of Use:
- Kombiglyze XR s not indicated for the treatment of type 1 diabetes mellitus or diabetic ketoacidosis.

Nesina
Nesina is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.
Limitations of Use:
- Nesina should not be used in patients with type 1 diabetes mellitus.

Onglyza
Monotherapy and Combination Therapy
Onglyza is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.
Limitations of Use:
- Onglyza is not indicated for the treatment of type 1 diabetes mellitus or diabetic ketoacidosis, as it would not be effective in these settings.

Oseni
Oseni is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.
Limitations of Use:
- Oseni should not be used in patients with type 1 diabetes mellitus.

Tradjenta
Tradjenta is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.
Limitations of Use:
- Tradjenta should not be used in patients with type 1 diabetes as it would not be effective.

- Tradjenta has not been studied in patients with a history of pancreatitis. It is unknown whether patients with a history of pancreatitis are at an increased risk for the development of pancreatitis while using Tradjenta.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has a diagnosis of type 2 diabetes mellitus

AND

- The patient has NOT been receiving a stable maintenance dose of the requested drug for at least 3 months **AND**
    - The patient has experienced an inadequate treatment response, intolerance, or has a contraindication to metformin

    OR
    - The patient requires combination therapy AND has an A1c (hemoglobin A1c) of 7.5 percent or greater

OR

- The patient has been receiving a stable maintenance dose of the requested drug for at least 3 months **AND**
    - The patient has demonstrated a reduction in A1c (hemoglobin A1c) since starting this therapy

REFERENCES

1. Janumet [package insert]. Whitehouse Station, NJ: Merck Sharp & Dohme Corp; December 2021.
2. Janumet XR [package insert]. Whitehouse Station, NJ: Merck Sharp & Dohme Corp; December 2021.
3. Januvia [package insert]. Whitehouse Station, NJ: Merck Sharp & Dohme Corp; December 2021.
4. Jentadueto [package insert]. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc.; April 2022.
5. Jentadueto XR [package insert]. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc.; October 2021.
6. Kazano [package insert]. Lexington, MA: Takeda Pharmaceuticals America, Inc.; March 2022.
7. Kombiglyze XR [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; October 2019.
8. Nesina [package insert]. Lexington, MA: Takeda Pharmaceuticals America, Inc.; March 2022.
9. Onglyza [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; October 2019.
10. Oseni [package insert]. Lexington, MA: Takeda Pharmaceuticals America, Inc.; March 2022.
11. Tradjenta [package insert]. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc.; April 2022.
12. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, Ohio: UpToDate, Inc.; 2022; Accessed June 9, 2022.
13. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed June 9, 2022.
14. American Diabetes Association. Standards of Medical Care in Diabetes—2022. *Diabetes Care* 2022;45(Suppl 1):S1-S264.
15. Garber AJ, Handelsman Y, Grunberger G, et al. Consensus Statement by the American Association of Clinical Endocrinologists and American College of Endocrinology on the Comprehensive Type 2 Diabetes Management Algorithm – 2020 Executive Summary. *Endocr Pract*. 2020;26(1):107-139.

STEP THERAPY CRITERIA

DRUG CLASS	**DIPEPTIDYL PEPTIDASE-4 (DPP-4) INHIBITORS**
BRAND NAME (generic)	**JANUMET (sitagliptin/metformin)** **JANUMET XR (sitagliptin/metformin extended-release)** **JANUVIA (sitagliptin)** **JENTADUETO (linagliptin/metformin)** **JENTADUETO XR (linagliptin/metformin extended-release)** **KAZANO (alogliptin/metformin)** **KOMBIGLYZE XR (saxagliptin/metformin extended-release)** **NESINA (alogliptin)** **ONGLYZA (saxagliptin)** **OSENI (alogliptin/pioglitazone)** **TRADJENTA (linagliptin)**

Status: CVS Caremark Criteria
Type: Initial Step Therapy; Post Step Therapy Prior Authorization

POLICY

FDA-APPROVED INDICATIONS
Janumet/Janumet XR

Janumet/Janumet XR are indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.
Limitations of Use
- Janumet/Janumet XR should not be used in patients with type 1 diabetes mellitus.
- Janumet/Janumet XR have not been studied in patients with a history of pancreatitis. It is unknown whether patients with a history of pancreatitis are at increased risk for the development of pancreatitis while using Janumet/Janumet XR.

Januvia
Januvia is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.
Limitations of Use:
- Januvia should not be used in patients with type 1 diabetes.
- Januvia has not been studied in patients with a history of pancreatitis. It is unknown whether patients with a history of pancreatitis are at increased risk for the development of pancreatitis while using Januvia.

Jentadueto/Jentadueto XR
Jentadueto/Jentadueto XR are indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.
Limitations of Use:
- Jentadueto/Jentadueto XR should not be used in patients with type 1 diabetes.
- Jentadueto/Jentadueto XR have not been studied in patients with a history of pancreatitis. It is unknown whether patients with a history of pancreatitis are at increased risk for the development of pancreatitis while using Jentadueto/Jentadueto XR.

Kazano
Kazano is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.
Limitations of Use:
- Kazano should not be used in patients with type 1 diabetes mellitus.

Kombiglyze XR
Kombiglyze XR is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus when treatment with both saxagliptin and metformin is appropriate.
Limitations of Use:
- Kombiglyze XR s not indicated for the treatment of type 1 diabetes mellitus or diabetic ketoacidosis.

Nesina
Nesina is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.
Limitations of Use:
- Nesina should not be used in patients with type 1 diabetes mellitus.

Onglyza
Monotherapy and Combination Therapy
Onglyza is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.
Limitations of Use:
- Onglyza is not indicated for the treatment of type 1 diabetes mellitus or diabetic ketoacidosis, as it would not be effective in these settings.

Oseni
Oseni is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.
Limitations of Use:
- Oseni should not be used in patients with type 1 diabetes mellitus.

Tradjenta
Tradjenta is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.
Limitations of Use:

- Tradjenta should not be used in patients with type 1 diabetes as it would not be effective.
- Tradjenta has not been studied in patients with a history of pancreatitis. It is unknown whether patients with a history of pancreatitis are at an increased risk for the development of pancreatitis while using Tradjenta.

INITIAL STEP THERAPY

**Include Rx and OTC products unless otherwise stated.*

If the patient has filled a prescription for at least a 30-day supply of metformin within the past 180 days under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit. If the patient does not meet the initial step therapy criteria, then the claim will reject with a message indicating that a prior authorization (PA) is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has a diagnosis of type 2 diabetes mellitus

AND

- The patient has NOT been receiving a stable maintenance dose of the requested drug for at least 3 months **AND**
    - The patient has experienced an inadequate treatment response, intolerance, or has a contraindication to metformin

    OR
    - The patient requires combination therapy AND has an A1c (hemoglobin A1c) of 7.5 percent or greater

OR

- The patient has been receiving a stable maintenance dose of the requested drug for at least 3 months **AND**
    - The patient has demonstrated a reduction in A1c (hemoglobin A1c) since starting this therapy

REFERENCES

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3. Januvia [package insert]. Whitehouse Station, NJ: Merck Sharp & Dohme Corp; December 2021.
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6. Kazano [package insert]. Lexington, MA: Takeda Pharmaceuticals America, Inc.; March 2022.
7. Kombiglyze XR [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; October 2019.
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9. Onglyza [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; October 2019.
10. Oseni [package insert]. Lexington, MA: Takeda Pharmaceuticals America, Inc.; March 2022.
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15. Garber AJ, Handelsman Y, Grunberger G, et al. Consensus Statement by the American Association of Clinical Endocrinologists and American College of Endocrinology on the Comprehensive Type 2 Diabetes Management Algorithm – 2020 Executive Summary. *Endocr Pract*. 2020;26(1):107-139.

STEP THERAPY CRITERIA

DRUG CLASS	**DIPEPTIDYL PEPTIDASE-4 (DPP-4) INHIBITORS**
BRAND NAME (generic)	
	JANUMET (sitagliptin/metformin)
	JANUMET XR (sitagliptin/metformin extended-release)
	JANUVIA (sitagliptin)
	JENTADUETO (linagliptin/metformin)
	JENTADUETO XR (linagliptin/metformin extended-release)
	KAZANO (alogliptin/metformin)
	KOMBIGLYZE XR (saxagliptin/metformin extended-release)
	NESINA (alogliptin)
	ONGLYZA (saxagliptin)
	OSENI (alogliptin/pioglitazone)
	TRADJENTA (linagliptin)
	ZITUVIMET (sitagliptin/metformin)
	ZITUVIO (sitagliptin)

Status: CVS Caremark® Criteria

POLICY

FDA-APPROVED INDICATIONS

Janumet/Janumet XR
Janumet/Janumet XR are indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Limitations of Use
- Janumet/Janumet XR should not be used in patients with type 1 diabetes mellitus.
- Janumet/Janumet XR have not been studied in patients with a history of pancreatitis. It is unknown whether patients with a history of pancreatitis are at increased risk for the development of pancreatitis while using Janumet/Janumet XR.

Januvia
Januvia is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Limitations of Use:
- Januvia should not be used in patients with type 1 diabetes.
- Januvia has not been studied in patients with a history of pancreatitis. It is unknown whether patients with a history of pancreatitis are at increased risk for the development of pancreatitis while using Januvia.

Jentadueto/Jentadueto XR
Jentadueto/Jentadueto XR are indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Limitations of Use:
- Jentadueto/Jentadueto XR should not be used in patients with type 1 diabetes.
- Jentadueto/Jentadueto XR have not been studied in patients with a history of pancreatitis. It is unknown whether patients with a history of pancreatitis are at increased risk for the development of pancreatitis while using Jentadueto/Jentadueto XR.

Kazano
Kazano is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Limitations of Use:
- Kazano should not be used in patients with type 1 diabetes mellitus.

Kombiglyze XR
Kombiglyze XR is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus when treatment with both saxagliptin and metformin is appropriate.

Limitations of Use:
- Kombiglyze XR s not indicated for the treatment of type 1 diabetes mellitus or diabetic ketoacidosis.

Nesina
Nesina is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Limitations of Use:
- Nesina should not be used in patients with type 1 diabetes mellitus.

Onglyza
Monotherapy and Combination Therapy
Onglyza is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Limitations of Use:

- Onglyza is not indicated for the treatment of type 1 diabetes mellitus or diabetic ketoacidosis, as it would not be effective in these settings.

Oseni
Oseni is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Limitations of Use:
- Oseni should not be used in patients with type 1 diabetes mellitus.

Tradjenta
Tradjenta is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Limitations of Use:
- Tradjenta should not be used in patients with type 1 diabetes as it would not be effective.
- Tradjenta has not been studied in patients with a history of pancreatitis. It is unknown whether patients with a history of pancreatitis are at an increased risk for the development of pancreatitis while using Tradjenta.

Zituvimet
Zituvimet is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Limitations of Use:
Zituvimet is not recommended in patients with type 1 diabetes mellitus.
Zituvimet has not been studied in patients with a history of pancreatitis. It is unknown whether patients with a history of pancreatitis are at increased risk for the development of pancreatitis while using Zituvimet.

Zituvio
Zituvio is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Limitations of Use:
Zituvio is not recommended in patients with type 1 diabetes mellitus.
Zituvio has not been studied in patients with a history of pancreatitis. It is unknown whether patients with a history of pancreatitis are at increased risk for the development of pancreatitis while using Zituvio.

INITIAL STEP THERAPY
**Include Rx and OTC products unless otherwise stated.*

If the patient has filled a prescription for at least a 30-day supply of metformin within the past 180 days under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit. If the patient does not meet the initial step therapy criteria, then the claim will reject with a message indicating that a prior authorization (PA) is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

COVERAGE CRITERIA
The requested drug will be covered with prior authorization when the following criteria are met:
- The patient has a diagnosis of type 2 diabetes mellitus **AND**
    - The patient has NOT been receiving a stable maintenance dose of the requested drug for at least 3 months **AND**
        - The patient has experienced an inadequate treatment response, intolerance, or has a contraindication to metformin

        OR
        - The patient requires combination therapy AND has an A1C of 7.5 percent or greater

    OR
    - The patient has been receiving a stable maintenance dose of the requested drug for at least 3 months **AND**

- The patient has demonstrated a reduction in A1C since starting this therapy

Duration of Approval (DOA):

- 1009-D: DOA: 36 months

REFERENCES

1. Janumet [package insert]. Rahway, NJ: Merck Sharp & Dohme LLC; July 2022.
2. Janumet XR [package insert]. Rahway, NJ: Merck Sharp & Dohme LLC; July 2022.
3. Januvia [package insert]. Rahway, NJ: Merck Sharp & Dohme LLC; July 2022.
4. Jentadueto [package insert]. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc.; April 2022.
5. Jentadueto XR [package insert]. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc.; October 2021.
6. Kazano [package insert]. Lexington, MA: Takeda Pharmaceuticals America, Inc.; March 2022.
7. Kombiglyze XR [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; October 2019.
8. Nesina [package insert]. Lexington, MA: Takeda Pharmaceuticals America, Inc.; March 2022.
9. Onglyza [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; October 2019.
10. Oseni [package insert]. Lexington, MA: Takeda Pharmaceuticals America, Inc.; March 2022.
11. Tradjenta [package insert]. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc.; April 2022.
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PRIOR AUTHORIZATION CRITERIA

DRUG CLASS	**DISPOSABLE INSULIN PUMPS**
BRAND NAME (generic)	**OMNIPOD (ALL RX PRODUCTS)** **V-GO (ALL PRODUCTS)**

Status: CVS Caremark Criteria
Type: Initial Prior Authorization with Quantity Limit

POLICY

COVERAGE CRITERIA

The requested medical device will be covered with prior authorization when the following criteria are met:

- The patient is currently established on therapy with an insulin pump **AND**
    - The patient has documented frequency of glucose self-testing an average of at least 4 times per day OR the patient is using a continuous glucose monitor (CGM)

OR

- The patient is managing their diabetes with multiple daily insulin injections (i.e., at least 3 injections per day) with frequent self-adjustments of the insulin dose for at least 6 months **AND**
    - The patient has documented frequency of glucose self-testing an average of at least 4 times per day for the past two months OR the patient has been using a continuous glucose monitor (CGM) for the past two months
      AND
    - The patient has completed a comprehensive diabetes education program
      AND
    - The patient has experienced any of the following while on multiple daily injections of insulin (i.e., more than 3 injections per day): A) elevated glycosylated hemoglobin level (e.g., HbA1c greater than 7 percent), B) history of recurrent hypoglycemia (e.g., blood glucose levels less than 70 mg/dL), C) wide fluctuations in blood glucose before mealtime, D) “dawn” phenomenon with fasting blood sugars frequently exceeding 200 mg/dL, E) history of severe glycemic excursions

Quantity Limits Apply.
Omnipod starter kit: 1 kit/999 days
Omnipod pod refills: 10 pods/25 days*
V-Go: 30 pumps/25 days*
**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*

REFERENCES

1. Omnipod, Omnipod DASH Insulin Management System. 510(k) Premarket Notification FDA Home Medical Devices Databases. Available at: https://www.accessdata.fda.gov/cdrh_docs/pdf19/K192659.pdf. Accessed August 3, 2022.
2. Omnipod 5 ACE Pump (Pod). 510(k) Premarket Notification FDA Home Medical Devices Databases. Available at: https://www.accessdata.fda.gov/cdrh_docs/pdf20/K203768.pdf. Accessed September 2, 2022.
3. V-Go. 510(k) Premarket Notification FDA Home Medical Devices Databases. Available at: https://www.accessdata.fda.gov/cdrh_docs/pdf10/K100504.pdf. Accessed August 3, 2022.
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5. McAdams BH, Rizvi AA. An Overview of Insulin Pumps and Glucose Sensors for the Generalist. *J Clin Med* 2016;5;1-17.
6. Peters AL, Ahmann AJ, Battelino T et al. Diabetes Technology – Continuous Subcutaneous Insulin Infusion Therapy and Continuous Glucose Monitoring in Adults: An Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab* 2016;101(11):3922-3937.
7. Grunberger G, Abelseth JM, Baily TS et al. Consensus statement by the American Association of Clinical Endocrinologist/American College of Endocrinology Insulin Pump Management Task Force. *Endocr Pract.* 2014;20(5):463-489.
8. Grunberger G, Handelsman Y, Bloomgarden ZT, et al. American Association of Clinical Endocrinologists and American College of Endocrinology 2018 Position Statement on Integration of Insulin Pumps and Continuous Glucose Monitoring in Patients with Diabetes Mellitus. *Endocr Pract*. 2018;24(3):302-308.
9. National Coverage Determination (NCD) for Infusion Pumps (280.14); Revision Effective Date 12/17/2004. Available at: https://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?NCDId=223&ncdver=2&NCAId=41&SearchType=Advanced&CoverageSelection=Both&NCSelection=NCA%7cCAL%7cNCD%7cMEDCAC%7cTA%7cMCD&ArticleType=BC%7cSAD%7cRTC%7cReg&PolicyType=Both&s=47&KeyWord=INSULIN+PUMP&KeyWordLookUp=Title&KeyWordSearchType=Exact&kq=true&bc=EAAAABAAIAAA&. Accessed August 3, 2022.

QUANTITY LIMIT CRITERIA

DRUG CLASS	**DRONABINOL PRODUCTS**
BRAND NAME* **(generic)**	**MARINOL** **(dronabinol)**
	SYNDROS **(dronabinol oral solution)**

Status: CVS Caremark Criteria
Type: Quantity Limit ***Ref # 137-H***

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Marinol and Syndros are indicated in adults for the treatment of:

- anorexia associated with weight loss in patients with Acquired Immune Deficiency Syndrome (AIDS).
- nausea and vomiting associated with cancer chemotherapy in patients who have failed to respond adequately to conventional antiemetic treatments.

INITIAL LIMIT QUANTITY

Limits do not accumulate together; patient is allowed the maximum limit for each drug and strength

Drug	1 Month Limit*	3 Month Limit*
Marinol 2.5 mg, 5 mg, 10 mg (dronabinol capsules)	60 capsules / 25 days	180 capsules / 75 days
Syndros (dronabinol oral solution)	120 mL / 25 days	360 mL / 75 days

**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*

RATIONALE

Marinol and Syndros are indicated in adults for the treatment of anorexia associated with weight loss in patients with Acquired Immune Deficiency Syndrome (AIDS). Marinol and Syndros are also indicated in adults for the treatment of nausea and vomiting associated with cancer chemotherapy in patients who have failed to respond adequately to conventional antiemetic treatments.[1-4]

Anorexia Associated with Weight Loss in Adult Patients with AIDS Dosage

Marinol

The recommended adult starting dosage of Marinol is 2.5 mg orally twice daily, one hour before lunch and dinner. The dosage may be increased gradually to 2.5 mg one hour before lunch and 5 mg one hour before dinner. Increase the dose of Marinol gradually in order to reduce the frequency of dose-related adverse reactions. Most patients respond to 2.5 mg twice daily, but the dose may be further increased to 5 mg one hour before lunch and 5 mg one hour before dinner, as tolerated to achieve a therapeutic effect. Maximum Dosage: 10 mg twice daily.[1]

Syndros
The recommended adult starting dosage of Syndros is 2.1 mg orally twice daily, one hour before lunch and one hour before dinner. The dosage may be increased gradually to 2.1 mg one hour before lunch and 4.2 mg one hour before dinner. Increase the dose of Syndros gradually in order to reduce the frequency of dose-related adverse reactions. Most patients respond to 2.1 mg twice daily, but the dose may be further increased to 4.2 mg one hour before lunch and 4.2 mg one hour before dinner, as tolerated to achieve a therapeutic effect. Maximum Dosage: 8.4 mg twice daily.[2]

Nausea and Vomiting Associated with Cancer Chemotherapy in Adult Patients Who Failed Conventional Antiemetics Dosage
Marinol
The recommended starting dosage of Marinol is 5 mg/m^2, orally administered 1 to 3 hours prior to the administration of chemotherapy and then every 2 to 4 hours after chemotherapy, for a total of 4 to 6 doses per day. The dosage can be titrated to clinical response during a chemotherapy cycle or subsequent cycles, based upon initial response, as tolerated to achieve a clinical effect, in increments of 2.5 mg/m^2. The maximum dosage is 15 mg/m^2 per dose for 4 to 6 doses per day. Adverse reactions are dose-related and psychiatric symptoms increase significantly at the maximum dosage. Monitor patients for adverse reactions and consider decreasing the dose to 2.5 mg once daily 1 to 3 hours prior to chemotherapy to reduce the risk of CNS adverse reactions.[1]
Syndros
The recommended starting dosage of Syndros is 4.2 mg/m^2 orally administered 1 to 3 hours prior to chemotherapy and then every 2 to 4 hours after chemotherapy for a total of 4 to 6 doses per day. The dosage can be titrated to clinical response during a chemotherapy cycle or subsequent cycles, based upon initial effect, as tolerated to achieve a clinical effect, in increments of 2.1 mg/m^2. Maximum Dosage: 12.6 mg/m^2 per dose for 4 to 6 doses per day. Adverse reactions are dose-related and psychiatric symptoms increase significantly at the maximum dosage. Monitor patients for adverse reactions and consider decreasing the dose to 2.1 mg once daily 1 to 3 hours prior to chemotherapy to reduce the risk of CNS adverse reactions.[2]

The initial quantity for Marinol (dronabinol) is set at 60 capsules per month or 180 capsules per 3 months. The initial quantity for Syndros (dronabinol) oral solution is set at 120 milliliters (mL) per month or 360 mL per 3 months. The Marinol and Syndros limits will accommodate the treatment of Acquired Immune Deficiency Syndrome (AIDS) associated weight loss at 20 mg or 16.8 mg per day respectively in divided doses. Also, the Marinol and Syndros limits will accommodate the risk of nausea and vomiting associated with cancer chemotherapy. Per the National Comprehensive Cancer Network (NCCN) Antiemesis Guideline, the risk for nausea and vomiting lasts for at least 3 days for highly emetogenic anticancer agents and 2 days for moderately emetogenic anticancer agents.[5] The limit takes into consideration the NCCN Antiemesis Guideline dosing recommendation of Marinol 5 to 10 mg and Syndros 2.1 to 4.2 mg/m^2 at 3 to 4 times daily for up to 3 days per chemotherapy cycle.[5] The limits will not accumulate to allow for dosage adjustments.

Marinol is available in 2.5 mg, 5 mg, and 10 mg capsules.[1] Syndros is available in a 5 mg/mL solution supplied in a 30 mL multi-dose glass bottle, (unused portion to be discarded 42 days after first opening).[2]

If the patient is requesting more than the initial quantity limit, the claim will reject with a message indicating that a prior authorization is required.

REFERENCES

1. Marinol [package insert]. Parsippany, N J: The Pharma Network, LLC; October 2020.
2. Syndros [package insert]. Round Rock, TX: Benuvia Therapeutics LLC; September 2022.
3. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2022; Accessed November 14, 2022.
4. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed November 11,2022.
5. National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology. Antiemesis. Version 2.2022. Available at: https://www.nccn.org/professionals/physician_gls/pdf/antiemesis.pdf. Accessed November 16, 2022.

Written by:	UM Development (LS)
Date Written:	01/2000
Revised:	(JG) 08/2002; (MG) 07/2003, 10/2004, 09/2005; (NB) 09/2006, 09/2007, 04/2008, 03/2009; (KD) 03/2010; (MS) 04/2011, 02/2012, 01/2013, 01/2014, 01/2015, 01/2016, 07/2016 (added Syndros), 01/2017 (no clinical changes); (KC) 01/2018 (no clinical changes), 01/2019 (no clinical changes); (TM) 01/2020 (no accumulation); (CJM) 01/2021 (no clinical changes), (VLS) 01/2022 (no clinical changes), (TM/KJ) 12/2022 (no clinical changes)
Reviewed:	Medical Affairs: 1/2000, 08/2002, 07/2003; (MM) 10/2004, 09/2005, 09/2006; (WF) 09/2007, 04/2008, 03/2009, 03/2010, (KP) 04/2011, 02/2012; (LS) 01/2013; (DC) 01/2014, 01/2015; (LS) 01/2016; (ME) 07/2016; (LS) 01/2017, (CHART) 01/30/20, 01/28/21, (CHART) 02/03/2022, 12/29/2022 External Review: 08/2003, 11/2004, 02/2006, 02/2007, 02/2008, 08/2008, 08/2009, 08/2010, 08/2011, 04/2012, 06/2013, 04/2014, 04/2015, 04/2016, 04/2017, 04/2018, 04/2019, 04/2020, 04/2021, 04/2022, 04/2023

PRIOR AUTHORIZATION CRITERIA

DRUG CLASS	**DRONABINOL PRODUCTS**
BRAND NAME (generic)	**MARINOL (dronabinol)** **SYNDROS (dronabinol oral solution)**

Status: CVS Caremark Criteria
Type: Post Limit Prior Authorization

POLICY

FDA-APPROVED INDICATIONS
Marinol and Syndros are indicated in adults for the treatment of:
- anorexia associated with weight loss in patients with Acquired Immune Deficiency Syndrome (AIDS).
- nausea and vomiting associated with cancer chemotherapy in patients who have failed to respond adequately to conventional antiemetic treatments.

COVERAGE CRITERIA
The requested drug will be covered with prior authorization when the following criteria are met:
- The requested drug is being prescribed for nausea and vomiting associated with cancer chemotherapy
  AND
- The patient has failed to respond adequately to a conventional antiemetic treatment [Note: Examples of conventional antiemetic treatments include dexamethasone, metoclopramide, olanzapine, prochlorperazine, and 5-HT3 receptor antagonists (e.g., Anzemet [dolasetron], granisetron, ondansetron)]

Quantity Limits apply.
Marinol (dronabinol) 120 capsules per 25 days*, 360 capsules per 75 days* or Syndros (dronabinol) oral solution 240 mL per 25 days *, 720 mL per 75 days*
**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*

REFERENCES

1. Marinol [package insert]. Parsippany, NJ: The Pharma Network LLC; October 2020.
2. Syndros [package insert]. Round Rock, TX: Benuvia Therapeutics LLC; September 2022.
3. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2022; Accessed November 14, 2022.
4. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed November 11, 2022.
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Written by:	UM Development (JG)
Date Written:	08/2002
Revised:	(MG) 07/2003, 10/2004, 09/2005; (NB) 09/2006(2), 09/2007, 04/2008, 03/2009; (KD) 03/2010; (MS) 04/2011, 02/2012, 01/2013, 01/2014, 01/2015, (LN) 04/2015 (Denial Reasons); (MS) 01/2016, 07/2016 (added Syndros), 01/2017; (KC) 01/2018, 01/2019 (no clinical changes), (TM) 01/2020 (revise Q2, no accumulation); (CJM) 01/2021 (no clinical changes); (PM) 08/2021 (updated denial verbiage), (VLS) 01/2022 (no clinical changes), (TM/KJ) 12/2022 (no clinical changes)
Reviewed:	Medical Affairs: 08/2002, 7/2003; (MM) 10/2004, 09/2005, 09/2006; (WF) 09/2007, 04/2008, 03/2009, 03/010; (KP) 04/2011, 02/2012; (LS) 01/2013; (DC) 01/2014, 01/2015; (LS) 01/2016; (ME) 07/2016; (LS) 01/2017, 01/2018, (CHART) 01/30/20, 01/28/21, (CHART) 02/03/2022, 12/29/2022 External Review: 10/2002, 08/2003, 11/2004, 02/2006, 02/2007, 02/2008, 08/2008, 08/2009, 08/2010, 08/2011, 04/2012, 06/2013, 04/2014, 04/2015, 04/2016, 04/2017, 04/2018, 04/2019, 04/2020, 04/2021, 04/2022, 04/2023

Reference number(s)
2020-A

SPECIALTY GUIDELINE MANAGEMENT

NORTHERA (droxidopa)
droxidopa (generic)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Treatment of orthostatic dizziness, lightheadedness, or the “feeling that you are about to black out” in adult patients with symptomatic neurogenic orthostatic hypotension (NOH) caused by primary autonomic failure [Parkinson's disease (PD), multiple system atrophy, and pure autonomic failure], dopamine beta-hydroxylase deficiency, and non-diabetic autonomic neuropathy. Effectiveness beyond 2 weeks of treatment has not been established. The continued effectiveness of Northera should be assessed periodically.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: blood pressure measurements demonstrating a persistent, consistent decrease in systolic blood pressure (SBP) of at least 20 mmHg or decrease in diastolic blood pressure (DBP) of at least 10 mmHg within 3 minutes of standing or head-up tilt test.

III. CRITERIA FOR INITIAL APPROVAL

Neurogenic orthostatic hypotension
Authorization of 3 months may be granted for treatment of neurogenic orthostatic hypotension when all of the following criteria are met:

A. Member has a persistent, consistent decrease in SBP of at least 20 mmHg or decrease in DBP of at least 10 mmHg within 3 minutes of standing or head-up tilt test.
B. Member has neurogenic orthostatic hypotension due to **ONE** of the following diagnoses:
    1. Primary autonomic failure due to Parkinson’s disease, multiple system atrophy, or pure autonomic failure, OR
    2. Dopamine beta hydroxylase deficiency, OR
    3. Non-diabetic autonomic neuropathy

IV. CONTINUATION OF THERAPY

Neurogenic orthostatic hypotension
Authorization of 6 months may be granted for treatment of neurogenic orthostatic hypotension when all of the following criteria are met:

A. Member has experienced a sustained decrease in dizziness
B. Member has neurogenic orthostatic hypotension due to **ONE** of the following diagnoses:
    1. Primary autonomic failure due to Parkinson's disease, multiple system atrophy, or pure autonomic failure, OR
    2. Dopamine beta hydroxylase deficiency, OR
    3. Non-diabetic autonomic neuropathy

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Reference number(s)
1690-A

SPECIALTY GUIDELINE MANAGEMENT

DUPIXENT (dupilumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

A. Dupixent is indicated for the treatment of patients aged 6 months and older with moderate-to-severe atopic dermatitis whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable. Dupixent can be used with or without topical corticosteroids.
B. Dupixent is indicated as an add-on maintenance treatment in patients with moderate-to-severe asthma aged 6 years and older with an eosinophilic phenotype or with oral corticosteroid dependent asthma.
C. Dupixent is indicated as an add-on maintenance treatment in adult patients with inadequately controlled chronic rhinosinusitis with nasal polyposis (CRSwNP).
D. Dupixent is indicated for the treatment of adult and pediatric patients aged 12 years and older, weighing at least 40 kg, with eosinophilic esophagitis (EoE).
E. Dupixent is indicated for the treatment of adult patients with prurigo nodularis (PN).

Limitation of Use: Dupixent is not indicated for the relief of acute bronchospasm or status asthmaticus

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

A. Atopic dermatitis (for initial requests): Member's chart or medical record showing prerequisite therapies (see section IV.A.2). If therapy is not advisable, documentation of clinical reason to avoid therapy.

B. Asthma

1. For initial requests:
   i. Member's chart or medical record showing pretreatment blood eosinophil count (where applicable)
   ii. Chart notes, medical record documentation, or claims history supporting previous medications tried including drug, dose, frequency, and duration.
2. For continuation requests: Chart notes or medical record documentation supporting improvement in asthma control.

C. Chronic rhinosinusitis with nasal polyposis

1. For initial requests:
   i. Member's chart or medical record showing nasal endoscopy, anterior rhinoscopy, or computed tomography (CT) details (e.g., location, size), or Meltzer Clinical Score or endoscopic nasal polyp score (NPS) (where applicable).
   ii. Chart notes, medical record documentation, or claims history supporting previous medications tried. If therapy is not advisable, documentation of clinical reason to avoid therapy.

2. For continuation requests: Chart notes or medical record documentation supporting positive clinical response.

D. Eosinophilic esophagitis

1. For initial requests:
   i. Member's chart or medical record showing endoscopic biopsy details including intraepithelial esophageal eosinophil count.
   ii. Chart notes, medical record documentation, or claims history supporting previous medications tried. If therapy is not advisable, documentation of clinical reason to avoid therapy.
2. For continuation requests: Chart notes or medical record documentation supporting positive clinical response.

E. Prurigo Nodularis

1. For initial requests:
   i. Member's chart or medical record of symptoms (e.g., pruritus, nodular lesions).
   ii. Member's chart, medical record, or claims history of prerequisite therapies including response to therapy. If therapy is not advisable, documentation of clinical reason to avoid therapy.
2. For continuation requests: Chart notes or medical record documentation supporting positive clinical response.

III. PRESCIBER SPECIALTIES

This medication must be prescribed by or in consultation with one of the following:

A. Atopic dermatitis: dermatologist or allergist/immunologist
B. Asthma: allergist/immunologist or pulmonologist
C. Chronic rhinosinusitis with nasal polyposis: allergist/immunologist or otolaryngologist
D. Eosinophilic esophagitis: gastroenterologist or allergist/immunologist
E. Prurigo nodularis: dermatologist or allergist/immunologist

IV. CRITERIA FOR INITIAL APPROVAL

A. Moderate-to-severe atopic dermatitis

Authorization of 4 months may be granted for treatment of moderate-to-severe atopic dermatitis in members 6 months of age or older when all of the following criteria are met:

1. Affected body surface is greater than or equal to 10% body surface area OR crucial body areas (e.g., hands, feet, face, neck, scalp, genitals/groin, intertriginous areas) are affected.
2. Member meets one of the following:
   i. Member has had an inadequate treatment response to one of the following in the past 180 days:
      a. A high potency or super-high potency topical corticosteroid (see Appendix A)
      b. A topical calcineurin inhibitor
   ii. The use of high potency or super-high potency topical corticosteroids and topical calcineurin inhibitors are not advisable for the member (e.g., due to contraindications, prior intolerances, potency not appropriate for member's age)

B. Asthma

Authorization of 6 months may be granted for treatment of asthma in members 6 years of age or older when all of the following criteria are met:

1. Member as uncontrolled asthma as demonstrated by experiencing at least one of the following within the past year:
   i. Two or more asthma exacerbations requiring oral or injectable corticosteroid treatment.

ii. One or more asthma exacerbation resulting in hospitalization or emergency medical care visit.
iii. Poor symptom control (frequent symptoms or reliever use, activity limited by asthma, night waking due to asthma).

2. Member meets one of the following criteria:
   i. Member has a baseline blood eosinophil count of at least 150 cells per microliter and inadequate asthma control despite current treatment with both of the following medications at optimized doses:
      a. Medium-to-high-dose inhaled corticosteroid
      b. Additional controller (i.e., long acting beta2-agonist, long acting muscarinic antagonist, leukotriene modifier, or sustained-release theophylline)
   ii. Member has inadequate asthma control despite current treatment with all of the following medications at optimized doses*:
      a. High-dose inhaled corticosteroid
      b. Additional controller (i.e., long acting beta2-agonist, long acting muscarinic antagonist, leukotriene modifier, or sustained-release theophylline)
      c. Oral glucocorticoids (at least 5 mg per day of prednisone/prednisolone or equivalent)
      *Members should be receiving treatment with inhaled corticosteroid and additional controller for at least the previous 3 months, and oral glucocorticoids for most days during the previous 6 months (e.g. 50% of days, 3 steroid bursts in the previous 6 months).[6]
3. Member will continue to use maintenance asthma treatments (e.g., inhaled corticosteroid, additional controller) in combination with Dupixent.

C. Chronic rhinosinusitis with nasal polyposis (CRSwNP)

Authorization of 6 months may be granted for treatment of CRSwNP in members 18 years of age or older when all of the following criteria are met:

1. Member has bilateral nasal polyposis and chronic symptoms of sinusitis despite intranasal corticosteroid treatment for at least 2 months unless contraindicated or not tolerated; and
2. The member has CRSwNP despite one of the following:
   i. Prior sino-nasal surgery; or
   ii. Prior treatment with systemic corticosteroids within the last two years was ineffective, unless contraindicated or not tolerated; and
3. Member has one of the following:
   i. A bilateral nasal endoscopy, anterior rhinoscopy, or computed tomography (CT) showing polyps reaching below the lower border of the middle turbinate or beyond in each nostril
   ii. Meltzer Clinical Score of 2 or higher in both nostrils
   iii. A total endoscopic nasal polyp score (NPS) of at least 5 with a minimum score of 2 for each nostril
4. Member has nasal blockage plus one additional symptom:
   i. Rhinorrhea (anterior/posterior); or
   ii. Reduction or loss of smell; or
   iii. Facial pain or pressure
5. Member will continue to use a daily intranasal corticosteroid while being treated with Dupixent, unless contraindicated or not tolerated.

D. Eosinophilic esophagitis (EoE)

Authorization of 6 months may be granted for treatment of EoE in members 12 years of age or older, weighing at least 40 kg, when all of the following criteria are met:

1. Member has history of an average of at least 2 episodes of dysphagia (with intake of solids) per week.
2. Diagnosis has been confirmed by esophageal biopsy as characterized by 15 or more intraepithelial esophageal eosinophils per high power field.
3. Member has had an inadequate treatment response to both of the following:
   i. Proton pump inhibitor

ii. Systemic corticosteroid or local therapies (e.g., budesonide, fluticasone [powder or suspension for inhalation] swallowed), unless contraindicated or not tolerated.

E. Prurigo Nodularis

Authorization of 6 months may be granted for treatment of prurigo nodularis in members 18 years of age or older when all of the following criteria are met:

1. Member must have pruritus lasting at least 6 weeks.
2. Member has history or signs of repeated itch-scratch cycle (e.g., scratching, picking, or rubbing).
3. Member must have a minimum of 20 nodular lesions.
4. Member meets one of the following:
   i. Member has had an inadequate response to one of the following:
      a. A medium to super-high potency topical corticosteroid (see Appendix A)
      b. A topical calcineurin inhibitor
      c. Phototherapy (e.g., UVB, PUVA)
      d. Pharmacologic treatment with methotrexate or cyclosporine
   ii. Member has had an intolerance or a clinical reason to avoid any of the following:
      a. Medium to super-high potency topical corticosteroid (see Appendix A) and topical calcineurin inhibitor
      b. Pharmacologic treatment with methotrexate and cyclosporine (see Appendix B)

V. CONTINUATION OF THERAPY

A. Moderate-to-severe atopic dermatitis

Authorization of 12 months may be granted for members 6 months of age or older who are using the requested medication for moderate-to-severe atopic dermatitis when the member has achieved or maintained positive clinical response with Dupixent therapy as evidenced by low disease activity (i.e., clear or almost clear skin), or improvement in signs and symptoms of atopic dermatitis (e.g., redness, itching, oozing/crusting).

B. Asthma

Authorization of 12 months may be granted for continuation of treatment of asthma in members 6 years of age or older when all of the following criteria are met:

1. Asthma control has improved on Dupixent treatment as demonstrated by at least one of the following:
   i. A reduction in the frequency and/or severity of symptoms and exacerbations
   ii. A reduction in the daily maintenance oral corticosteroid dose
2. Member will continue to use maintenance asthma treatments (e.g., inhaled corticosteroid, additional controller) in combination with Dupixent.

C. Chronic rhinosinusitis with nasal polyposis (CRSwNP)

Authorization of 12 months may be granted for continuation of treatment of chronic rhinosinusitis with nasal polyposis when all of the following are met:

1. Member is 18 years of age or older.
2. Member has achieved or maintained positive clinical response to Dupixent therapy as evidenced by improvement in signs and symptoms of CRSwNP (e.g., improvement in nasal congestion, nasal polyp size, loss of smell, anterior or posterior rhinorrhea, sinonasal inflammation, hyposmia and/or facial pressure or pain or reduction in corticosteroid use).

D. Eosinophilic Esophagitis

Authorization of 12 months may be granted for continuation of treatment of eosinophilic esophagitis in members 12 years of age or older, weighing at least 40 kg, when member has achieved or maintained

positive clinical response with Dupixent therapy as evidenced by improvement in signs and symptoms of eosinophilic esophagitis (e.g., dysphagia, heartburn, chest pain, emesis).

E. Prurigo Nodularis

Authorization of 12 months may be granted for members 18 years of age or older who are using Dupixent for prurigo nodularis when the member has achieved or maintained positive clinical response with Dupixent therapy as evidenced by one of the following:

1. Low disease activity (i.e., clear or almost clear skin).
2. Reduction in pruritis intensity and improvement in extent and severity of nodular lesions.

VI. OTHER

For all indications: Member cannot use Dupixent concomitantly with any other biologic drug or targeted synthetic drug.

Note: If the member is a current smoker or vaper, they should be counseled on the harmful effects of smoking and vaping on pulmonary conditions and available smoking and vaping cessation options.

VII. APPENDICES

Appendix A: Table. Relative potency of select topical corticosteroid products

Potency	Drug	Dosage form	Strength
I. Super-high potency (group 1)	Augmented betamethasone dipropionate	Ointment, Lotion, Gel	0.05%
	Clobetasol propionate	Cream, Gel, Ointment, Solution, Cream (emollient), Lotion, Shampoo, Foam, Spray	0.05%
	Fluocinonide	Cream	0.1%
	Flurandrenolide	Tape	4 mcg/cm^2
	Halobetasol propionate	Cream, Lotion, Ointment, Foam	0.05%
II. High potency (group 2)	Amcinonide	Ointment	0.1%
	Augmented betamethasone dipropionate	Cream	0.05%
	Betamethasone dipropionate	Ointment	0.05%
	Clobetasol propionate	Cream	0.025%
	Desoximetasone	Cream, Ointment, Spray	0.25%
		Gel	0.05%
	Diflorasone diacetate	Ointment, Cream (emollient)	0.05%
	Fluocinonide	Cream, Ointment, Gel, Solution	0.05%
	Halcinonide	Cream, Ointment	0.1%
	Halobetasol propionate	Lotion	0.01%
Potency	**Drug**	**Dosage form**	**Strength**
III. High potency (group 3)	Amcinonide	Cream, Lotion	0.1%
	Betamethasone dipropionate	Cream, hydrophilic emollient	0.05%
	Betamethasone valerate	Ointment	0.1%
		Foam	0.12%
	Desoximetasone	Cream, Ointment	0.05%
	Diflorasone diacetate	Cream	0.05%

Potency	Drug	Dosage form	Strength
	Fluocinonide	Cream, aqueous emollient	0.05%
	Fluticasone propionate	Ointment	0.005%
	Mometasone furoate	Ointment	0.1%
	Triamcinolone acetonide	Cream, Ointment	0.5%
IV. Medium potency (group 4)	Betamethasone dipropionate	Spray	0.05%
	Clocortolone pivalate	Cream	0.1%
	Fluocinolone acetonide	Ointment	0.025%
	Flurandrenolide	Ointment	0.05%
	Hydrocortisone valerate	Ointment	0.2%
	Mometasone furoate	Cream, Lotion, Solution	0.1%
	Triamcinolone acetonide	Cream	0.1%
		Ointment	0.05% and 0.1%
		Aerosol Spray	0.2 mg per 2-second spray
V. Lower-mid potency (group 5)	Betamethasone dipropionate	Lotion	0.05%
	Betamethasone valerate	Cream	0.1%
	Desonide	Ointment, Gel	0.05%
	Fluocinolone acetonide	Cream	0.025%
	Flurandrenolide	Cream, Lotion	0.05%
	Fluticasone propionate	Cream, Lotion	0.05%
	Hydrocortisone butyrate	Cream, Lotion, Ointment, Solution	0.1%
	Hydrocortisone probutate	Cream	0.1%
	Hydrocortisone valerate	Cream	0.2%
	Prednicarbate	Cream (emollient), Ointment	0.1%
	Triamcinolone acetonide	Lotion	0.1%
		Ointment	0.025%
VI. Low potency (group 6)	Alclometasone dipropionate	Cream, Ointment	0.05%
	Betamethasone valerate	Lotion	0.1%
	Desonide	Cream, Lotion, Foam	0.05%
	Fluocinolone acetonide	Cream, Solution, Shampoo, Oil	0.01%
	Triamcinolone acetonide	Cream, lotion	0.025%
VII. Least potent (group 7)	Hydrocortisone (base, less than 2%)	Cream, Ointment, Solution	2.5%
		Lotion	2%
		Cream, Ointment, Gel, Lotion, Spray, Solution	1%
		Cream, Ointment	0.5%
	Hydrocortisone acetate	Cream	2.5%
		Lotion	2%
		Cream	1%

Appendix B: Examples of Clinical Reasons to Avoid Pharmacologic Treatment with Methotrexate or Cyclosporine

1. Clinical diagnosis of alcohol use disorder, alcoholic liver disease or other chronic liver disease
2. Breastfeeding

3. Drug interaction
4. Cannot be used due to risk of treatment-related toxicity
5. Pregnancy or currently planning pregnancy
6. Significant comorbidity prohibits use of systemic agents (examples include liver or kidney disease, blood dyscrasias, uncontrolled hypertension)

VIII. REFERENCES

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Reference number(s)
1743-A

ENHANCED SPECIALTY GUIDELINE MANAGEMENT

DUPIXENT (dupilumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

A. Dupixent is indicated for the treatment of patients aged 6 months and older with moderate-to-severe atopic dermatitis whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable. Dupixent can be used with or without topical corticosteroids.
B. Dupixent is indicated as an add-on maintenance treatment in patients with moderate-to-severe asthma aged 6 years and older with an eosinophilic phenotype or with oral corticosteroid dependent asthma.
C. Dupixent is indicated as an add-on maintenance treatment in adult patients with inadequately controlled chronic rhinosinusitis with nasal polyposis (CRSwNP).
D. Dupixent is indicated for the treatment of adult and pediatric patients aged 12 years and older, weighing at least 40 kg, with eosinophilic esophagitis (EoE).

Limitation of Use: Dupixent is not indicated for the relief of acute bronchospasm or status asthmaticus

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

A. Atopic dermatitis

1. Initial requests:
   i. Member's chart notes or medical records showing affected area(s) and body surface area (see section IV.A.1).
   ii. Member's chart notes or medical record documentation and claims history of prerequisite therapies (including topical calcineurin inhibitors and topical corticosteroids) (see section IV.A.2) including dosage, duration, and response to therapy. If prerequisite therapy is not advisable, documentation of why topical calcineurin inhibitors and/or topical corticosteroids are not advisable for the member.
2. Continuation requests: Documentation (e.g., chart notes) that the member has experienced a positive clinical response to therapy as evidenced by low disease activity or improvement in signs or symptoms of atopic dermatitis.

B. Asthma

1. Initial requests:
   i. Member's chart or medical record showing pretreatment blood eosinophil count (where applicable).
   ii. Chart notes, medical record documentation, or claims history supporting previous medications tried including drug, dose, frequency, and duration.

2. Continuation requests: Chart notes or medical record documentation of positive clinical response.

C. Chronic rhinosinusitis with nasal polyposis

1. Initial requests:
   i. Member's chart or medical record showing nasal endoscopy, anterior rhinoscopy details, or computed tomography (CT) (e.g., location, size), or Meltzer Clinical Score or endoscopic nasal polyps score (NPS) (where applicable).
   ii. Chart notes, medical record documentation, or claims history supporting previous medications tried. If therapy is not advisable, documentation of clinical reason to avoid therapy.
2. Continuation requests: Chart notes or medical record documentation of positive clinical response.

D. Eosinophilic esophagitis

1. For initial requests:
   i. Member's chart or medical record showing endoscopic biopsy details including intraepithelial esophageal eosinophil count.
   ii. Chart notes, medical record documentation, or claims history supporting previous medications tried. If therapy is not advisable, documentation of clinical reason to avoid therapy.
2. For continuation requests: Chart notes or medical record documentation supporting positive clinical response.

III. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with one of the following:

A. Atopic dermatitis: dermatologist or allergist/immunologist
B. Asthma: allergist/immunologist or pulmonologist
C. Chronic rhinosinusitis with nasal polyposis: allergist/immunologist or otolaryngologist
D. Eosinophilic esophagitis: gastroenterologist or allergist/immunologist

IV. CRITERIA FOR INITIAL APPROVAL

A. Moderate-to-severe atopic dermatitis

Authorization of 4 months may be granted for treatment of moderate-to-severe atopic dermatitis in members 6 months of age or older when all of the following criteria are met:

1. Affected body surface area is greater than or equal to 10% OR crucial body areas (e.g., hands, feet, face, neck, scalp, genitals/groin, intertriginous areas) are affected.
2. Member has had an inadequate treatment response to both of the following in the past 180 days:
   i. A high potency or super-high potency topical corticosteroid (see Appendix), or the use of topical corticosteroids is not advisable for the member (e.g., due to contraindications, prior intolerances, potency not appropriate for member's age)
   ii. A topical calcineurin inhibitor, or the use of topical calcineurin inhibitors is not advisable for the member (e.g., due to contraindications or prior intolerances).
3. Member's dose will not exceed the following:
   i. Pediatric members (6 months to 5 years of age) 5 kg to less than 15 kg: 200 mg every 4 weeks
   ii. Pediatric members (6 months to 5 years of age) 15 kg to less than 30 kg: 300 mg every 4 weeks
   iii. Pediatric members (6 to 17 years of age) 15 kg to less than 30 kg: Initial 600 mg dose followed by 300 mg every 4 weeks
   iv. Pediatric members (6 to 17 years of age) 30 kg to less than 60 kg: Initial 400 mg dose followed by 200 mg every other week

v. Pediatric members (6 to 17 years of age) 60 kg or more: Initial 600 mg dose followed by 300 mg every other week
vi. Adult members: Initial 600 mg dose followed by 300 mg every other week

B. Moderate-to-severe asthma

Authorization of 6 months may be granted for treatment of moderate-to-severe asthma in members 6 years of age or older when all of the following criteria are met:

1. Member as uncontrolled asthma as demonstrated by experiencing at least one of the following within the past year:
   i. Two or more asthma exacerbations requiring oral or injectable corticosteroid treatment.
   ii. One or more asthma exacerbation resulting in hospitalization or emergency medical care visit.
   iii. Poor symptom control (frequent symptoms or reliever use, activity limited by asthma, night waking due to asthma).
2. Member meets one of the following criteria:
   i. Member has a baseline blood eosinophil count of at least 150 cells per microliter and asthma is inadequately controlled despite treatment for at least 3 months with both of the following at optimized doses:
      a. Medium-to-high-dose inhaled corticosteroid
         1. Adult and adolescent members (12 years age and older): greater than 250 microgram total daily dose of fluticasone propionate or equivalent
         2. Pediatric members (6 to 11 years of age): greater than 100 microgram total daily dose of fluticasone propionate or equivalent
      b. Additional controller (i.e., long acting beta2-agonist, long acting muscarinic antagonist, leukotriene modifier, or sustained-release theophylline)
   ii. Member has inadequate asthma control despite current treatment with all of the following medications at optimized doses*:
      a. High-dose inhaled corticosteroid
         1. Adult and adolescent members (12 years of age and older): greater than 500 microgram total daily dose of fluticasone propionate or equivalent
         2. Pediatric members (6 to 11 years of age): greater than 200 microgram total daily dose of fluticasone propionate or equivalent
      b. Additional controller (i.e., long acting $beta_2$-agonist, long acting muscarinic antagonist, leukotriene modifier, or sustained-release theophylline)
      c. Oral glucocorticoids (at least 5 mg per day of prednisone/prednisolone or equivalent)

      *Members should be receiving treatment with inhaled corticosteroid and additional controller for at least the previous 3 months, and oral glucocorticoids for most days during the previous 6 months (e.g., 50% of days, 3 steroid bursts in the previous 6 months)[10].
3. Member will continue to use maintenance asthma treatments (e.g., inhaled corticosteroid, additional controller) in combination with Dupixent.
4. Member's dose will not exceed the following:
   i. Adult and adolescent members (12 years of age and older): Initial dose 600 mg followed by 300 mg every other week or initial dose 400 mg followed by 200 mg every other week
   ii. Adult adolescent members (12 years of age and older) with co-morbid moderate-to-severe atopic dermatitis: initial dose 600 mg followed by 300 mg every other week
   iii. Pediatric members (6 to 11 years of age) 15 to less than 30 kg: 100 mg every other week or 300 mg every four weeks
   iv. Pediatric members (6 to 11 years of age) ≥ 30 kg: 200 mg every other week
   v. Pediatric members (6 to 11 years of age) with co-morbid moderate-to-severe atopic dermatitis:
      a. 15 kg to less than 30 kg: Initial 600 mg dose followed by 300 mg every 4 weeks
      b. 30 kg to less than 60 kg: Initial 400 mg dose followed by 200 mg every other week

c. 60 kg or more: Initial 600 mg dose followed by 300 mg every other week

C. Chronic rhinosinusitis with nasal polyposis (CRSwNP)

Authorization of 6 months may be granted for treatment of CRSwNP in members 18 years of age or older when all of the following criteria are met:

1. Member has bilateral nasal polyposis and chronic symptoms of sinusitis despite intranasal corticosteroid treatment for at least 2 months unless contraindicated or not tolerated; and
2. The member has CRSwNP despite one of the following:
   i. Prior sino-nasal surgery; or
   ii. Prior treatment with systemic corticosteroids within the last two years was ineffective, unless contraindicated or not tolerated; and
3. Member has one of the following:
   i. A bilateral nasal endoscopy, anterior rhinoscopy, or computed tomography (CT) showing polyps reaching below the lower border of the middle turbinate or beyond in each nostril
   ii. Meltzer Clinical Score of 2 or higher in both nostrils
   iii. A total endoscopic nasal polyp score (NPS) of at least 5 with a minimum score of 2 for each nostril
4. Member has nasal blockage plus one additional symptom:
   i. Rhinorrhea (anterior/posterior); or
   ii. Reduction or loss of smell; or
   iii. Facial pain or pressure
5. Member will continue to use a daily intranasal corticosteroid while being treated with Dupixent, unless contraindicated or not tolerated.
6. Member's dose will not exceed the following:
   i. 300 mg every other week
   ii. Members with co-morbid moderate-to-severe asthma: initial dose of 600 mg followed by 300 mg every other week

D. Eosinophilic esophagitis (EoE)

Authorization of 6 months may be granted for treatment of EoE in members 12 years of age or older, weighing at least 40 kg, when all of the following criteria are met:

1. Member has history of an average of at least 2 episodes of dysphagia (with intake of solids) per week
2. Diagnosis has been confirmed by esophageal biopsy as characterized by 15 or more intraepithelial esophageal eosinophils per high power field
3. Member has had an inadequate treatment response to both of the following:
   i. Proton pump inhibitor
   ii. Systemic corticosteroid or local therapies (e.g., budesonide, fluticasone [powder or suspension for inhalation] swallowed), unless contraindicated or not tolerated.
4. Member's dose will not exceed 300 mg every week

V. CONTINUATION OF THERAPY

A. Moderate-to-severe atopic dermatitis

Authorization of 6 months may be granted for members 6 months of age or older when all of the following criteria is met:

1. Member has achieved or maintained positive clinical response with Dupixent therapy for moderate-to-severe atopic dermatitis as evidenced by low disease activity (i.e., clear or almost clear skin) or improvement in signs and symptoms of atopic dermatitis (e.g., redness, itching, oozing/crusting).
2. Member's dose will not exceed the following:

i. Pediatric members (6 months to 5 years of age) 5 kg to less than 15 kg: 200 mg every 4 weeks
ii. Pediatric members (6 months to 5 years of age) 15 kg to less than 30 kg: 300 mg every 4 weeks
iii. Pediatric members (6 to 17 years of age) 15 kg to less than 30 kg: Initial 600 mg dose followed by 300 mg every 4 weeks
iv. Pediatric members (6 to 17 years of age) 30 kg to less than 60 kg: Initial 400 mg dose followed by 200 mg every other week
v. Pediatric members (6 to 17 years of age) 60 kg or more: Initial 600 mg dose followed by 300 mg every other week
vi. Adult members: Initial 600 mg dose followed by 300 mg every other week

B. Moderate-to-severe asthma

Authorization of 12 months may be granted for continuation of treatment of moderate-to-severe asthma in members 6 years of age or older when all of the following criteria are met:

1. Member has achieved and maintained positive clinical response with Dupixent therapy for asthma as evidenced by at least one of the following:
   i. A reduction in the frequency and/or severity of symptoms and exacerbations
   ii. A reduction in the daily maintenance oral corticosteroid dose
2. Member will continue to use maintenance asthma treatments (e.g., inhaled corticosteroid, additional controller) in combination with Dupixent.
3. Member's dose will not exceed the following:
   i. Adult and adolescent members (12 years of age and older): Initial dose of 600 mg followed by 300 mg every other week or initial dose of 400 mg followed by 200 mg every other week
   ii. Adult and adolescent members (12 years of age and older) with co-morbid moderate-to-severe atopic dermatitis: initial dose 600 mg followed by 300 mg every other week
   iii. Pediatric members (6 to 11 years of age) 15 to less than 30 kg: 100 mg every other week or 300 mg every four weeks
   iv. Pediatric members (6 to 11 years of age): ≥ 30 kg: 200 mg every other week
   v. Pediatric members (6 to 11 years of age) with co-morbid moderate-to-severe atopic dermatitis
      a. 15 kg to less than 30 kg: Initial 600 mg dose followed by 300 mg every 4 weeks
      b. 30 kg to less than 60 kg: Initial 400 mg dose followed by 200 mg every other week
      c. 60 kg or more: Initial 600 mg dose followed by 300 mg every other week

C. Chronic rhinosinusitis with nasal polyposis (CRSwNP)

Authorization of 12 months may be granted for continuation of treatment of chronic rhinosinusitis with nasal polyposis in members 18 years of age or older when all of the following are met:

1. Member has achieved or maintained positive clinical response to Dupixent therapy as evidenced by improvement in signs and symptoms of CRSwNP (e.g., improvement in nasal congestion, nasal polyp size, loss of smell, anterior or posterior rhinorrhea, sinonasal inflammation, hyposmia and/or facial pressure or pain or reduction in corticosteroid use)
2. Member's dose will not exceed the following:
   i. 300 mg every other week
   ii. Members with co-morbid moderate-to-severe asthma: initial dose 600 mg followed by 300 mg every other week

D. Eosinophilic Esophagitis

Authorization of 12 months may be granted for continuation of treatment of eosinophilic esophagitis in members 12 years of age or older, weighing at least 40 kg, when all of the following are met:

1. Member has achieved or maintained positive clinical response with Dupixent therapy as evidenced by improvement in signs and symptoms of eosinophilic esophagitis (e.g., dysphagia, heartburn, chest pain, emesis).

2. Member will not exceed 300 mg every week

VI. OTHER

For all indications: Member cannot use Dupixent concomitantly with any other biologic drug or targeted synthetic drug.

Note: If the member is a current smoker or vaper, they should be counseled on the harmful effects of smoking and vaping on pulmonary conditions and available smoking and vaping cessation options.

VII. APPENDIX

Table. Relative potency of select topical corticosteroid products

Potency	**Drug**	**Dosage form**	**Strength**
I. Super-high potency (group 1)	Augmented betamethasone dipropionate	Ointment, Lotion, Gel	0.05%
	Clobetasol propionate	Cream, Gel, Ointment, Solution, Cream (emollient), Lotion, Shampoo, Foam, Spray	0.05%
	Fluocinonide	Cream	0.1%
	Flurandrenolide	Tape	4 mcg/cm^2
	Halobetasol propionate	Cream, Lotion, Ointment, Foam	0.05%
II. High potency (group 2)	Amcinonide	Ointment	0.1%
	Augmented betamethasone dipropionate	Cream	0.05%
	Betamethasone dipropionate	Ointment	0.05%
	Clobetasol propionate	Cream	0.025%
	Desoximetasone	Cream, Ointment, Spray	0.25%
		Gel	0.05%
	Diflorasone diacetate	Ointment, Cream (emollient)	0.05%
	Fluocinonide	Cream, Ointment, Gel, Solution	0.05%
	Halcinonide	Cream, Ointment	0.1%
	Halobetasol propionate	Lotion	0.01%
Potency	**Drug**	**Dosage form**	**Strength**
III. High potency (group 3)	Amcinonide	Cream, Lotion	0.1%
	Betamethasone dipropionate	Cream, hydrophilic emollient	0.05%
	Betamethasone valerate	Ointment	0.1%
		Foam	0.12%
	Desoximetasone	Cream, Ointment	0.05%
	Diflorasone diacetate	Cream	0.05%
	Fluocinonide	Cream, aqueous emollient	0.05%
	Fluticasone propionate	Ointment	0.005%
	Mometasone furoate	Ointment	0.1%
	Triamcinolone acetonide	Cream, Ointment	0.5%
	Betamethasone dipropionate	Spray	0.05%

Potency	Drug	Dosage form	Strength
	Clocortolone pivalate	Cream	0.1%
	Fluocinolone acetonide	Ointment	0.025%
	Flurandrenolide	Ointment	0.05%
IV. Medium potency (group 4)	Hydrocortisone valerate	Ointment	0.2%
	Mometasone furoate	Cream, Lotion, Solution	0.1%
	Triamcinolone acetonide	Cream	0.1%
		Ointment	0.05% and 0.1%
		Aerosol Spray	0.2 mg per 2-second spray
V. Lower-mid potency (group 5)	Betamethasone dipropionate	Lotion	0.05%
	Betamethasone valerate	Cream	0.1%
	Desonide	Ointment, Gel	0.05%
	Fluocinolone acetonide	Cream	0.025%
	Flurandrenolide	Cream, Lotion	0.05%
	Fluticasone propionate	Cream, Lotion	0.05%
	Hydrocortisone butyrate	Cream, Lotion, Ointment, Solution	0.1%
	Hydrocortisone probutate	Cream	0.1%
	Hydrocortisone valerate	Cream	0.2%
	Prednicarbate	Cream (emollient), Ointment	0.1%
	Triamcinolone acetonide	Lotion	0.1%
		Ointment	0.025%
VI. Low potency (group 6)	Alclometasone dipropionate	Cream, Ointment	0.05%
	Betamethasone valerate	Lotion	0.1%
	Desonide	Cream, Lotion, Foam	0.05%
	Fluocinolone acetonide	Cream, Solution, Shampoo, Oil	0.01%
	Triamcinolone acetonide	Cream, lotion	0.025%
VII. Least potent (group 7)	Hydrocortisone (base, less than 2%)	Cream, Ointment, Solution	2.5%
		Lotion	2%
		Cream, Ointment, Gel, Lotion, Spray, Solution	1%
		Cream, Ointment	0.5%
	Hydrocortisone acetate	Cream	2.5%
		Lotion	2%
		Cream	1%

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DOCUMENT HISTORY

Created:	Specialty Clinical Development (IP) 04/2017
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	(label update-asthma age, duplicate indication dosing), CNg 01/2022 (derm annual + AD-no concomitant use with biologics/JAK), CNg 03/2022 (asthma annual-uncontrolled asthma, LAMA; CRSwNP: no concomitant biologic, align with Nucala), CNg 05/2022 (label update- eos esophagitis), CNg 06/2022 (label update-AD age 6 mo & up, AD 3 topical steps to 2, add CT/Meltzer score/NPS to CRSwNP)
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External Review:	04/2017, 02/2018, 12/2018, 01/2019, 05/2019, 01/2020, 05/2020, 12/2020, 05/2021, 11/2021, 12/2021, 02/2022. 05/2022, 06/2022 (P&T SG only)

QUANTITY LIMIT CRITERIA

DRUG CLASS	**ERECTILE DYSFUNCTION - BPH DRUGS**
BRAND NAME* **(generic)**	
ALPROSTADILS:	
	CAVERJECT **(alprostadil)**
	EDEX **(alprostadil)**
	MUSE **(alprostadil)**
PHOSPHODIESTERASE TYPE 5 (PDE-5) INHIBITORS:	
	CIALIS **(tadalafil)**
	LEVITRA **(vardenafil hydrochloride)**
	STAXYN **(vardenafil hydrochloride orally disintegrating)**
	STENDRA **(avanafil)**
	VIAGRA **(sildenafil)**
Status: CVS Caremark Criteria	
Type: Quantity Limit	***Ref # 84-H***

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATION

ALPROSTADILS

Caverject

Caverject is indicated for the treatment of erectile dysfunction.
Caverject is also indicated as an adjunct to other diagnostic tests in the diagnosis of erectile dysfunction.

Edex

Edex is indicated for the treatment of erectile dysfunction due to neurogenic, vasculogenic, psychogenic, or mixed etiology.

MUSE
MUSE is indicated for the treatment of erectile dysfunction. Studies that established benefit demonstrated improvements in success rates for sexual intercourse compared with similarly administered placebo.

PHOSPHODIESTERASE TYPE 5 (PDE-5) INHIBITORS
Cialis
Erectile Dysfunction
Cialis is indicated for the treatment of erectile dysfunction (ED).
Benign Prostatic Hyperplasia
Cialis is indicated for the treatment of the signs and symptoms of benign prostatic hyperplasia (BPH).
Erectile Dysfunction and Benign Prostatic Hyperplasia
Cialis is indicated for the treatment of ED and the signs and symptoms of BPH (ED/BPH).
Limitation of Use
If Cialis is used with finasteride to initiate BPH treatment, such use is recommended for up to 26 weeks because the incremental benefit of Cialis decreases from 4 weeks until 26 weeks, and the incremental benefit of Cialis beyond 26 weeks is unknown.

Levitra
Levitra is indicated for the treatment of erectile dysfunction.

Staxyn
Staxyn is indicated for the treatment of erectile dysfunction.

Stendra
Stendra is a phosphodiesterase 5 (PDE5) inhibitor indicated for the treatment of erectile dysfunction.

Viagra
Viagra is indicated for the treatment of erectile dysfunction.

RATIONALE
Alprostadil and Phosphodiesterase type 5 (PDE-5) Inhibitors [Caverject (alprostadil), Edex (alprostadil), MUSE (alprostadil), Cialis (tadalafil), Levitra (vardenafil hydrochloride), Staxyn (vardenafil hydrochloride orally disintegrating), Stendra (avanafil), Viagra (sildenafil)] are indicated for the treatment of erectile dysfunction (ED). Cialis is also indicated for the treatment of the signs and symptoms of benign prostatic hyperplasia (BPH), and for the treatment of ED and the signs and symptoms of BPH (ED/BPH).[1-11]

Since erectile dysfunction drugs are used as needed (excluding Cialis 2.5 mg and 5 mg), the quantity limits are based upon coital frequency from studies of data analysis. According to the Predictors of Adult Sexual Activity in The United States survey, men and women between the ages of 25 and 45 have sex a mean 5.7 and 6.4 times per month, respectively.[13] A Study of Sexuality and Health among Older Adults in the United States found that the prevalence of sexual activity declined with age and that 54% of sexually active persons age 75-85 reported having sex at least two to three times per month.[14] A 2020 publication, Trends in Frequency of Sexual Activity and Number of Sexual Partners Among Adults Aged 18 to 44 Years in the US, 2000-2018, assessed the proportion of US men and women by category of sexual frequency and number of sexual partners in 2016-2018. Overall, most men and women reported having had weekly or more sexual activity and 1 sexual partner in the past year, with these percentages increasing with age.[15] A Study of Declines in Sexual Frequency among American Adults found that age had a strong effect on sexual frequency: Americans in their 20s had sex an average of about 80 times per year, declining to about 60 times per year by age 45 and about 20 times per year by age 65.[16] Among the studies, the highest average coital frequency reported amongst age groups is approximately 6 times per month. Therefore, the quantity limit for erectile dysfunction drugs (excluding Cialis 2.5 mg and 5 mg) will be set at 6 units per month.

The recommended starting dose of Cialis for daily use for ED is 2.5 mg taken at approximately the same time every day, without regard to timing of sexual activity. The Cialis dose for once daily use may be increased to 5 mg based on individual efficacy and tolerability.[3,10,11] The recommended dose of Cialis for once daily use for BPH and ED/BPH is 5 mg, taken at approximately the same time every day, without regard to timing of sexual activity. For BPH and ED/BPH a starting dose of 2.5 mg is recommended for creatinine clearance 30 to 50 mL/min.[3] Therefore, the initial quantity limit for Cialis 2.5 mg and 5 mg will be 30 tablets per month for once daily use.

If the patient is requesting more than the initial quantity limit, then the claim will reject with a message indicating that quantity limits are exceeded.

Please note manufacturer package sizes may vary. It is the discretion of the dispensing pharmacy to fill quantities per package size up to these quantity limits. In such cases, the filling limit and day supply may be less than what is indicated in the Limit Criteria chart.

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Date Written:	03/1998
Last Revised:	(LS) 12/1998, 04/2000, 02/2001; (JG) 12/2002, 08/2003, 11/2003, 08/2004; (PJ) 10/2005; (CT) 01/2006, 09/2006, 01/2007; (NB) 07/2007; (MS) 07/2008; (NB) 08/2009; (TM) 08/2010, 07/2011, 10/2011, 04/2012, 04/2013; (CF) 04/2014, 04/2015; (JH) 04/2016 (no clinical changes); (KM) 04/2017 (no clinical changes); (KC) 04/2018 (no clinical changes); (CF/KC) 04/2019 (no clinical changes), 07/2019 (increased Cialis 5 mg QL to 30); (KC) 04/2020 (no clinical changes), 04/2021 (no clinical changes), (VLS) 03/2022 (no clinical changes)
Reviewed:	Medical Affairs: 12/1998, 04/2000, 01/2001, 12/2002, 08/2003, 11/2003, 08/2004, 10/2005; (MM) 01/2006, 09/2006; (WF) 01/2007, 07/2007, 07/200, 08/2009; (KP) 08/2010, 07/2011, 10/2011; (LB) 05/2012; (DC) 04/2013; (SES) 04/2014; (ADA) 04/2015; (CHART) 8/22/19, 04/30/20, 04/22/21, (CHART) 04/28/2022 External Review: 02/2003, 10/2003, 12/2003, 10/2004, 04/2006, 12/2006, 02/2008, 02/2009, 12/2009, 12/2010, 12/2011, 06/2012, 08/2013, 08/2014, 08/2015, 08/2016, 08/2017, 08/2018, 08/2019, 08/2020, 08/2022

LIMIT CRITERIA

Limits should accumulate across all drugs and strengths up to highest quantity listed depending on the order the claims are processed.

PLEASE NOTE: Since manufacturer package sizes may vary, it is the discretion of the dispensing pharmacy to fill quantities per package size up to these quantity limits. In such cases the filling limit and day supply may be less than what is indicated.

Medication	1 Month Limit*	3 Month Limit*
Cialis (tadalafil) 2.5 mg, 5 mg	30 tablets / 25 days	90 tablets / 75 days
Cialis (tadalafil) 10 mg, 20 mg	6 tablets / 25 days	18 tablets / 75 days
Levitra (vardenafil HCl)	6 tablets / 25 days	18 tablets / 75 days
Staxyn (vardenafil HCl orally disintegrating)	6 tablets / 25 days	18 tablets / 75 days
Stendra (avanafil)	6 tablets / 25 days	18 tablets / 75 days
Viagra (sildenafil)	6 tablets / 25 days	18 tablets / 75 days
Caverject (alprostadil)	6 units / 25 days	18 units / 75 days
Edex (alprostadil)	6 units / 25 days	18 units / 75 days
MUSE (alprostadil)	6 units / 25 days	18 units / 75 days

** The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*

STEP THERAPY CRITERIA

BRAND NAME*
(generic)

CIALIS 2.5 mg, 5 mg
(tadalafil)

Status: CVS Caremark Criteria
Type: Initial Step Therapy with Quantity Limit;
Post Step Therapy Prior Authorization with Quantity Limit ***Ref # 710-E***

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Erectile Dysfunction
Cialis is indicated for the treatment of erectile dysfunction (ED).
Benign Prostatic Hyperplasia
Cialis is indicated for the treatment of the signs and symptoms of benign prostatic hyperplasia (BPH).
Erectile Dysfunction and Benign Prostatic Hyperplasia
Cialis is indicated for the treatment of ED and the signs and symptoms of BPH (ED/BPH).

Limitation of Use
If Cialis is used with finasteride to initiate BPH treatment, such use is recommended for up to 26 weeks because the incremental benefit of Cialis decreases from 4 weeks until 26 weeks, and the incremental benefit of Cialis beyond 26 weeks is unknown.

INITIAL STEP THERAPY with QUANTITY LIMIT*
**Include Rx and OTC products unless otherwise stated.*

If the patient has filled a prescription for at least a 30-day supply of at least one alpha-blocker (e.g., alfuzosin, doxazosin, silodosin, tamsulosin, or terazosin), 5 alpha-reductase inhibitor (5-ARI) (e.g., dutasteride, finasteride 5 mg), or combination alpha-blocker and 5-ARI [e.g., Jalyn (dutasteride/tamsulosin)] within the past 180 days under a prescription benefit administered by CVS Caremark, then the requested Cialis 2.5 mg or Cialis 5 mg will be paid under that prescription benefit.** If the patient does not meet the initial step therapy criteria, then the claim will reject with a message indicating that a prior authorization (PA) is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

**If the patient meets the initial step therapy criteria, then the initial limit criteria will apply. If the patient is requesting more than the initial quantity limit, then the claim will reject with a message indicating that a PA is required.

****INITIAL LIMIT CRITERIA**
Limits should accumulate across all drugs and strengths up to highest quantity listed depending on the order the claims are processed.

Drug	1 Month Limit*	3 Month Limit*
Cialis (tadalafil) 2.5 mg, 5 mg	30 tablets / 25 days	90 tablets / 75 days

**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*

COVERAGE CRITERIA

CVS caremark

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for daily use for symptomatic benign prostatic hyperplasia (BPH) with or without erectile dysfunction (ED) in a patient that is 18 years of age or older
  [Note: Examples of signs and symptoms of BPH are incomplete emptying, weak stream, straining, urinary frequency, intermittency, or urgency.]
  AND
  - The patient has experienced an inadequate treatment response, intolerance, or has a contraindication to an alpha-blocker and/or a 5 alpha-reductase inhibitor (5-ARI) [Note: Examples of trial drugs are alfuzosin, doxazosin, silodosin, tamsulosin, terazosin, dutasteride, finasteride 5 mg, Jalyn (dutasteride/tamsulosin).]

OR

- The requested drug is being prescribed for erectile dysfunction in a patient that is 18 years of age or older

Quantity Limits apply.

RATIONALE

If the patient has filled a prescription for at least a 30-day supply of at least one alpha-blocker (e.g., alfuzosin, doxazosin, silodosin, tamsulosin, or terazosin), 5 alpha-reductase inhibitor (5-ARI) (e.g., dutasteride, finasteride 5 mg), or combination alpha-blocker and 5-ARI [e.g., Jalyn (dutasteride/tamsulosin)] within the past 180 days under a prescription benefit administered by CVS Caremark, then the requested Cialis 2.5 mg or Cialis 5 mg will be paid under that prescription benefit for up to 30 tablets per month.

If the patient does not meet the initial step therapy criteria, then the claim will reject indicating a prior authorization is required. If the patient does not meet the initial limit criteria, then the claim will reject indicating a prior authorization is required.

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Cialis is indicated for the treatment of erectile dysfunction (ED), for the treatment of the signs and symptoms of benign prostatic hyperplasia (BPH), and for the treatment of ED and the signs and symptoms of BPH (ED/BPH).[1-3] Cialis is not indicated for use in pediatric patients. Safety and efficacy in patients below the age of 18 years have not been established.[1-3]

ED only

According to the American Urological Association (AUA) Guideline on the Management of Erectile Dysfunction, patients presenting with symptoms of erectile dysfunction (ED) should undergo a thorough medical, sexual, and psychosocial history; a physical examination; and selective laboratory testing. Shared decision-making is the cornerstone of patient-centered care for ED. Determining an appropriate treatment requires that the patient, his clinician, and ideally the partner navigate all of these issues in order to arrive at a treatment choice that is aligned with the patient and the partner's priorities and values. Patients should be informed of all treatment options that are not medically contraindicated and supported in the shared decision-making process to determine the appropriate treatment.[4]

The recommended starting dose of Cialis for daily use for ED is 2.5 mg taken at approximately the same time every day, without regard to timing of sexual activity. The Cialis dose for once daily use may be increased to 5 mg based on individual efficacy and tolerability.[1-3] Therefore, the quantity for approval for Cialis 2.5 mg and 5 mg will be 30 tablets per month for ED for once daily use.

BPH and ED/BPH

According to the American Urological Association (AUA) BPH guidelines, the most prevalent and generally first line approach to the treatment of male lower urinary tract symptoms secondary/attributed to BPH (LUTS/BPH) is behavioral and lifestyle modifications followed by medical therapy, including alpha-adrenergic antagonists (alpha blockers), 5-alpha reductase inhibitors (5-ARIs), phosphodiesterase 5 selective inhibitors (PDE5s), anticholinergics, and beta-3 agonists - which may be utilized alone, or in combination to take advantage of their different mechanisms of action. Clinicians should offer one of the following alpha blockers as a treatment option for patients with bothersome, moderate to severe LUTS/BPH: alfuzosin, doxazosin, silodosin, tamsulosin, or terazosin. 5-ARIs alone or in combination with alpha blockers are recommended as a treatment option to prevent progression of LUTS/BPH and/or reduce the risks of urinary retention

and need for future prostate-related surgery. For patients with LUTS/BPH irrespective of comorbid erectile dysfunction (ED), 5 mg daily tadalafil should be discussed as a treatment option.[5] In clinical studies, tadalafil improved lower urinary tract symptoms associated with BPH (e.g., urinary frequency, urgency, nocturia, straining, incomplete emptying, weak urinary stream) but generally did not affect peak urinary flow rate or postvoid residual volume.[2]

The recommended dose of Cialis for once daily use for BPH and ED/BPH is 5 mg, taken at approximately the same time every day, without regard to timing of sexual activity. For BPH and ED/BPH, a starting dose of 2.5 mg is recommended for creatinine clearance 30 to 50 mL/min.[1-3] The quantity for approval for Cialis 2.5 mg and 5 mg will be 30 tablets per month for once daily use for BPH and ED/BPH.

REFERENCES

1. Cialis [package insert]. Indianapolis, IN: Eli Lilly and Company; June 2020.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2022; Accessed March 31, 2022.
3. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed March 31, 2022.
4. American Urological Association Guideline on the Management of Erectile Dysfunction. 2018. Available at https://www.auanet.org/guidelines/erectile-dysfunction-(ed)-guideline. Accessed March 2022.
5. American Urological Association Guideline Management of Benign Prostatic Hyperplasia (BPH). 2010. Available at https://www.auanet.org/guidelines/benign-prostatic-hyperplasia-(bph)-guideline/benign-prostatic-hyperplasia-(2010-reviewed-and-validity-confirmed-2014). Accessed April 2021.

Written by:	UM Development (TM)
Date Written:	10/2011
Revised:	(TM) 11/2011, 03/2012 (add dup questions for Web), 05/2012 (add Cialis 2.5 & revise questions for Web), 10/2012 (extended duration), 04/2013; (CF) 04/2014, 09/2014 (changed Cialis 5 mg qty), 04/2015; (JH) 04/2016, 09/2016 (updated for TGC); (KM) 04/2017 (removed contraindication question, added partial approval questions); (KC) 04/2018; (KC/CF) 04/2019 (no clinical changes), 07/2019 (increased Cialis 5 mg QL to 30 for ED); (KC) 04/2020 (no clinical changes), 08/2020 (updated note in BPH question), 04/2021 (no clinical changes), (VLS) 03/2022 (no clinical changes)
Reviewed:	Medical Affairs: (KP) 10/2011, 11/2011; (LB) 05/2012; (KP) 10/2012; (DC) 04/2013; (SES) 04/2014, 09/2014; (ADA) 04/2015; (TP) 04/2016; (ME) 09/2016; (JG) 04/2017; (PA) 04/2018; (CHART) 08/22/19, 04/30/20, 09/03/20, 04/22/21, (CHART) 04/28/2022 External Review: 12/2011, 06/2012, 08/2013, 08/2014, 09/2014, 10/2014, 08/2015, 08/2016, 08/2017, 08/2018, 08/2019, 08/2020, 08/2021, 08/2022

CRITERIA FOR APPROVAL

1	Is the requested drug being prescribed for daily use for symptomatic benign prostatic hyperplasia (BPH) with or without erectile dysfunction (ED) in a patient that is 18 years of age or older? [Note: Examples of signs and symptoms of BPH are incomplete emptying, weak stream, straining, urinary frequency, intermittency, or urgency.] [If no, then skip to question 3.]	Yes	No
2	Has the patient experienced an inadequate treatment response, intolerance, or does the patient have a contraindication to an alpha-blocker and/or a 5 alpha-reductase inhibitor (5-ARI)? [Note: Examples of trial drugs are alfuzosin, doxazosin, silodosin, tamsulosin, terazosin, dutasteride, finasteride 5 mg, Jalyn (dutasteride/tamsulosin).] [If yes, then skip to question 4.] [If no, then no further questions.]	Yes	No
3	Is the requested drug being prescribed for erectile dysfunction in a patient that is 18 years of age or older? [If no, then no further questions.]	Yes	No

4	Does the patient require MORE than the plan allowance of 1 tablet per day? [RPh Note: If yes, then deny and enter a partial approval for 30 tablets / 25 days or 90 tablets / 75 days of the requested drug.]	Yes	No

Mapping Instructions			
	Yes	**No**	**DENIAL REASONS – DO NOT USE FOR MEDICARE PART D**
1.	Go to 2	Go to 3	
2.	Go to 4	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you meet all of these conditions: - You tried another drug for benign prostatic hyperplasia (BPH) first, and it did not work for you or you cannot take it Your request has been denied based on the information we have. [Short Description: No inadequate response, intolerance, or contraindication to an alpha-blocker and/or a 5 alpha-reductase inhibitor (5-ARI).]
3.	Go to 4	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you meet any of these conditions: - You are 18 years of age or older and you have erectile dysfunction - You are 18 years of age or older and you have male lower urinary tract symptoms secondary/attributed to benign prostatic hyperplasia (BPH) Your request has been denied based on the information we have. [Short Description: No approvable diagnosis.]
4.	Deny	Approve, 36 months 30 tablets per 25 days* 90 tablets per 75 days*	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 30 tablets per month of the requested drug and strength. Your request has been partially approved. You have been approved for the maximum quantity that your plan covers for a duration of 36 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity.]

**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*

Reference number
1872-A

SPECIALTY GUIDELINE MANAGEMENT

EGRIFTA SV (tesamorelin)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Egrifta SV is indicated for the reduction of excess abdominal fat in human immunodeficiency virus (HIV)-infected adult patients with lipodystrophy.

Limitations of Use:
A. Long-term cardiovascular safety of Egrifta SV has not been established.
B. Egrifta SV is not indicated for weight loss management as it has a weight neutral effect.
C. There are no data to support improved compliance with anti-retroviral therapies in HIV-positive patients taking Egrifta SV.

All other indications are considered experimental/investigational and not medically necessary.

II. EXCLUSIONS

Coverage will not be provided for weight loss.

III. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with an infectious disease specialist.

IV. CRITERIA FOR INITIAL APPROVAL

Reduction of excess abdominal fat in human immunodeficiency virus (HIV)-infected patients with lipodystrophy
Authorization of 6 months may be granted for reduction of excess abdominal fat in HIV-infected patients with lipodystrophy when the patient is currently receiving anti-retroviral therapy.

V. CONTINUATION OF THERAPY

Authorization of 6 months may be granted for continued treatment in members requesting reauthorization for reduction of excess abdominal fat when all of the following criteria are met:
A. The member has HIV infection and lipodystrophy
B. The member is currently receiving anti-retroviral therapy

C. The member has demonstrated a clear clinical improvement from baseline that is supported by waist circumference measurement or computed tomography (CT) scan

VI. REFERENCES

1. Egrifta SV [package insert]. Montreal, Québec: Theratechnologies, Inc.; October 2019.
2. Brown TT. Approach to the human immunodeficiency virus-infected patient with lipodystrophy. *J Clin Endocrinol Metab*. 2008;93(8):2937-2945.

STEP THERAPY CRITERIA

BRAND NAME
(generic)

ELIDEL
(pimecrolimus)

Status: CVS Caremark Criteria
Type: Initial Step Therapy; Post Step Therapy Prior Authorization

POLICY

FDA-APPROVED INDICATIONS

Elidel is indicated as second-line therapy for the short-term and non-continuous chronic treatment of mild to moderate atopic dermatitis in non-immunocompromised adults and children 2 years of age and older, who have failed to respond adequately to other topical prescription treatments, or when those treatments are not advisable.
Elidel is not indicated for use in children less than 2 years of age.

Compendial Uses
Psoriasis[3] - on the face, genitals, or skin folds[6]
Atopic Dermatitis for patients under 2 years of age[4, 5]
Vitiligo on the head or neck[7, 8]

INITIAL STEP THERAPY

**Include Rx and OTC products unless otherwise stated.*

If the patient has filled a prescription for at least a 14 day supply of at least one corticosteroid of medium or higher potency within the past 180 days (see examples in Table 1) under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit. If the patient does not meet the initial step therapy criteria, then the claim will reject with a message indicating that a prior authorization (PA) is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

TABLE 1: EXAMPLES OF TOPICAL CORTICOSTEROIDS FOR TREATMENT OF ATOPIC DERMATITIS [2,3,4]	
Medium Potency	betamethasone dipropionate lotion, spray 0.05%
	betamethasone valerate crm/lotion 0.1%/foam 0.12%
	clocortolone pivalate crm 0.1%
	desonide lotion, ointment 0.05%
	desoximetasone crm 0.05%
	fluocinolone acetonide crm/oint/kit 0.025%
	flurandrenolide crm/oint/lotion 0.05%
	fluticasone propionate crm/lotion 0.05%/oint 0.005%
	hydrocortisone butyrate cream/lipocream/lotion/oint/soln 0.1%
	hydrocortisone probutate crm 0.1%
	hydrocortisone valerate crm/oint 0.2%
	mometasone furoate crm/lotion/solution 0.1%
	prednicarbate crm/oint 0.1%
	triamcinolone acetonide crm/oint/lotion/kit 0.1%
	triamcinolone acetonide crm/oint/lotion 0.025%
	triamcinolone acetonide ointment 0.05%
High Potency	amcinonide crm/oint/lotion 0.1%
	betamethasone dipropionate crm/oint 0.05%
	betamethasone dipropionate augmented crm/lotion 0.05%
	betamethasone valerate oint 0.1%
	desoximetasone crm/oint/spray 0.25%/gel/oint 0.05%

	diflorasone diacetate crm (emollient base) 0.05% diflorasone cream 0.05%
	halcinonide crm/oint 0.1%
	fluocinonide crm/emulsified cream/oint/gel/soln 0.05%
	mometasone furoate oint 0.1%
	triamcinolone acetonide crm/oint 0.5%
	triamcinolone acetonide aerosol soln 0.147 mg/g
Very High Potency	betamethasone dipropionate augmented oint/gel 0.05%
	clobetasol propionate crm/oint/foam/shampoo/gel/lotion/soln/spray 0.05%/cream 0.025%
	diflorasone diacetate oint 0.05%
	flurandrenolide tape 4mcg/cm^2
	halobetasol propionate crm/oint/lotion/kit 0.05%
	fluocinonide crm 0.1%

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for psoriasis on the face, genitals, or skin folds OR vitiligo on the head or neck

OR

- The requested drug is being prescribed for mild to moderate atopic dermatitis (eczema) **AND**
  - The patient is less than 2 years of age
    OR
  - The requested drug will be used on sensitive skin areas (e.g., face, genitals, or skin folds)
    OR
  - The patient has experienced an inadequate treatment response, intolerance, or contraindication to at least one first line therapy agent (e.g., medium or higher potency topical corticosteroid)

REFERENCES

1. Elidel [package insert]. Bridgewater, NJ: Bausch Health US, LLC; September 2020.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2022; Accessed February 14, 2022.
3. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed February 14, 2022.
4. Eichenfield L, Tom W, Berger T, et al. Guidelines of Care for the Management of Atopic Dermatitis. *J Am Acad Dermatol.* 2014 Jul;71:116-32.
5. Sigurgeirsson B, Boznanski A, et al. Safety and Efficacy of Pimecrolimus in Atopic Dermatitis: A 5-Year Randomized Trial. *Pediatrics*. 2015:135(4): 594-606.
6. Elmets CA, Korman NJ, Prater EF, et al. Joint AAD-NPF Guidelines of care for the management and treatment of psoriasis with topical therapy and alternative medicine modalities for psoriasis severity measures. *J Am Acad Dermatol*. 2021 Feb;84(2):432-470.
7. Kubelis-López DE, Zapata-Salazar NA, et al. Updates and new medical treatments for vitiligo (Review). *Exp Ther Med*. 2021;22(2):797.
8. Eleftheriadou V, Atkar R, et al. British Association of Dermatologists guidelines for the management of people with vitiligo 2021. *The British Journal of Dermatology*. 2021;186(1):18-29.

QUANTITY LIMIT CRITERIA

BRAND NAME
(generic)

(aprepitant)

CINVANTI
(aprepitant)

EMEND
(aprepitant)

EMEND INJECTION
(fosaprepitant dimeglumine)

VARUBI
(rolapitant)

Status: CVS Caremark Criteria
Type: Quantity Limit

POLICY

FDA-APPROVED INDICATIONS

Aprepitant capsules

Prevention of Chemotherapy Induced Nausea and Vomiting (CINV)

Aprepitant capsules, in combination with other antiemetic agents, are indicated in patients 12 years of age and older for the prevention of:

- acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy (HEC) including high-dose cisplatin.
- nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy (MEC).

Prevention of Postoperative Nausea and Vomiting (PONV)

Aprepitant capsules are indicated in adults for the prevention of postoperative nausea and vomiting.

Limitations of Use

- Aprepitant has not been studied for the treatment of established nausea and vomiting.
- Chronic continuous administration of aprepitant is not recommended because it has not been studied, and because the drug interaction profile may change during chronic continuous use.

Cinvanti (aprepitant) injectable emulsion

Cinvanti, in combination with other antiemetic agents, is indicated in adults for the prevention of:

- acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy (HEC) including high-dose cisplatin as a single dose regimen.
- delayed nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy (MEC) as a single dose regimen.
- nausea and vomiting associated with initial and repeat courses of MEC as a 3-day regimen.

Limitations of Use

- Cinvanti has not been studied for the treatment of established nausea and vomiting.

Emend (aprepitant) capsules and oral suspension
Emend for oral suspension, in combination with other antiemetic agents, is indicated in patients 6 months of age and older for the prevention of:

- acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy (HEC) including high-dose cisplatin.
- nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy (MEC).

Emend capsules, in combination with other antiemetic agents, is indicated in patients 12 years of age and older for the prevention of:

- acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy (HEC) including high-dose cisplatin.
- nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy (MEC).

Limitations of Use

- Emend has not been studied for the treatment of established nausea and vomiting.
- Chronic continuous administration of Emend is not recommended because it has not been studied, and because the drug interaction profile may change during chronic continuous use.

Emend (fosaprepitant dimeglumine) for injection
Emend for injection, in combination with other antiemetic agents, is indicated in adults and pediatric patients 6 months of age and older for the prevention of:

- acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy (HEC) including high-dose cisplatin.
- delayed nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy (MEC).

Limitations of Use

- Emend has not been studied for the treatment of established nausea and vomiting.

Varubi (rolapitant) tablets
Varubi is indicated in combination with other antiemetic agents in adults for the prevention of delayed nausea and vomiting associated with initial and repeat courses of emetogenic cancer chemotherapy, including, but not limited to, highly emetogenic chemotherapy.

INITIAL LIMIT QUANTITY
Limits do not accumulate together; patient is allowed the maximum limit for each drug and strength

Drug	4 Week Limit*	12 Week Limit*
Cinvanti (aprepitant) 130 mg Injection (Single-Dose 130 mg/18 mL Vial)	2 vials (36 mL) / 21 days	Does Not Apply**
Emend (aprepitant) 80 mg Capsule	4 capsules / 21 days	Does Not Apply**
Emend (aprepitant) 125 mg Capsule	2 capsules / 21 days	Does Not Apply**
Emend (aprepitant) 125 mg-80 mg Capsules (Tri-pack contains one 125 mg capsule and two 80 mg capsules)	2 packs (6 capsules) / 21 days	Does Not Apply**
Emend (aprepitant) 125 mg for Oral Suspension (Single-Dose Kit contains 125 mg / 5 mL)	6 kits / 21 days	Does Not Apply**
Emend (fosaprepitant dimeglumine) 150 mg Injection (Single-Dose 150 mg Vial)	2 vials / 21 days	Does Not Apply**
Varubi (rolapitant) 90 mg Tablet (Single Dose Package contains two 90 mg tablets as one set of twinned blisters)	2 packs (4 tablets) / 21 days	Does Not Apply**

** The duration of 21 days is used for a 28-day fill period to allow time for refill processing.*
*** These drugs are for short-term acute use; therefore, the mail limit will be the same as the retail limit. The intent is for prescriptions of the requested drug to be filled one month at a time, even if filled at mail order; there should be no 3 month supplies filled.*

Drug	Limit***
Aprepitant 40 mg Capsule	3 capsules / 6 months
*** These drugs are for short-term acute use.	

REFERENCES

1. Aprepitant capsules [package insert]. Princeton, NJ: Sandoz Inc.; December 2020.
2. Cinvanti [package insert]. San Diego, CA: Heron Therapeutics, Inc.; March 2022.
3. Emend capsules and oral suspension [package insert]. Rahway, NJ: Merck Sharp & Dohme LLC; May 2022.
4. Emend for injection [package insert]. Whitehouse Station, NJ: Merck Sharp & Dohme Corp., a subsidiary of Merck and Co., Inc.; May 2022.
5. Varubi [package insert]. Deerfield, IL: TerSera Therapeutics LLC; August 2020.
6. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2022; Accessed November 14, 2022.
7. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed November 11, 2022.
8. National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology. Antiemesis. Version 2.2022. Available at: https://www.nccn.org/professionals/physician_gls/pdf/antiemesis.pdf. Accessed November 16, 2022.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME
(generic)

(aprepitant)

CINVANTI
(aprepitant)

EMEND
(aprepitant)

EMEND INJECTION
(fosaprepitant dimeglumine)

VARUBI
(rolapitant)

Status: CVS Caremark Criteria
Type: Post Limit Prior Authorization

POLICY

FDA-APPROVED INDICATIONS

Aprepitant capsules

Prevention of Chemotherapy Induced Nausea and Vomiting (CINV)

Aprepitant capsules, in combination with other antiemetic agents, are indicated in patients 12 years of age and older for the prevention of:

- acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy (HEC) including high-dose cisplatin.
- nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy (MEC).

Prevention of Postoperative Nausea and Vomiting (PONV)

Aprepitant capsules are indicated in adults for the prevention of postoperative nausea and vomiting.

Limitations of Use

- Aprepitant has not been studied for the treatment of established nausea and vomiting.
- Chronic continuous administration of aprepitant is not recommended because it has not been studied, and because the drug interaction profile may change during chronic continuous use.

Cinvanti (aprepitant) injectable emulsion

Cinvanti, in combination with other antiemetic agents, is indicated in adults for the prevention of:

- acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy (HEC) including high-dose cisplatin as a single dose regimen.
- delayed nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy (MEC) as a single dose regimen.
- nausea and vomiting associated with initial and repeat courses of MEC as a 3-day regimen.

Limitations of Use

- Cinvanti has not been studied for the treatment of established nausea and vomiting.

Emend (aprepitant) capsules and oral suspension

Emend for oral suspension, in combination with other antiemetic agents, is indicated in patients 6 months of age and older for the prevention of:

- acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy (HEC) including high-dose cisplatin.
- nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy (MEC).

Emend capsules, in combination with other antiemetic agents, is indicated in patients 12 years of age and older for the prevention of:

- acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy (HEC) including high-dose cisplatin.
- nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy (MEC).

Limitations of Use

- Emend has not been studied for the treatment of established nausea and vomiting.
- Chronic continuous administration of Emend is not recommended because it has not been studied, and because the drug interaction profile may change during chronic continuous use.

Emend (fosaprepitant dimeglumine) for injection

Emend for injection, in combination with other antiemetic agents, is indicated in adults and pediatric patients 6 months of age and older for the prevention of:

- acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy (HEC) including high-dose cisplatin.
- delayed nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy (MEC).

Limitations of Use

- Emend has not been studied for the treatment of established nausea and vomiting.

Varubi (rolapitant) tablets

Varubi is indicated in combination with other antiemetic agents in adults for the prevention of delayed nausea and vomiting associated with initial and repeat courses of emetogenic cancer chemotherapy, including, but not limited to, highly emetogenic chemotherapy.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The request is not for Varubi, and the requested drug is being prescribed for the prevention of nausea and vomiting associated with highly or moderately emetogenic cancer chemotherapy
  AND
  - The requested drug will be used in combination with other antiemetic agents

OR

- Aprepitant capsules are being prescribed for the prevention of postoperative nausea and vomiting

Quantity Limits apply.

POST LIMIT QUANTITY

Drug	4 Week Limit*	12 Week Limit*
Cinvanti (aprepitant) 130 mg Injection (Single-Dose 130 mg/18 mL Vial)	4 vials (72 mL) / 21 days	Does Not Apply**
Emend (aprepitant) 80 mg Capsule	16 capsules / 21 days	Does Not Apply**
Emend (aprepitant) 125 mg Capsule	4 capsules / 21 days	Does Not Apply**
Emend (aprepitant) 125 mg-80 mg Capsules (Tri-pack contains one 125 mg capsule and two 80 mg capsules)	4 packs (12 capsules) / 21 days	Does Not Apply**

Emend (aprepitant) 125 mg Oral Suspension (Single-Dose Kit contains 125 mg / 5 mL)	12 kits / 21 days	Does Not Apply**
Emend (fosaprepitant dimeglumine) 150 mg Injection (Single-Dose 150 mg Vial)	4 vials / 21 days	Does Not Apply**
** The duration of 21 days is used for a 28-day fill period to allow time for refill processing.* *** These drugs are for short-term acute use; therefore, the mail limit will be the same as the retail limit. The intent is for prescriptions of the requested drug to be filled one month at a time, even if filled at mail order; there should be no 3 month supplies filled.*		

Drug	**Limit*****
Aprepitant 40 mg Capsule	6 capsules / 6 months
**** These drugs are for short-term acute use.*	

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Reference number(s)
1636-A

SPECIALTY GUIDELINE MANAGEMENT

EMFLAZA (deflazacort)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Emflaza is indicated for the treatment of Duchenne muscular dystrophy (DMD) in patients 2 years of age and older.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
A. Laboratory confirmation of DMD diagnosis by genetic testing or muscle biopsy
B. Chart documentation of weight gain/obesity or persistent psychiatric/behavioral issues with previous prednisone or prednisolone treatment.

III. CRITERIA FOR INITIAL APPROVAL

Duchenne Muscular Dystrophy
Authorization of 6 months may be granted for treatment of DMD when all of the following criteria are met:
A. The diagnosis of DMD was confirmed by one of the following criteria:
   1. Genetic testing demonstrating a mutation in the *DMD* gene.
   2. Muscle biopsy demonstrating absent dystrophin.
B. The member is 2 years of age or older.
C. The member has tried prednisone or prednisolone and experienced unmanageable and clinically significant weight gain/obesity or psychiatric/behavioral issues (e.g., abnormal behavior, aggression, irritability):
   1. For weight gain/obesity: body mass index is in the overweight or obese category while receiving treatment with prednisone or prednisolone (refer to Appendix for weight status categories for children and adults).
   2. For psychiatric/behavioral issues: psychiatric/behavioral issues persisted beyond the first 6 weeks of treatment with prednisone or prednisolone.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for members requesting continuation of therapy when all of the following criteria are met:
A. The member meets all initial authorization criteria.

B. The member is receiving a clinical benefit from Emflaza therapy, such as improvement or stabilization of muscle strength or pulmonary function.

V. APPENDIX

Body Mass Index Percentile and Weight Status Category for Children 2 Through 19 Years of Age

Body Mass Index Percentile Range	Weight Status
Less than the 5th percentile	Underweight
5th percentile to less than the 85th percentile	Normal or Healthy Weight
85th to less than the 95th percentile	Overweight
Equal to or greater than the 95th percentile	Obese

Body Mass Index and Weight Status Category for Adults (20 Years of Age and Older)

Body Mass Index	Weight Status
Below 18.5	Underweight
18.5 – 24.9	Normal or Healthy Weight
25.0 – 29.9	Overweight
30.0 and Above	Obese

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PRIOR AUTHORIZATION CRITERIA

BRAND NAME
(generic)

EMSAM
(selegiline transdermal system)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

POLICY

FDA-APPROVED INDICATIONS
Emsam (selegiline transdermal system) is a monoamine oxidase inhibitor (MAOI) indicated for the treatment of adults with major depressive disorder (MDD).

COVERAGE CRITERIA
The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for the treatment of an adult patient with major depressive disorder (MDD)
  AND
  - The patient has experienced an inadequate treatment response, intolerance, or the patient has a contraindication to ANY of the following: A) a serotonin and norepinephrine reuptake inhibitor (SNRI), B) a selective serotonin reuptake inhibitor (SSRI), C) mirtazapine, D) bupropion

  OR
  - The patient is unable to swallow oral formulations

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Reference number(s)
2003-A

SPECIALTY GUIDELINE MANAGEMENT

ENBREL (etanercept)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. Moderately to severely active rheumatoid arthritis (RA)
   2. Moderately to severely active polyarticular juvenile idiopathic arthritis (pJIA) in patients aged 2 years or older
   3. Active psoriatic arthritis (PsA)
   4. Active ankylosing spondylitis (AS)
   5. Chronic moderate to severe plaque psoriasis (PsO) in patients aged 4 years or older

B. Compendial Uses
   1. Axial spondyloarthritis
   2. Oligoarticular juvenile idiopathic arthritis
   3. Reactive arthritis
   4. Hidradenitis suppurativa, severe, refractory
   5. Behcet's disease
   6. Graft versus host disease
   7. Immunotherapy-related inflammatory arthritis

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

A. Rheumatoid arthritis (RA)
   1. For initial requests:
      i. Chart notes, medical record documentation, or claims history supporting previous medications tried (if applicable), including response to therapy. If therapy is not advisable, documentation of clinical reason to avoid therapy.
      ii. Laboratory results, chart notes, or medical record documentation of biomarker testing (i.e., rheumatoid factor [RF], anti-cyclic citrullinated peptide [anti-CCP], and C-reactive protein [CRP] and/or erythrocyte sedimentation rate [ESR]) (if applicable).
   2. For continuation requests: Chart notes or medical record documentation supporting positive clinical response.

B. Articular juvenile idiopathic arthritis, ankylosing spondylitis (AS), active axial spondyloarthritis, and reactive arthritis:

1. Initial requests: Chart notes, medical record documentation, or claims history supporting previous medications tried (if applicable), including response to therapy. If therapy is not advisable, documentation of clinical reason to avoid therapy.
2. Continuation requests: Chart notes or medical record documentation supporting positive clinical response.

C. Psoriatic arthritis (PsA): For continuation requests: Chart notes or medical record documentation supporting positive clinical response.

D. Plaque psoriasis
   1. Initial requests:
      i. Chart notes or medical record documentation of affected area(s) and body surface area (BSA) affected (if applicable).
      ii. Chart notes, medical record documentation, or claims history supporting previous medications tried (if applicable), including response to therapy. If therapy is not advisable, documentation of clinical reason to avoid therapy.
   2. Continuation requests: Chart notes or medical record documentation of decreased body surface area (BSA) affected and/or improvement in signs and symptoms
      .

E. Hidradenitis suppurativa
   1. Initial requests: Chart notes, medical record documentation, or claims history supporting previous medications tried (if applicable), including response to therapy. If therapy is not advisable, documentation of clinical reason to avoid therapy.
   2. Continuation requests: Chart notes or medical record documentation supporting positive clinical response to therapy.

F. Graft versus host disease, and immunotherapy-related inflammatory arthritis (initial requests only): Chart notes, medical record documentation, or claims history supporting previous medications tried (if applicable), including response to therapy. If therapy is not advisable, documentation of clinical reason to avoid therapy.

G. Behcet's disease (initial requests only): Chart notes, medical record documentation, or claims history supporting previous medications tried, including response to therapy (if applicable).

III. CRITERIA FOR INITIAL APPROVAL

A. Moderately to severely active rheumatoid arthritis (RA)

1. Authorization of 12 months may be granted for members who have previously received a biologic or targeted synthetic DMARD (e.g., Rinvoq, Xeljanz) indicated for moderately to severely active rheumatoid arthritis.

2. Authorization of 12 months may be granted for treatment of moderately to severely active RA when all of the following criteria are met:
   i. Member meets either of the following criteria:
      a. Member has been tested for either of the following biomarkers and the test was positive:
         1. Rheumatoid factor (RF)
         2. Anti-cyclic citrullinated peptide (anti-CCP)
      b. Member has been tested for ALL of the following biomarkers:
         1. RF
         2. Anti-CCP

3. C-reactive protein (CRP) and/or erythrocyte sedimentation rate (ESR)

ii. Member meets either of the following criteria:
   a. Member has experienced an inadequate response to at least a 3-month trial of methotrexate despite adequate dosing (i.e., titrated to at least 15 mg/week).
   b. Member has an intolerance or contraindication to methotrexate (see Appendix A)

B. Moderately to severely active articular juvenile idiopathic arthritis

1. Authorization of 12 months may be granted for members who have previously received a biologic or targeted synthetic DMARD indicated for moderately to severely active articular juvenile idiopathic arthritis.

2. Authorization of 12 months may be granted for the treatment of moderately to severely active articular juvenile idiopathic arthritis when any of the following criteria are met:
   i. The member has had an inadequate response to methotrexate or another non-biologic DMARD administered at an adequate dose and duration.
   ii. The member has risk factors (See Appendix C) and the member also meets one of the following:
      a. High-risk joints are involved (e.g., cervical spine, wrist, or hip).
      b. High disease activity.
      c. Are judged to be at high risk for disabling joint disease.

C. Active psoriatic arthritis (PsA)

Authorization of 12 months may be granted for treatment of active psoriatic arthritis (PsA).

D. Active ankylosing spondylitis (AS) and active axial spondyloarthritis

1. Authorization of 12 months may be granted for members who have previously received a biologic indicated for active ankylosing spondylitis or active axial spondyloarthritis.

2. Authorization of 12 months may be granted for treatment of active ankylosing spondylitis or active axial spondyloarthritis when any of the following criteria is met:
   i. Member has experienced an inadequate response to at least two non-steroidal anti-inflammatory drugs (NSAIDs).
   ii. Member has an intolerance or contraindication to two or more NSAIDs.

E. Moderate to severe plaque psoriasis

1. Authorization of 12 months may be granted for members who have previously received Otezla or a biologic indicated for the treatment of moderate to severe plaque psoriasis.

2. Authorization of 12 months may be granted for treatment of moderate to severe plaque psoriasis in members when any of the following criteria is met:
   i. Crucial body areas (e.g., hands, feet, face, neck, scalp, genitals/groin, intertriginous areas) are affected.
   ii. At least 10% of the body surface area (BSA) is affected
   iii. At least 3% of body surface area (BSA) is affected and the member meets any of the following criteria:
      a. Member has had an inadequate response or intolerance to either phototherapy (e.g., UVB, PUVA) or pharmacologic treatment with methotrexate, cyclosporine, or acitretin.
      b. Member has a clinical reason to avoid pharmacologic treatment with methotrexate, cyclosporine, and acitretin (see Appendix B).

F. Reactive arthritis

1. Authorization of 12 months may be granted for members who have previously received a biologic indicated for reactive arthritis.

2. Authorization of 12 months may be granted for treatment of reactive arthritis when any of the following criteria is met:
   i. Member has experienced an inadequate response to at least a 3-month trial of methotrexate despite adequate dosing (i.e., titrated at least 15 mg/week).
   ii. Member has an intolerance or contraindication to methotrexate (see Appendix A).

G. Hidradenitis suppurativa

1. Authorization of 12 months may be granted for members who have previously received a biologic indicated for the treatment of severe, refractory hidradenitis suppurativa.

2. Authorization of 12 months may be granted for treatment of severe, refractory hidradenitis suppurativa when either of the following is met:
   i. Member has experienced an inadequate response to oral antibiotics for at least 90 days.
   ii. Member has an intolerance or contraindication to oral antibiotics.

H. Graft versus host disease

Authorization of 12 months may be granted for treatment of graft versus host disease when either of the following criteria is met:
1. Member has experienced an inadequate response to systemic corticosteroids.
2. Member has an intolerance or contraindication to corticosteroids.

I. Behcet's disease

1. Authorization of 12 months may be granted for members who have previously received Otezla or a biologic indicated for the treatment of Behcet's disease.

2. Authorization of 12 months may be granted for the treatment of Behcet's disease when the member has had an inadequate response to at least one nonbiologic medication for Behcet's disease (e.g., apremilast, colchicine, systemic glucocorticoids, azathioprine).

J. Immunotherapy-related inflammatory arthritis

Authorization of 12 months may be granted for treatment of severe/refractory immunotherapy-related inflammatory arthritis that is not responding to corticosteroids and anti-inflammatory agents.

IV. CONTINUATION OF THERAPY

A. Moderately to severely active rheumatoid arthritis (RA)

Authorization of 12 months may be granted for all members (including new members) who are using the requested medication for moderately to severely active rheumatoid arthritis and who achieve or maintain a positive clinical response as evidenced by disease activity improvement of at least 20% from baseline in tender joint count, swollen joint count, pain, or disability.

B. Moderately to severely active articular juvenile idiopathic arthritis

Authorization of 12 months may be granted for all members (including new members) who are using the requested medication for moderately to severely active articular juvenile idiopathic arthritis and who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition when there is improvement in any of the following from baseline:
1. Number of joints with active arthritis (e.g., swelling, pain, limitation of motion)

2. Number of joints with limitation of movement
3. Functional ability

C. Active psoriatic arthritis

Authorization of 12 months may be granted for all members (including new members) who are using the requested medication for active psoriatic arthritis and who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition when there is improvement in any of the following from baseline:

1. Number of swollen joints
2. Number of tender joints
3. Dactylitis
4. Enthesitis
5. Skin and/or nail involvement

D. Active ankylosing spondylitis (AS) and active axial spondylarthritis

Authorization of 12 months may be granted for all members (including new members) who are using the requested medication for active ankylosing spondylitis or active axial spondyloarthritis and who achieve or maintain a positive clinical response with the requested medication as evidenced by low disease activity or improvement in signs and symptoms of the condition when there is improvement in any of the following from baseline:

1. Functional status
2. Total spinal pain
3. Inflammation (e.g. morning stiffness)

E. Moderate to severe plaque psoriasis

Authorization of 12 months may be granted for all members (including new members) who are using the requested medication for moderate to severe plaque psoriasis and who achieve or maintain positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition when any of the following is met:

1. Reduction in body surface area (BSA) affected from baseline
2. Improvement in signs and symptoms from baseline (e.g., itching, redness, flaking, scaling, burning, cracking, pain)

F. Reactive arthritis

Authorization of 12 months may be granted for all members (including new members) who are using the requested medication for reactive arthritis and who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition (e.g., tender joint count, swollen joint count, or pain).

G. Hidradenitis suppurativa

Authorization of 12 months may be granted for all members (including new members) who are using the requested medication for severe, refractory hidradenitis suppurativa and who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition when any of the following is met:

1. Reduction in abscess and inflammatory nodule count from baseline
2. Reduced formation of new sinus tracts and scarring
3. Decrease in frequency of inflammatory lesions from baseline
4. Reduction in pain from baseline
5. Reduction in suppuration from baseline
6. Improvement in frequency of relapses from baseline
7. Improvement in quality of life from baseline

8. Improvement on a disease severity assessment tool from baseline

H. Graft versus host disease and immunotherapy-related inflammatory arthritis
All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

I. All other diagnoses
Authorization of 12 months may be granted for all members (including new members) who are using the requested medication for an indication outlined in Section III and who achieve or maintain positive clinical response with the requested medication as evidenced by low disease activity or improvement in signs and symptoms of the condition.

V. OTHER

For all indications: Member has had a documented negative TB test (which can include a tuberculosis skin test [PPD], an interferon-release assay [IGRA], or a chest x-ray)* within 6 months of initiating therapy for persons who are naïve to biologic DMARDs or targeted synthetic DMARDs associated with an increased risk of TB.

* If the screening testing for TB is positive, there must be further testing to confirm there is no active disease. Do not administer the requested medication to members with active TB infection. If there is latent disease, TB treatment must be started before initiation of the requested medication.

For all indications: Member cannot use the requested medication concomitantly with any other biologic DMARD or targeted synthetic DMARD.

VI. DOSAGE AND ADMINISTRATION

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. Dose optimization with 50 mg product formulations should be used when possible. Exceptions for higher quantities of 25 mg vials will be allowed when the member has a latex allergy or is following FDA-approved weight-based dosing.

VII. APPENDICES

Appendix A: Examples of Contraindications to Methotrexate
1. Clinical diagnosis of alcohol use disorder, alcoholic liver disease, or other chronic liver disease
2. Breastfeeding
3. Blood dyscrasias (e.g., thrombocytopenia, leukopenia, significant anemia)
4. Elevated liver transaminases
5. History of intolerance or adverse event
6. Hypersensitivity
7. Interstitial pneumonitis or clinically significant pulmonary fibrosis
8. Myelodysplasia
9. Pregnancy or currently planning pregnancy
10. Renal impairment
11. Significant drug interaction

Appendix B: Examples of Clinical Reasons to Avoid Pharmacologic Treatment with Methotrexate, Cyclosporine or Acitretin.

1. Clinical diagnosis of alcohol use disorder, alcoholic liver disease, or other chronic liver disease
2. Breastfeeding
3. Drug interaction
4. Cannot be used due to risk of treatment-related toxicity
5. Pregnancy or currently planning pregnancy
6. Significant comorbidity prohibits use of systemic agents (examples include liver or kidney disease, blood dyscrasias, uncontrolled hypertension)

APPENDIX C: Risk factors for articular juvenile idiopathic arthritis

1. Positive rheumatoid factor
2. Positive anti-cyclic citrullinated peptide antibodies
3. Pre-existing joint damage

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30. Smolen JS, Aletaha D. Assessment of rheumatoid arthritis activity in clinical trials and clinical practice. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. Available with subscription. URL: www.uptodate.com. Accessed March 19, 2021.
31. Fraenkel L, Bathon JM, England BR, et al. 2021 American College of Rheumatology guideline for the treatment of rheumatoid arthritis. *Arthrit Care Res*. 2021;0:1-16.

Reference number(s)
2208-A

SPECIALTY GUIDELINE MANAGEMENT

ENDARI (L-glutamine oral powder)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Endari is indicated to reduce the acute complications of sickle cell disease in adult and pediatric patients 5 years of age and older.

All other indications are considered experimental/investigational and not medically necessary.

II. PRESCRIBER SPECIALITIES

Endari must be prescribed by or in consultation with a hematologist or specialist in sickle cell disease.

III. CRITERIA FOR INITIAL APPROVAL

Sickle cell disease, to reduce the acute complications
Authorization of 12 months may be granted for use in reducing the acute complications of sickle cell disease in members 5 years of age or older when either of the following criteria is met:

A. Member has sickle hemoglobin C (HbSC) or sickle β^+-thalassemia (HbSβ^+) genotype
B. Member has homozygous hemoglobin S (HbSS) or sickle β^0-thalassemia (HbSβ^0) genotype AND meets any of the following:
    1. Has experienced, at any time in the past, an inadequate response or intolerance to a trial of hydroxyurea.
    2. Has a contraindication to hydroxyurea.
    3. Will be using Endari with concurrent hydroxyurea therapy.

IV. CONTINUATION OF THERAPY

Sickle cell disease, to reduce the acute complications
Authorization of 12 months may be granted for continued treatment when the member experienced a reduction in acute complications of sickle cell disease (e.g., reduction in the number of painful vaso-occlusive episodes, acute chest syndrome episodes, fever, occurrences of priapism, splenic sequestration) since initiating therapy with Endari.

V. REFERENCES

1. Endari [package insert]. Torrance, CA: Emmaus Medical, Inc; October 2020.
2. Niihara Y, Miller ST, et al. A phase 3 trial of l-glutamine in sickle cell disease. *N Engl J Med*. 2018;379(3):226-235.

Reference number(s)
4100-A

SPECIALTY GUIDELINE MANAGEMENT

ENSPRYNG (satralizumab-mwge)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Enspryng is an interleukin-6 (IL-6) receptor antagonist indicated for the treatment of neuromyelitis optica spectrum disorder (NMOSD) in adult patients who are anti-aquaporin-4 (AQP4) antibody positive.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
A. For initial requests: Immunoassay used to confirm anti-aquaporin-4 (AQP4) antibody is present.
B. For continuation requests: Chart notes or medical record documentation supporting positive clinical response.

III. CRITERIA FOR INITIAL APPROVAL

Neuromyelitis optica spectrum disorder (NMOSD)
Authorization of 12 months may be granted for treatment of neuromyelitis optica spectrum disorder (NMOSD) when all of the following criteria are met:
A. Anti-aquaporin-4 (AQPR) antibody positive
B. Member exhibits one of the following core clinical characteristics of NMOSD:
    1. Optic neuritis
    2. Acute myelitis
    3. Area postrema syndrome (episode of otherwise unexplained hiccups or nausea and vomiting)
    4. Acute brainstem syndrome
    5. Symptomatic narcolepsy or acute diencephalic clinical syndrome with NMOSD-typical diencephalic magnetic resonance imaging (MRI) lesions
    6. Symptomatic cerebral syndrome with NMOSD-typical brain lesions
C. The member will not receive the requested drug concomitantly with other biologics for the treatment of NMOSD.

IV. CONTINUATION OF THERAPY

Authorization of 12 months for continuation of therapy may be granted when both of the following criteria are met:
A. The member demonstrates a positive response to therapy (e.g., reduction in number of relapses).

B. The member will not receive the requested drug concomitantly with other biologics for the treatment of NMOSD.

V. REFERENCES

1. Enspryng [package insert]. South San Francisco, CA: Genentech, Inc.; March 2022.
2. Wingerchuk DM, Banwell B, Bennett JL, et al. International consensus diagnostic criteria for neuromyelitis optica spectrum disorders. Neurology. 2015; 85:177-189.

Reference number(s)
2137-A, 2676-A

SPECIALTY GUIDELINE MANAGEMENT

EPCLUSA (sofosbuvir and velpatasvir)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Epclusa is indicated for the treatment of adults and pediatric patients 3 years of age and older with chronic hepatitis C virus (HCV) genotype 1, 2, 3, 4, 5 or 6 infection:
A. without cirrhosis or with compensated cirrhosis
B. with decompensated cirrhosis for use in combination with ribavirin

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Hepatitis C virus infection, without ribavirin

1. Genotype 1, 2, 3, 4, 5 or 6 infection
Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who are treatment-naïve or who failed prior treatment with peginterferon alfa (PEG-IFN) and ribavirin (RBV) with or without an HCV protease inhibitor (boceprevir, simeprevir or telaprevir).

2. Unknown genotype/genotype could not be determined
Authorization of up to 12 weeks total may be granted for members with unknown or undetermined genotype without cirrhosis who are treatment-naïve and do not have any of the following characteristics:
i. HIV or HBsAG positive
ii. Current pregnancy
iii. Known or suspected hepatocellular carcinoma
iv. Prior liver transplantation

Note: Genotype testing is required for members with any of the characteristics listed.

3. Decompensated cirrhosis (Child Turcotte Pugh [CTP] class B or C)
Authorization of up to 24 weeks total may be granted for members with genotype 1, 2, 3, 4, 5 or 6 infection who have decompensated cirrhosis and documented anemia (baseline hemoglobin [Hgb] below 10 g/dL) or RBV ineligibility (see Section IV).

4. Recurrent HCV infection post liver transplantation
Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis and recurrent HCV genotype 1, 2, 3, 4, 5 or 6 infection post liver transplantation.

5. **Kidney transplant recipients**
   Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who have HCV genotype 1, 2, 3, 4, 5 or 6 infection and are treatment-naïve or who have not failed prior treatment with a direct-acting antiviral.

6. **Organ recipient from HCV-viremic donor**
   Authorization of up to 12 weeks total may be granted for members who have received a liver or non-liver organ transplant from an HCV-viremic donor.

B. Hepatitis C virus infection, in combination with ribavirin

1. **Genotype 3 infection**
   Authorization of up to 12 weeks total may be granted for treatment naïve members with compensated cirrhosis who have the Y93H substitution associated with velpatasvir resistance.

2. **Decompensated cirrhosis (CTP class B or C)**
   i. Authorization of up to 12 weeks total may be granted for members with genotype 1, 2, 3, 4, 5 or 6 infection and decompensated cirrhosis.
   ii. Authorization of up to 24 weeks total may be granted for members with genotype 1, 2, 3, 4, 5 or 6 infection and decompensated cirrhosis who failed prior treatment with a sofosbuvir- or NS5A inhibitor-based regimen.

3. **Recurrent HCV infection post liver transplantation**
   i. Authorization of up to 12 weeks total may be granted for treatment-naïve members with decompensated cirrhosis and recurrent HCV genotype 1, 2, 3, 4, 5 or 6 infection post liver transplantation.
   ii. Authorization of up to 24 weeks total may be granted for treatment experienced members with decompensated cirrhosis and recurrent HCV genotype 1, 2, 3, 4, 5 or 6 infection post liver transplantation.

C. HCV and HIV coinfection
Authorization may be granted for members with HCV and HIV coinfection when the criteria for approval of the requested regimen in Section A or B above are met.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. APPENDIX: RIBAVIRIN INELIGIBILITY

RBV ineligibility is defined as one or more of the below:
- Intolerance to RBV
- Pregnant female or male whose female partner is pregnant
- Hemoglobinopathy
- Coadministration with didanosine
- History of significant or unstable cardiac disease

V. REFERENCES

1. Epclusa [package insert]. Foster City, CA: Gilead Sciences, Inc.; June 2021.
2. AASLD/IDSA/IAS–USA. Recommendations for testing, managing, and treating hepatitis C. https://www.hcvguidelines.org. Last changes made September 29, 2021. Accessed October 15, 2021.

Reference number(s)
2609-A

SPECIALTY GUIDELINE MANAGEMENT

EPIDIOLEX (cannabidiol)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Epidiolex is indicated for the treatment of seizures associated with Lennox-Gastaut syndrome (LGS), Dravet syndrome (DS), or tuberous sclerosis complex (TSC) in patients 1 year of age and older.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Seizures associated with Lennox-Gastaut syndrome or Dravet syndrome
Authorization of 12 months may be granted for treatment of seizures associated with Lennox-Gastaut syndrome or Dravet syndrome in members 1 year of age and older.

B. Seizures associated with Tuberous Sclerosis Complex
Authorization of 12 months may be granted for treatment of seizures associated with tuberous sclerosis complex in members 1 year of age and older.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continuation of treatment in members (including new members) 1 year of age or older requesting reauthorization for an indication listed in Section II when the member has achieved or maintained a positive clinical response as evidenced by reduction in frequency or duration of seizures compared with seizure activity prior to initiating Epidiolex.

IV. REFERENCE

1. Epidiolex [package insert]. Palo Alto, CA: Jazz Pharmaceuticals, Inc.; January 2023.

PRIOR AUTHORIZATION CRITERIA

DRUG CLASS	**RETINOID/BENZOYL PEROXIDE COMBINATIONS (TOPICAL)**
BRAND NAME (generic)	**EPIDUO (adapalene/benzoyl peroxide)** **EPIDUO FORTE (adapalene/benzoyl peroxide)**

Status: CVS Caremark® Criteria
Type: Initial Prior Authorization

POLICY

FDA-APPROVED INDICATIONS

Epiduo
Epiduo gel is indicated for the topical treatment of acne vulgaris in patients 9 years of age and older.

Epiduo Forte
Epiduo Forte gel is indicated for the topical treatment of acne vulgaris in adults and pediatric patients 12 years of age and older.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has a diagnosis of acne vulgaris

REFERENCES

1. Epiduo [package insert]. Fort Worth, TX: Galderma Laboratories, L.P.; February 2018.
2. Epiduo Forte [package insert]. Fort Worth, TX: Galderma Laboratories, L.P.; April 2022.
3. Lexicomp Online, Lexi-Drugs Online, Hudson, OH: UpToDate, Inc.; 2023; Accessed March 9, 2023.
4. Micromedex (electronic version). Merative, Ann Arbor, Michigan, USA. Available at: https://www.micromedexsolutions.com/ (cited: 03/09/2023).
5. Zaenglein AL, Pathy AL, Schlosser BJ, et al. Guidelines of Care for the Management of Acne Vulgaris. *J Am Acad Dermatol*. 2016;74(5):945-73.

QUANTITY LIMIT PRIOR AUTHORIZATION CRITERIA

BRAND NAME*
(generic)

AUVI-Q
(epinephrine solution auto-injector)

(epinephrine solution auto-injector)

EPIPEN, EPIPEN JR
(epinephrine solution auto-injector)

SYMJEPI
(epinephrine solution prefilled syringe)

Status: CVS Caremark Criteria
Type: Quantity Limit; Post Limit Prior Authorization ***Ref # 2927-HJ***

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

AUVI-Q

AUVI-Q is indicated in the emergency treatment of allergic reactions (Type I) including anaphylaxis to stinging insects (e.g., order Hymenoptera, which include bees, wasps, hornets, yellow jackets and fire ants) and biting insects (e.g., triatoma, mosquitoes), allergen immunotherapy, foods, drugs, diagnostic testing substances (e.g., radiocontrast media) and other allergens, as well as idiopathic anaphylaxis or exercise-induced anaphylaxis.
AUVI-Q is intended for immediate administration in patients who are determined to be at increased risk for anaphylaxis, including individuals with a history of anaphylactic reactions.
Anaphylactic reactions may occur within minutes after exposure and consist of flushing, apprehension, syncope, tachycardia, thready or unobtainable pulse associated with a fall in blood pressure, convulsions, vomiting, diarrhea and abdominal cramps, involuntary voiding, wheezing, dyspnea due to laryngeal spasm, pruritus, rashes, urticaria or angioedema.
AUVI-Q is intended for immediate self-administration as emergency supportive therapy only and is not a substitute for immediate medical care.

Epipen and Epipen Jr.

EpiPen and EpiPen Jr are indicated in the emergency treatment of allergic reactions (Type I) including anaphylaxis to stinging insects (e.g., order Hymenoptera, which include bees, wasps, hornets, yellow jackets and fire ants) and biting insects (e.g., triatoma, mosquitoes), allergen immunotherapy, foods, drugs, diagnostic testing substances (e.g., radiocontrast media) and other allergens, as well as idiopathic anaphylaxis or exercise-induced anaphylaxis.
EpiPen and EpiPen Jr are intended for immediate administration in patients who are determined to be at increased risk for anaphylaxis, including individuals with a history of anaphylactic reactions.
Anaphylactic reactions may occur within minutes after exposure and consist of flushing, apprehension, syncope, tachycardia, thready or unobtainable pulse associated with a fall in blood pressure, convulsions, vomiting, diarrhea and abdominal cramps, involuntary voiding, wheezing, dyspnea due to laryngeal spasm, pruritus, rashes, urticaria or angioedema.
EpiPen and EpiPen Jr are intended for immediate administration as emergency supportive therapy only and are not a substitute for immediate medical care.

Symjepi

Symjepi is indicated in the emergency treatment of allergic reactions (Type I) including anaphylaxis to stinging insects (e.g., order Hymenoptera, which include bees, wasps, hornets, yellow jackets and fire ants) and biting insects (e.g., triatoma, mosquitoes), allergen immunotherapy, foods, drugs, diagnostic testing substances (e.g., radiocontrast media) and other allergens, as well as idiopathic anaphylaxis or exercise-induced anaphylaxis.
Symjepi is intended for immediate administration in patients who are determined to be at increased risk for anaphylaxis, including individuals with a history of anaphylactic reactions.
Anaphylactic reactions may occur within minutes after exposure and consist of flushing, apprehension, syncope, tachycardia, thready or unobtainable pulse associated with a fall in blood pressure, convulsions, vomiting, diarrhea and abdominal cramps, involuntary voiding, wheezing, dyspnea due to laryngeal spasm, pruritus, rashes, urticaria or angioedema.
Symjepi is intended for immediate administration as emergency supportive therapy only and is not a substitute for immediate medical care.

INITIAL QUANTITY LIMIT**

LIMIT CRITERIA
Limits should accumulate across all drugs and strengths up to highest quantity listed depending on the order the claims are processed.

Drug	1 Month Limit*	3 Month Limit*
epinephrine solution auto-injector	4 auto-injectors / 25 days	12 auto-injectors / 75 days
epinephrine prefilled syringe	4 prefilled syringes / 25 days	12 prefilled syringes / 75 days

**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*

**If the patient is requesting more than the initial quantity limit, the claim will reject with a message indicating that a prior authorization is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

COVERAGE CRITERIA
The requested drug will be covered with prior authorization when the following criteria are met:
- The patient needs more than 4 epinephrine auto-injectors or prefilled syringes per 30 days due to a need for availability in multiple locations or as replacement due to use

Quantity Limits apply.

RATIONALE
Inject epinephrine auto-injection or prefilled syringe intramuscularly or subcutaneously into the anterolateral aspect of the thigh, through clothing if necessary. Each epinephrine device contains a single dose of epinephrine for single-use injection. The prescriber should carefully assess each patient to determine the most appropriate dose of epinephrine, recognizing the life-threatening nature of the reactions for which this drug is indicated. With severe persistent anaphylaxis, repeat injections with an additional epinephrine auto-injection or prefilled syringe may be necessary. More than two sequential doses of epinephrine should only be administered under direct medical supervision.[1-5] The initial limit allows for two anaphylaxis incidences needing a repeat injection per episode per month which may occur without medical supervision.

If the patient is requesting more than the initial quantity limit, then the claim will reject with a message indicating that a prior authorization is required.

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Epinephrine auto-injection or prefilled syringe is indicated in the emergency treatment of allergic reactions (Type I) including anaphylaxis to stinging insects (e.g., order

Hymenoptera, which include bees, wasps, hornets, yellow jackets and fire ants) and biting insects (e.g., triatoma, mosquitoes), allergen immunotherapy, foods, drugs, diagnostic testing substances (e.g., radiocontrast media) and other allergens, as well as idiopathic anaphylaxis or exercise-induced anaphylaxis.[1-3]

Epinephrine auto-injection or prefilled syringe is intended for immediate administration in patients who are determined to be at increased risk for anaphylaxis, including individuals with a history of anaphylactic reactions. Anaphylactic reactions may occur within minutes after exposure and consist of flushing, apprehension, syncope, tachycardia, thready or unobtainable pulse associated with a fall in blood pressure, convulsions, vomiting, diarrhea and abdominal cramps, involuntary voiding, wheezing, dyspnea due to laryngeal spasm, pruritus, rashes, urticaria or angioedema. Epinephrine auto-injection or prefilled syringe is intended for immediate self-administration as emergency supportive therapy only and is not a substitute for immediate medical care.[1-5]

In the event that the patient requires additional quantities of epinephrine auto-injection or prefilled syringe within 30 days, epinephrine auto-injection or prefilled syringe may be covered if criteria are met. The post limit quantity for approval will be an additional 4 auto-injectors or prefilled syringes of epinephrine for a total of 8 auto-injections or prefilled syringes per 30 days.

Due to numerous socio-economic factors, patients may need to have epinephrine auto-injectors or prefilled syringes available in multiple locations (e.g., work, school, multiple caregivers). The choice is left to physician discretion with patient input after consideration of benefit and burden. If a patient had a need to use an injector or prefilled syringe, they could receive a replacement.

The requested drug will be covered with prior authorization when the following criteria are met:
The patient needs more than 4 epinephrine auto-injectors or prefilled syringes per 30 days due to a need for availability in multiple locations or as replacement due to use.

REFERENCES

1. Auvi-Q [package insert]. Richmond, VA: Kaleo, Inc.: September 2019.
2. EpiPen [package insert]. Columbia, MD: Mylan Inc.: December 2020.
3. Symjepi [package insert]. San Diego, CA: Adamis Pharmaceuticals Corp.: July 2021.
4. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2022; Accessed February 21, 2022.
5. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed February 21, 2022.

Written by:	UM Development (SF)
Date Written:	04/2019
Revised:	07/2019, 03/2020 (no clinical changes), 11/2020 (clarified accumulation), 03/2021. (DRS) 03/2022(no clinical changes)
Reviewed:	Medical Affairs (GAD) 04/2019, 07/2019, (CHART) 03/26/2020, 03/25/2021, (CHART) 03/31/22 External Review: 08/2019, 06/2020, 06/2021, 06/2022

CRITERIA FOR APPROVAL

1	Does the patient need more than 4 epinephrine auto-injectors or prefilled syringes per 30 days due to a need for availability in multiple locations or as replacement due to use? [If no, then no further questions.]	Yes	No
2	Does the patient require more than the plan allowance of 8 epinephrine auto-injectors or prefilled syringes per month? [RPh Note: If yes, then deny and enter a partial approval for 8 auto-injectors or prefilled syringes per month of epinephrine auto-injector.]	Yes	No

Mapping Instructions			
	Yes	**No**	**DENIAL REASONS – DO NOT USE FOR MEDICARE PART D**
1.	Go to 2	Deny	You do not meet the requirements of your plan. Your plan covers additional quantities of this drug when you meet any of these conditions: -You need to have epinephrine auto-injectors or prefilled syringes in multiple locations -You need to replace used epinephrine auto-injectors or prefilled syringes Your request has been denied based on the information we have. [Short Description: No need to have in multiple locations or replacement due to use]
2.	Deny	Approve, 12 months, 8 auto-injectors or prefilled syringes per month of epinephrine auto-injector or prefilled syringes /25 days or 24 auto-injectors or prefilled syringes /75 days*	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 8 auto-injectors or prefilled syringes per month of epinephrine. Your request has been partially approved. You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity]

**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*

PRIOR AUTHORIZATION CRITERIA

BRAND NAME
(generic)

AUVI-Q
(epinephrine solution auto-injector)

(epinephrine solution auto-injector)

EPIPEN, EPIPEN JR
(epinephrine solution auto-injector)

SYMJEPI
(epinephrine solution prefilled syringe)

Status: Client Requested Criteria
Type: Quantity Limit; Post Limit Prior Authorization ***Ref # C17721-HJ***

INITIAL QUANTITY LIMIT**

Drug	300 Day Limit*
epinephrine solution auto-injector	6 auto-injectors
epinephrine prefilled syringe	6 prefilled syringes

**If the patient is requesting more than the initial quantity limit, the claim will reject with a message indicating that a prior authorization is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

CRITERIA FOR APPROVAL

1	Does the patient need more than 6 epinephrine auto-injectors or prefilled syringes per 300 days due to a need for availability in multiple locations or as replacement due to use?	Yes	No
2	Does the patient require more than the plan allowance of 10 epinephrine auto-injectors or prefilled syringes per 300 days?	Yes	No

REFERENCES

1. Carefirst Prior Authorization Approval Policy.

Written by: UM Development (ME)
Date Written: 01/2020
Revised:
Reviewed: Medical Affairs: (SG) 01/2020

CVS caremark™

QUANTITY LIMIT PRIOR AUTHORIZATION CRITERIA

BRAND NAME
(generic)

AUVI-Q
(epinephrine solution auto-injector)

(epinephrine solution auto-injector)

EPIPEN, EPIPEN JR
(epinephrine solution auto-injector)

SYMJEPI
(epinephrine solution prefilled syringe)

Status: CVS Caremark Criteria
Type: Quantity Limit; Post Limit Prior Authorization

POLICY

FDA-APPROVED INDICATIONS

AUVI-Q

AUVI-Q is indicated in the emergency treatment of allergic reactions (Type I) including anaphylaxis to stinging insects (e.g., order Hymenoptera, which include bees, wasps, hornets, yellow jackets and fire ants) and biting insects (e.g., triatoma, mosquitoes), allergen immunotherapy, foods, drugs, diagnostic testing substances (e.g., radiocontrast media) and other allergens, as well as idiopathic anaphylaxis or exercise-induced anaphylaxis.
AUVI-Q is intended for immediate administration in patients who are determined to be at increased risk for anaphylaxis, including individuals with a history of anaphylactic reactions.
Anaphylactic reactions may occur within minutes after exposure and consist of flushing, apprehension, syncope, tachycardia, thready or unobtainable pulse associated with a fall in blood pressure, convulsions, vomiting, diarrhea and abdominal cramps, involuntary voiding, wheezing, dyspnea due to laryngeal spasm, pruritus, rashes, urticaria or angioedema.
AUVI-Q is intended for immediate self-administration as emergency supportive therapy only and is not a substitute for immediate medical care.

Epinephrine Injection (generic for Adrenaclick)

Epinephrine injection is indicated in the emergency treatment of allergic reactions (Type I) including anaphylaxis to stinging insects (e.g., order Hymenoptera, which includes bees, wasps, hornets, yellow jackets and fire ants), and biting insects (e.g., triatoma, mosquitoes), allergen immunotherapy, foods, drugs, diagnostic testing substances (e.g., radiocontrast media), and other allergens, as well as idiopathic anaphylaxis or exercise-induced anaphylaxis.
Epinephrine injection is intended for immediate administration in patients who are determined to be at increased risk for anaphylaxis, including individuals with a history of anaphylactic reactions.
Anaphylactic reactions may occur within minutes after exposure and consist of flushing, apprehension, syncope, tachycardia, thready or unobtainable pulse associated with a fall in blood pressure, convulsions, vomiting, diarrhea and abdominal cramps, involuntary voiding, wheezing, dyspnea due to laryngeal spasm, pruritus, rashes, urticaria, or angioedema.
Epinephrine injection is intended for immediate administration as emergency supportive therapy only and is not a replacement or substitute for immediate medical care.

Epipen and Epipen Jr.

EpiPen and EpiPen Jr are indicated in the emergency treatment of allergic reactions (Type I) including anaphylaxis to stinging insects (e.g., order Hymenoptera, which include bees, wasps, hornets, yellow jackets and fire ants) and biting

insects (e.g., triatoma, mosquitoes), allergen immunotherapy, foods, drugs, diagnostic testing substances (e.g., radiocontrast media) and other allergens, as well as idiopathic anaphylaxis or exercise-induced anaphylaxis.
EpiPen and EpiPen Jr are intended for immediate administration in patients who are determined to be at increased risk for anaphylaxis, including individuals with a history of anaphylactic reactions.
Anaphylactic reactions may occur within minutes after exposure and consist of flushing, apprehension, syncope, tachycardia, thready or unobtainable pulse associated with a fall in blood pressure, convulsions, vomiting, diarrhea and abdominal cramps, involuntary voiding, wheezing, dyspnea due to laryngeal spasm, pruritus, rashes, urticaria or angioedema.
EpiPen and EpiPen Jr are intended for immediate administration as emergency supportive therapy only and are not a substitute for immediate medical care.

Symjepi
Symjepi is indicated in the emergency treatment of allergic reactions (Type I) including anaphylaxis to stinging insects (e.g., order Hymenoptera, which include bees, wasps, hornets, yellow jackets and fire ants) and biting insects (e.g., triatoma, mosquitoes), allergen immunotherapy, foods, drugs, diagnostic testing substances (e.g., radiocontrast media) and other allergens, as well as idiopathic anaphylaxis or exercise-induced anaphylaxis.
Symjepi is intended for immediate administration in patients who are determined to be at increased risk for anaphylaxis, including individuals with a history of anaphylactic reactions.
Anaphylactic reactions may occur within minutes after exposure and consist of flushing, apprehension, syncope, tachycardia, thready or unobtainable pulse associated with a fall in blood pressure, convulsions, vomiting, diarrhea and abdominal cramps, involuntary voiding, wheezing, dyspnea due to laryngeal spasm, pruritus, rashes, urticaria or angioedema.
Symjepi is intended for immediate administration as emergency supportive therapy only and is not a substitute for immediate medical care.

INITIAL QUANTITY LIMIT**

LIMIT CRITERIA
Limits should accumulate across all drugs and strengths up to highest quantity listed depending on the order the claims are processed.

Drug	1 Month Limit*	3 Month Limit*
epinephrine solution auto-injector	4 auto-injectors / 25 days	12 auto-injectors / 75 days
epinephrine prefilled syringe	4 prefilled syringes / 25 days	12 prefilled syringes / 75 days

**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*

**If the patient is requesting more than the initial quantity limit, the claim will reject with a message indicating that a prior authorization is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

COVERAGE CRITERIA
The requested drug will be covered with prior authorization when the following criteria are met:
- The patient needs more than 4 epinephrine auto-injectors or prefilled syringes per 30 days due to a need for availability in multiple locations or as replacement due to use

Quantity Limits apply.
8 auto-injectors or prefilled syringes / 25 days*
**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*

REFERENCES

1. Auvi-Q [package insert]. Richmond, VA: Kaleo, Inc.: September 2019.
2. EpiPen [package insert]. Morgantown, WV: Mylan Specialty L.P.: December 2020.

3. Symjepi [package insert]. Louisville, KY: USWM, LLC: July 2021.
4. Epinephrine [package insert]. Bridgewater, NJ: Amneal Pharmaceuticals LLC.: January 2021.
5. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2022; Accessed December 29, 2022.
6. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed December 29, 2022.

Reference number(s)
1785-A

SPECIALTY GUIDELINE MANAGEMENT

ERIVEDGE (vismodegib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication
Erivedge is indicated for the treatment of adults with metastatic basal cell carcinoma, or with locally advanced basal cell carcinoma that has recurred following surgery or who are not candidates for surgery, and who are not candidates for radiation.

B. Compendial Uses
1. Basal cell carcinoma
2. Adult medulloblastoma

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Basal Cell Carcinoma (BCC)
Authorization of 12 months may be granted for treatment of advanced, diffuse (e.g., Gorlin syndrome), recurrent, or metastatic basal cell carcinoma.

B. Adult Medulloblastoma
Authorization of 12 months may be granted for treatment of recurrent adult medulloblastoma in patients who have received prior systemic therapy and whose tumor(s) have mutations in the sonic hedgehog pathway, as a single agent.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

IV. REFERENCES

1. Erivedge [package insert]. South San Francisco, CA: Genentech USA, Inc.; July 2020.
2. The NCCN Drugs & Biologics Compendium™ © 2022 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed November 1, 2022.

Reference number(s)
2498-A

SPECIALTY GUIDELINE MANAGEMENT

ERLEADA (apalutamide)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. Erleada is indicated for the treatment of patients with non-metastatic castration-resistant prostate cancer.
   2. Erleada is indicated for the treatment of patients with metastatic castration-sensitive prostate cancer.

B. Compendial Use
   Prostate Cancer

All other indications are considered experimental/investigational and not medically necessary.

II. EXCLUSIONS

Coverage will not be provided if the requested medication is used in combination with a second-generation oral anti-androgen (e.g., enzalutamide [Xtandi]) or an oral androgen metabolism inhibitor (e.g., abiraterone acetate [Zytiga]).

III. CRITERIA FOR INITIAL APPROVAL

1. Non-metastatic castration-resistant prostate cancer
Authorization of 12 months may be granted for treatment of non-metastatic castration-resistant prostate cancer when the member has had a bilateral orchiectomy or will be using the requested medication in combination with a gonadotropin-releasing hormone (GnRH) agonist or degarelix.

2. Metastatic castration-sensitive prostate cancer
Authorization of 12 months may be granted for treatment of metastatic castration-sensitive prostate cancer when the member has had a bilateral orchiectomy or will be using the requested medication in combination with a gonadotropin-releasing hormone (GnRH) agonist or degarelix.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

V. REFERENCES

1. Erleada [package insert]. Horsham, PA: Janssen Products, LP; February 2023.
2. The NCCN Drugs & Biologics Compendium™ © 2023 National Comprehensive Cancer Network, Inc. https://www.nccn.org Accessed August 6, 2023.

Reference number(s)
4074-A

SPECIALTY GUIDELINE MANAGEMENT

EVRYSDI (risdiplam)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Evrysdi is indicated for the treatment of spinal muscular atrophy (SMA) in pediatric and adult patients.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

A. Initiation of therapy:
   1. Deletion or mutation at the SMN1 allele confirmed by genetic testing
   2. Medical records (e.g., chart notes, laboratory values) of the baseline assessment for at least one of the following assessment tools (based on patient age and motor ability) to establish baseline motor ability:
      i. Hammersmith Infant Neurological Exam Part 2 (HINE-2)
      ii. Hammersmith Functional Motor Scale Expanded (HFMSE)
      iii. Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP-INTEND)
      iv. Motor Function Measure 32 (MFM32)
      v. Bayley Scales of Infant and Toddler Development – Third Edition (BSID-III)

B. Continuation of therapy:
   Medical records (e.g., chart notes, laboratory values) of the most recent (less than 1 month prior to continuation request) assessment by at least one of the following assessments:
      i. HINE-2
      ii. HFMSE
      iii. CHOP-INTEND
      iv. MFM32
      v. BSID-III
      vi. For members prescribed Evrysdi due to clinical worsening after receiving gene replacement therapy (e.g., Zolgensma): documentation of the impact of Evrysdi therapy (e.g., impact on motor milestones)

III. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with a physician who specializes in treatment of spinal muscular atrophy.

IV. CRITERIA FOR INITIAL APPROVAL

Spinal Muscular Atrophy (SMA)
Authorization of 12 months may be granted for treatment of SMA when all of the following criteria are met:

A. Member has type 1, type 2, or type 3 SMA
B. There is genetic documentation of 5q SMA homozygous gene mutation, homozygous gene deletion, or compound heterozygote
C. The member is 25 years of age or younger at the initiation of treatment
D. Member is not dependent on either of the following:
    1. Invasive ventilation or tracheostomy
    2. Use of non-invasive ventilation beyond naps and nighttime sleep
E. Member meets one of the following criteria:
    1. Member has not previously received gene replacement therapy for SMA (e.g., Zolgensma), or
    2. Member has previously received gene replacement therapy for SMA (e.g., Zolgensma) and has experienced a worsening in clinical status since receiving gene replacement therapy as demonstrated by a decline of minimally clinical important difference from highest score achieved or baseline on one of the following exams (based on member age, motor ability, and specific exam)
        i. HINE-2: Decline of at least 2 points on kicking and 1 point on any other milestone (excluding voluntary grasp)
        ii. HFMSE: Decline of at least 3 points
        iii. CHOP-INTEND: Decline of at least 4 points
        iv. MFM32: Decline from baseline
        v. BSID-III: Inability to sit without support for more than 5 seconds per item 22 of test
F. Member will not use Evrysdi and Spinraza concomitantly
G. Member's daily dose will not exceed the following:
    1. Members less than 2 months of age: 0.15 mg/kg
    2. Members 2 months to less than 2 years of age: 0.2 mg/kg
    3. Members 2 years of age and older weighing less than 20 kg: 0.25 mg/kg
    4. Members 2 years of age and older weighing 20 kg or more: 5 mg

V. CONTINUATION OF THERAPY

Note: Members who were previously established on Evrysdi and subsequently administered gene replacement therapy (e.g., Zolgensma) must meet all initial criteria prior to re-starting therapy on Evrysdi.

Authorization of 12 months may be granted for continued treatment of SMA when all of the following criteria are met:

A. Member has type 1, type 2, or type 3 SMA
B. Member is not dependent on either of the following:
    1. Invasive ventilation or tracheostomy
    2. Use of non-invasive ventilation beyond naps and nighttime sleep
C. Submission of medical records (e.g., chart notes, laboratory values) of the most recent (less than 1 month prior to continuation request) assessment documenting a positive clinical response from pretreatment baseline to Evrysdi therapy, as demonstrated by at least one of the following assessments:
    1. HINE-2
        i. One of the following:
            a. Member exhibited improvement or maintenance of previous improvement of at least a 2-point (or maximal score) increase in ability to kick; *or*

b. Member exhibited improvement or maintenance of previous improvement of at least a 1-point (or maximal score) increase in any other HINE-2 milestone (e.g., head control, rolling, sitting, crawling, standing, or walking) excluding voluntary grasp; *and*

ii. One of the following:

a. Member exhibited improvement or maintenance of previous improvement in more HINE-2 motor milestones than worsening (net positive improvement); *or*

b. Member achieved and maintained any new motor milestones when they would otherwise be unexpected to do so (e.g., sit or stand unassisted, walk)

2. HFMSE
   i. One of the following:
      a. Member exhibited improvement or maintenance of previous improvement of at least a 3-point increase in score; *or*
      b. Member has achieved and maintained any new motor milestone from pretreatment baseline when they would otherwise be unexpected to do so
3. CHOP-INTEND
   i. One of the following:
      a. Member exhibited improvement or maintenance of previous improvement of at least a 4-point increase in score; *or*
      b. Member has achieved and maintained any new motor milestone from pretreatment baseline when they would otherwise be unexpected to do so
4. MFM32
   i. Member has experienced an increase in their MFM32 score from baseline and that increase correlates with a clinically significant functional improvement
5. BSID-III
   i. Member exhibited the ability to sit without support for at least 5 seconds after 12 months of treatment
6. Member was prescribed Evrysdi due to clinical worsening after receiving gene replacement therapy (e.g., Zolgensma) and there is documentation of stabilization or improvement in clinical status with Evrysdi therapy (e.g., impact on motor milestones).

D. Member will not use Evrysdi and Spinraza concomitantly
E. Member's daily dose will not exceed the following:
   1. Members less than 2 months of age: 0.15 mg/kg
   2. Members 2 months to less than 2 years of age: 0.2 mg/kg
   3. Members 2 years of age and older weighing less than 20 kg: 0.25 mg/kg
   4. Members 2 years of age and older weighing 20 kg or more: 5 mg

VI. REFERENCES

1. Evrysdi [package insert]. South San Francisco, CA: Genentech, Inc; May 2022.
2. Arnold WD, Kassar D, Kissel JT, et al. Spinal muscular atrophy: diagnosis and management in a new therapeutic era. *Muscle & Nerve*. 2015;51(2):157-167.
3. Burgunder JM, Schols L, Baets J, et al. EFNS guidelines for the molecular diagnosis of neurogenetic disorders: motoneuron, peripheral nerve and muscle disorders. *European J Neurol*. 2011;18:207-217.
4. Wang CH, Finkel RS, Bertini ES, et al. Consensus statement for standard care in spinal muscular atrophy. *J Child Neurol*. 2007;22(8):1027-1049.

Reference number(s)
4074-A

QUANTITY LIMIT PRIOR AUTHORIZATION CRITERIA

DRUG CLASS	**TOPICAL ANTIFUNGALS**
BRAND NAME (generic)	**EXELDERM (sulconazole cream and solution)**

Status: CVS Caremark® Criteria
Type: Quantity Limit; Post Limit Prior Authorization

POLICY

FDA-APPROVED INDICATIONS

Exelderm Cream
Exelderm (sulconazole nitrate, USP) cream, 1.0% is an antifungal agent indicated for the treatment of tinea pedis (athlete's foot), tinea cruris, and tinea corporis caused by *Trichophyton rubrum, Trichophyton mentagrophytes, Epidermophyton floccosum,* and *Microsporum canis*,* and for the treatment of tinea versicolor.

*Efficacy for this organism in the organ system was studied in fewer than ten infections.

Exelderm Solution
Exelderm (sulconazole nitrate, USP) solution, 1.0% is a broad-spectrum antifungal agent indicated for the treatment of tinea cruris and tinea corporis caused by *Trichophyton rubrum*, *Trichophyton mentagrophytes*, *Epidermophyton floccosum*, and *Microsporum canis*; and for the treatment of tinea versicolor. Effectiveness has not been proven in tinea pedis (athlete's foot).

Symptomatic relief usually occurs within a few days after starting Exelderm solution and clinical improvement usually occurs within one week.

INITIAL QUANTITY LIMIT**

INITIAL LIMIT QUANTITY
Limits should accumulate across all drugs and strengths up to highest quantity listed depending on the order the claims are processed. Accumulation does not apply if limit is coded for daily dose.

Drug	1 Month Limit*	3 Month Limit*
Exelderm Cream (sulconazole cream)	60 gm / 25 days	Does Not Apply
Exelderm Solution (sulconazole solution)	60 mL / 25 days	Does Not Apply

** The duration of 25 days is used for a 30-day fill period to allow time for refill processing.*
**These drugs are for short-term acute use; therefore, the mail limit will be the same as the retail limit. The intent is for prescriptions of the requested drug to be filled 1 month at a time, even if filled at mail order; there should be no 3-month supplies filled.*

**If the patient is requesting more than the initial quantity limit, the claim will reject with a message indicating that a prior authorization is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- Exelderm solution is being prescribed for any of the following: A) Tinea cruris, B) Tinea corporis, C) Tinea versicolor

  OR
- Exelderm cream is being prescribed for any of the following: A) Tinea cruris, B) Tinea corporis, C) Tinea versicolor, D) Tinea pedis

AND

- The requested drug is not being used in a footbath

Quantity Limits apply.
Exelderm (sulconazole) cream: 120 gm per 25 days*
Exelderm (sulconazole) solution: 120 mL per 25 days*
**The duration of 25 days is used for a 30-day fill period to allow time for refill processing. These drugs are for short-term acute use; therefore, the mail limit will be the same as the retail limit. The intent is for prescriptions of the requested drug to be filled one month at a time, even if filled at mail order; there should be no 3-month supplies filled.*

Duration of Approval (DOA):

- 2929-HJ: DOA: 3 months

REFERENCES

1. Exelderm Cream [package insert]. Scottsdale, AZ: Journey Medical Corp.; March 2021.
2. Exelderm Solution [package insert]. Scottsdale, AZ: Journey Medical Corp.; March 2021.
3. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Waltham, MA: UpToDate, Inc.; 2023. https://online.lexi.com. Accessed July 5, 2023.
4. Micromedex (electronic version). Merative, Ann Arbor, Michigan, USA. Available at: https://www.micromedexsolutions.com/ (cited: 07/05/2023).
5. Eichenfield L, Tom W, Berger T, et al. Guidelines of Care for the Management of Atopic Dermatitis Section 2. Management and Treatment of Atopic Dermatitis with Topical Therapies. J Am Acad Dermatol 2014; 71:116-32.
6. Elmets C, Korman N, Prater E, et al. Joint AAD–NPF Guidelines of Care for the Management and Treatment of Psoriasis with Topical Therapy and Alternative Medicine Modalities for Psoriasis Severity Measures. J Am Acad Dermatol 2021; 84:432-70.
7. U.S. Department of Health & Human Services. Burn Triage and Treatment – Thermal Injuries. Chemical Hazards Emergency Medical Management. August 16, 2021. Available at: https://chemm.hhs.gov/burns.htm. Accessed July 5, 2023.
8. Moore RA, Waheed A, Burns B. Rule of Nines. 2022 May 30. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan. Available at: https://www.ncbi.nlm.nih.gov/books/NBK513287/. Accessed July 5, 2023

PRIOR AUTHORIZATION CRITERIA

BRAND NAME*
(generic)

EXELON
(rivastigmine)

Status: CVS Caremark Criteria ***Ref # 85-A***
Type: Initial Prior Authorization ***Ref # 509-A***

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Alzheimer's Disease

Exelon Patch is indicated for the treatment of dementia of the Alzheimer's type (AD). Efficacy has been demonstrated in patients with mild, moderate, and severe Alzheimer's disease.
Rivastigmine tartrate capsules are indicated for the treatment of mild to moderate dementia of the Alzheimer's type (AD).

Parkinson's Disease Dementia

Exelon Patch and **rivastigmine tartrate capsules** are indicated for the treatment of mild to moderate dementia associated with Parkinson's disease (PDD).

Compendial Uses

Dementia with Lewy bodies[3,5]

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has any of the following diagnoses: A) dementia of the Alzheimer's type, B) mild to moderate dementia associated with Parkinson's disease, C) dementia with Lewy bodies

AND

- If the request is for continuation of therapy, the medication continues to provide benefit to the patient
  [Note: If slowing decline of cognitive function is no longer a goal, or if the patient is rapidly declining, treatment with the medication is no longer appropriate.]
  OR
- If the request is NOT for continuation of therapy, the diagnosis is supported by a validated cognitive assessment within the past 12 months

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Exelon Patch (rivastigmine transdermal system) is indicated for the treatment of dementia of the Alzheimer's type (AD); efficacy has been demonstrated in patients with mild, moderate, and severe AD. Exelon Patch is also indicated for the treatment of mild to moderate dementia associated with Parkinson's disease (PDD). Rivastigmine tartrate capsules are indicated for the treatment of mild to moderate dementia of the Alzheimer's type and mild to moderate dementia associated with Parkinson's disease. The 9.5mg/24 hour Exelon Patch gave approximately the same exposure as that provided by an oral rivastigmine dose of 6 mg twice daily (i.e., 12mg/day).[1,2]

Rivastigmine has also been effective in treating dementia with Lewy bodies. In a double-blind, placebo-controlled trial, treatment with rivastigmine (6 to 12 mg daily) led to significant and clinically relevant improvements in behavior in patients

diagnosed with probable Lewy-body dementia. Almost twice as many patients receiving rivastigmine, compared to placebo, experienced at least a 30% improvement from baseline (63% versus 30%, respectively). These patients also experienced less apathy, less anxiousness, and had fewer delusions and hallucinations than the placebo group. Additionally, patients receiving rivastigmine performed faster and better on computerized cognitive and neurological tests compared to those receiving placebo. The overall safety and tolerability of the drug was judged as acceptable.[3,5] Furthermore, per the American Psychiatric Association practice guidelines for the treatment of patients with Alzheimer's disease and other dementias, cholinesterase inhibitors could be considered for patients with dementia with Lewy bodies.[6]

The treatment of patients with dementia should be based on a thorough psychiatric, neurological, and general medical evaluation of the nature and cause of the cognitive deficits and associated noncognitive symptoms.[6] According to the Diagnostic and Statistical Manual of Mental Disorders 5th Edition (DSM-5), diagnostic criteria for Major Neurocognitive Disorder (dementia) or Mild Neurocognitive Disorder includes evidence of cognitive decline from a previous level of performance in one or more cognitive domains based on: 1) Concern of the individual, a knowledgeable informant, or the clinician that there has been a decline in cognitive function and 2) An impairment in cognitive performance, preferably documented by standardized neuropsychological testing or, in its absence, another quantified clinical assessment.[8] Tests commonly used in clinical studies to evaluate the efficacy of available therapies in the treatment of Alzheimer's dementia, the treatment of Parkinson's Disease Dementia, and the treatment of dementia with Lewy bodies include but are not limited to, the Mini-Mental State Exam (MMSE) and the Alzheimer's Disease Assessment Scale—Cognitive Subscale (ADAS-Cog).[1-7,9] The decision to initiate therapy should be based on evaluation of the benefits and risks associated with an individual patient. In more advanced dementia, decision makers may not view stabilization or slowing of decline as a desirable goal if quality of life is judged to be poor. Cholinesterase inhibitors have known adverse events, and the decision to manage patients with dementia should balance harms against benefit.[9] Therefore, prior to initiating therapy with rivastigmine, patients should receive a validated cognitive assessment within the past 12 months.

Ongoing assessment includes routine monitoring of the development and change in cognitive and noncognitive psychiatric symptoms and their response to intervention. In order to offer prompt treatment, enhance safety, and provide timely advice to the patient and family, it is usually necessary to see patients in routine follow-up at least every 3 to 6 months.[6] Currently, the available evidence is insufficient to determine the optimal duration of therapy of cholinesterase inhibitors. A beneficial effect (e.g., improvement, stabilization, slowing of decline), if any, would generally be observed within 3 months on the basis of duration of trials.[9] Therefore, if the request is for continuation of therapy, the medication must continue to provide benefit to the patient.

No medication treatment has been shown to delay the progression of neurodegeneration. If a patient is declining rapidly despite taking a cholinesterase inhibitor, they may be considered a medication non-responder and the medication can be discontinued. Additionally, if slowing decline is no longer a goal, treatment with a cholinesterase inhibitor is no longer appropriate.[6,9]

REFERENCES

1. Exelon Patch [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation. June 2020.
2. Rivastigmine Tartrate Capsules [package insert]. Berlin, CT: Breckenridge Pharmaceutical, Inc. June 2020.
3. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed April 28, 2022.
4. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2022; Accessed April 28, 2022.
5. McKeith I, Del Ser T, Spano P, et al. Efficacy of Rivastigmine in Dementia with Lewy Bodies: A Randomised, Double-Blind, Placebo-Controlled International Study. *Lancet.* 2000;356:2031-36.
6. Rabins P, Blacker D, Rovner B, et al. Practice Guideline for the Treatment of Patients with Alzheimer's Disease and Other Dementias, Second Edition. *Am J Psychiatry*. 2007;164(12S):1-56.
7. Rabins P, Rovner B, Rummans T, et al. Guideline Watch (October 2014): Practice Guideline for the Treatment of Patients with Alzheimer's Disease and Other Dementias. 2014;1-26.
8. American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition. Arlington, VA, American Psychiatric Association, 2013.

9. Qaseem A, Snow V, Cross T, et al. Current Pharmacological Treatment of Dementia: A Clinical Practice Guideline from the American College of Physicians and the American Academy of Family Physicians. *Ann Intern Med.* 2008;148:370-78.

Written by: UM Development (LS)
Date Written: 05/2000
Revised: 06/2001; (AD) 12/2002; (MG) 10/2003; (NB) 12/2004; (AK) 12/2005; (NB) 06/2006, 07/2006 (new indication); (AM) 10/2007 (new non-MDC version), 05/2008, 05/2009, (TM) 05/2010; (RP) 07/2011, 06/2012, 08/2012; (NB)10/2012 (extended duration); (RP) 06/2013, 06/2014, 05/2015 (combined with MDC-2 ref#); (JH) 05/2016 (no clinical changes); (RP) 05/2017, 05/2018 (no clinical changes); (ME) 05/2019 (removed MDC from title/document); (PM) 05/2020 (no clinical changes), 12/2020 (added continuation of therapy), 05/2021 (no clinical changes); (CJH) 05/2022 (no clinical changes)
Reviewed: CRC 05/2000, 07/30/2001, 12/2002, 11/2003; CDPR/Medical Affairs (MM): 12/2004, 12/2005, 06/2006; (WF): 10/2007, 05/2008, 05/2009, 05/2010; (KP) 07/2011, 06/2012, 10/2012, 07/2013; (LMS) 06/2014; (DNC) 05/2015; (ABM) 05/2017; (CHART) 05/28/20, 01/21/21, 05/27/21, 05/26/22
External Review: 12/2002, 12/2003, 01/2005, 02/2006, 08/2006, 12/2006, 02/2008, 08/2008, 10/2009, 09/2010, 10/2011, 10/2012, 02/2013, 10/2013, 02/2014, 10/2014, 10/2015, 10/2016, 10/2017, 10/2018, 10/2019, 10/2020, 04/2021, 10/2021, 08/2022

CRITERIA FOR APPROVAL

1	Does the patient have any of the following diagnoses: A) dementia of the Alzheimer's type, B) mild to moderate dementia associated with Parkinson's disease, C) dementia with Lewy bodies? [If no, then no further questions.]	Yes	No
2	Is this request for continuation of therapy? [If no, then skip to question 4.]	Yes	No
3	Does the medication continue to provide benefit to the patient? [Note: If slowing decline of cognitive function is no longer a goal, or if the patient is rapidly declining, treatment with the medication is no longer appropriate.] [No further questions.]	Yes	No
4	Is the diagnosis supported by a validated cognitive assessment within the past 12 months?	Yes	No

Mapping Instructions (85-A)			
	Yes	**No**	**DENIAL REASONS – DO NOT USE FOR MEDICARE PART D**
1.	Go to 2	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have any of these conditions: – Dementia of the Alzheimer's type – Mild to moderate dementia associated with Parkinson's disease – Dementia with Lewy bodies Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]
2.	Go to 3	Go to 4	
3.	Approve, 36 Months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when it continues to provide benefit to you. Your request has been denied based on the information we have. [Short Description: No continued benefit]

4.	Approve, 36 Months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have had an assessment in the past 12 months that supports your condition. Your request has been denied based on the information we have. [Short Description: No recent assessment]

Mapping Instructions (509-A)			
	Yes	**No**	**DENIAL REASONS – DO NOT USE FOR MEDICARE PART D**
1.	Go to 2	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have any of these conditions: – Dementia of the Alzheimer's type – Mild to moderate dementia associated with Parkinson's disease – Dementia with Lewy bodies Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]
2.	Go to 3	Go to 4	
3.	Approve, 12 Months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when it continues to provide benefit to you. Your request has been denied based on the information we have. [Short Description: No continued benefit]
4.	Approve, 12 Months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have had an assessment in the past 12 months that supports your condition. Your request has been denied based on the information we have. [Short Description: No recent assessment]

Reference number(s)
4941-A

SPECIALTY GUIDELINE MANAGEMENT

EXKIVITY (mobocertinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication
Exkivity is a kinase inhibitor indicated for the treatment of adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) exon 20 insertion mutations, as detected by an FDA-approved test, whose disease has progressed on or after platinum-based chemotherapy.

B. Compendial Use
Non-small cell lung cancer

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: test results showing the presence of EGFR exon 20 insertion mutations

III. CRITERIA FOR INITIAL APPROVAL

Non-Small Cell Lung Cancer (NSCLC)
Authorization of 12 months may be granted for treatment of NSCLC when all of the following criteria are met:
1. Member has locally advanced, recurrent, or metastatic disease
2. Member has EGFR exon 20 insertion mutations
3. Disease has progressed on or after platinum-based chemotherapy
4. The requested medication is used as a single agent

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

V. REFERENCES

1. Exkivity [package insert]. Lexington, MA: Takeda Pharmaceuticals America, Inc; March 2023.
2. The NCCN Drugs & Biologics Compendium® © 2023 National Comprehensive Cancer Network, Inc. Available at: https://www.nccn.org. Accessed July 6, 2023.

QUANTITY LIMIT PRIOR AUTHORIZATION CRITERIA

BRAND NAME
(generic)

EXTINA
(ketoconazole)

Status: CVS Caremark® Criteria
Type: Quantity Limit; Post Limit Prior Authorization

POLICY

FDA-APPROVED INDICATIONS

Extina is indicated for the topical treatment of seborrheic dermatitis in immunocompetent adults and children 12 years of age and older.

Limitations of Use
Safety and efficacy of Extina for treatment of fungal infections have not been established.

INITIAL QUANTITY LIMIT**

LIMIT CRITERIA

Drug	1 Month Limit*	3 Month Limit*
Extina (ketoconazole 2% topical foam)	100 grams / 25 days	Does Not Apply*

**The duration of 25 days is used for a 30-day fill period to allow time for refill processing.*
**This drug is for short-term acute use; therefore, the mail limit will be the same as the retail limit. The intent is for prescriptions of the requested drug to be filled one month at a time, even if filled at mail order; there should be no 3 month supplies filled.*

**If the patient is requesting more than the initial quantity limit, the claim will reject with a message indicating that a prior authorization is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for the treatment of seborrheic dermatitis

AND

- The requested drug is not being used in a footbath

Quantity Limits apply.
200 grams per 25 days*, 3 month limit does not apply

** The duration of 25 days is used for a 30-day fill period to allow time for refill processing. These drugs are for short-term acute use; therefore, the mail limit will be the same as the retail limit. The intent is for prescriptions of the requested drug to be filled one month at a time, even if filled at mail order; there should be no 3 month supplies filled.*

REFERENCES

1. Extina [package insert]. Morgantown, WV: Mylan Pharmaceuticals Inc.; August 2018.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Waltham, MA: UpToDate, Inc.; 2023. https://online.lexi.com. Accessed March 21, 2023.
3. Micromedex (electronic version). Merative, Ann Arbor, Michigan, USA. Available at: https://www.micromedexsolutions.com/ (cited: 03/21/2023).
4. Eichenfield L, Tom W, Berger T, et al. Guidelines of Care for the Management of Atopic Dermatitis Section 2. Management and Treatment of Atopic Dermatitis with Topical Therapies. *J Am Acad Dermatol*. 2014;71:116-32.
5. U.S. Department of Health & Human Services. Burn Triage and Treatment – Thermal Injuries. Chemical Hazards Emergency Medical Management. August 16, 2021. Available at: https://chemm.hhs.gov/burns.htm. Accessed March 6, 2023.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME*
(generic)

EYSUVIS
(loteprednol etabonate ophthalmic suspension 0.25%)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization with Quantity Limits ***Ref # 4348-C***

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Eysuvis is a corticosteroid indicated for the short-term (up to two weeks) treatment of the signs and symptoms of dry eye disease.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for the treatment of the signs and symptoms of dry eye disease
  AND
- The requested drug is being prescribed for short-term use (up to two weeks)
  AND
- The patient has experienced an inadequate treatment response to an artificial tears product
  OR
- The patient has experienced an intolerance to an artificial tears product
  OR
- The patient has a contraindication that would prohibit a trial of an artificial tears product

Quantity Limits apply.

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Eysuvis is a corticosteroid indicated for the short-term (up to two weeks) treatment of the signs and symptoms of dry eye disease.[1]

The Preferred Practice Pattern (PPP) for Dry Eye Syndrome by the American Academy of Ophthalmology classifies dry eye as mild, moderate, and severe based on both symptoms and signs, but with an emphasis on symptoms over signs. The PPP notes that this classification is imprecise because characteristics at each level overlap due to the nature of dry eye disease. Dry eye syndrome is also categorized into one of two forms, aqueous tear deficiency and evaporative dry eye, which coexist in the majority of the patients with the disease. Ocular lubricants, such as artificial tear substitutes, are a Step-1 treatment option for dry eye. Artificial tear substitutes have been found to be a safe and effective treatment for dry eye. Topical corticosteroids, like Eysuvis, are a Step-2 treatment option.[5] Therefore, coverage for Eysuvis will be provided for patients with dry eye disease who have experienced an inadequate treatment response or intolerance to, or who have a contraindication that would prohibit a trial of an artificial tears product.

Dosage for Eysuvis is one to two drops into each eye four times daily for up to two weeks. Eysuvis is available as an 8.3 mL multi-dose bottle.[1] According to the Centers for Medicare and Medicaid Services, it is appropriate to use a conversion factor of 20 drops per mL to calculate a days' supply.[5] Using this conversion, there are 166 drops per bottle. Given the max daily dose of 16 drops, there is at least a 10-day supply in each bottle. According to the PPP, low-dose topical corticosteroid therapy can be used at infrequent intervals for short periods of time (i.e., several weeks) to suppress ocular

surface inflammation.[4] Because Eysuvis is indicated for the short-term treatment of the signs and symptoms of dry eye disease, the limit and duration of approval for Eysuvis will be 2 bottles per 90 days.

REFERENCES

1. Eysuvis [package insert]. Watertown, MA: Kala Pharmaceuticals, Inc.; October 2020.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. http://online.lexi.com/. Accessed October 19, 2021.
3. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. http://www.micromedexsolutions.com/. Accessed October 19, 2021.
4. Preferred Practice Pattern. Dry Eye Syndrome. American Academy of Ophthalmology. November 2018.
5. Pharmacy Auditing and Dispensing Job Aid: Billing Other Dosage Forms. Centers for Medicare and Medicaid Services. December 2015.

Written by:	UM Development (DS)
Date Written:	11/2020
Revised:	10/2021 (no clinical changes)
Reviewed:	Medical Affairs: (CHART) 12/17/2020, 10/28/2021 External Review: 02/2021, 12/2021

CRITERIA FOR APPROVAL

1	Is the requested drug being prescribed for the treatment of the signs and symptoms of dry eye disease? [If no, then no further questions.]	Yes	No
2	Is the requested drug being prescribed for short-term (up to two weeks) use? [If no, then no further questions.]	Yes	No
3	Has the patient experienced an inadequate treatment response to an artificial tears product? [If yes, then skip to question 6.]	Yes	No
4	Has the patient experienced an intolerance to an artificial tears product? [If yes, then skip to question 6.]	Yes	No
5	Does the patient have a contraindication that would prohibit a trial of an artificial tears product? [If no, then no further questions.]	Yes	No
6	Does the patient require more than the plan allowance of 2 bottles per 90 days of the requested drug? [RPh Note: If yes, then deny and enter a partial approval for 2 bottles (16.6 mL) per 90 days of the requested drug.]	Yes	No

Mapping Instructions			
	Yes	**No**	**DENIAL REASONS – DO NOT USE FOR MEDICARE PART D**
1.	Go to 2	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you are using it for the treatment of the signs and symptoms of dry eye disease. Your request has been denied based on the information we have.

			[Short Description: No approvable diagnosis]
2.	Go to 3	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you are using it short-term (up to two weeks). Your request has been denied based on the information we have. [Short Description: Use longer than two weeks]
3.	Go to 6	Go to 4	
4.	Go to 6	Go to 5	
5.	Go to 6	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have tried an artificial tears product and it either did not work for you or you cannot use it. Your request has been denied based on the information we have. [Short Description: No inadequate response, intolerance or contraindication to artificial tears]
6.	Deny	Approve, 3 months, 2 bottles (16.6 mL)/90 days*	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 2 bottles per 90 days of Eysuvis. Your request has been partially approved. You have been approved for the maximum quantity that your plan covers for a duration of 3 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity]

**This drug is for short-term acute use; therefore, the mail limit will be the same as the retail limit. The intent is for prescriptions of the requested drug to be filled one month at a time, even if filled at mail order; there should be no 3 month supplies filled.*

PRIOR AUTHORIZATION CRITERIA

BRAND NAME
(generic)

FABIOR
(tazarotene foam)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

POLICY

FDA-APPROVED INDICATIONS
Fabior (tazarotene) Foam, 0.1% is indicated for the topical treatment of acne vulgaris in patients 12 years of age or older.

COVERAGE CRITERIA
The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has the diagnosis of acne vulgaris

REFERENCES

1. Fabior Foam [package insert]. Greenville, NC: Mayne Pharma LLC; June 2018.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2022; Accessed July 1, 2022.
3. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed July 1, 2022.
4. Zaenglein AL, Pathy AL, Schlosser BJ, et al. Guidelines of care for the management of acne vulgaris. *J Am Acad Dermatol*. 2016;74(5):945-973.

Reference number(s)
2231-A

SPECIALTY GUIDELINE MANAGEMENT

FARYDAK (panobinostat)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication
Farydak, in combination with bortezomib and dexamethasone, is indicated for the treatment of patients with multiple myeloma who have received at least 2 prior regimens, including bortezomib and an immunomodulatory agent.

B. Compendial Uses
1. In combination with bortezomib and dexamethasone for previously treated multiple myeloma
2. In combination with carfilzomib or in combination with dexamethasone and lenalidomide for previously treated multiple myeloma for patients who have received at least 2 prior regimens, including bortezomib and an immunomodulatory agent

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Multiple Myeloma
Authorization of 12 months may be granted for the treatment of previously treated multiple myeloma when any of the following criteria are met:
1. The requested medication will be used in combination with bortezomib and dexamethasone
2. The member has received at least two prior regimens, including bortezomib and an immunomodulatory agent, and will be used in combination with carfilzomib or with lenalidomide and dexamethasone.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

IV. REFERENCES

1. Farydak [package insert]. Las Vegas, NV: Secura Bio, Inc.; September 2019.
2. The NCCN Drugs & Biologics Compendium 2021 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed October 6, 2021.

QUANTITY LIMIT PRIOR AUTHORIZATION CRITERIA

DRUG CLASS **CONDOMS**

BRAND NAME (generic)

FEMALE CONDOMS (OTC)

Status: CVS Caremark Criteria
Type: Quantity Limit; Post Limit Prior Authorization

POLICY

INDICATIONS AND USES
Female (internal) condoms are used for the prevention of pregnancy. Female condoms can also effectively protect against sexually transmitted infections (STIs) and human immunodeficiency virus (HIV) transmission.[2-3] Specifically, the FC2 Female Condom is indicated for vaginal use for the prevention of unplanned pregnancy and the transmission of STIs, including HIV.[1]

INITIAL QUANTITY LIMIT**

LIMIT CRITERIA
Limits should accumulate across all drugs and strengths up to highest quantity listed depending on the order the claims are processed.

PLEASE NOTE: Since manufacturer package sizes may vary, it is the discretion of the dispensing pharmacy to fill quantities per package size up to these quantity limits. In such cases the filling limit and day supply may be less than what is indicated.

Drug	1 Month Limit*	3 Month Limit*
Female Condoms	12 condoms / 25 days	36 condoms / 75 days

** The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*

**If the patient is requesting more than the initial quantity limit, the claim will reject with a message indicating that a prior authorization is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

COVERAGE CRITERIA
The requested drug will be covered with prior authorization when the following criteria are met:

- The patient requires more than 12 condoms per month due to a clinical need (e.g., increased sexual activity, condom breakage, or other need to have multiple condoms available for each sexual encounter)

Quantity Limits apply.
24 condoms/25 days* OR 72 condoms/75 days*

REFERENCES

Reference number(s)
2413-A

SPECIALTY GUIDELINE MANAGEMENT

FASENRA (benralizumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Fasenra is indicated for the add-on maintenance treatment of patients with severe asthma aged 12 years and older, and with an eosinophilic phenotype.

Limitations of Use:
- Not for treatment of other eosinophilic conditions
- Not for relief of acute bronchospasm or status asthmaticus

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
A. For initial requests:
   1. Member's chart notes or medical record showing pretreatment blood eosinophil count, dependance on systemic corticosteroids if applicable.
   2. Chart notes, medical record documentation, or claims history supporting previous medications tried including drug, dose, frequency, and duration.
B. For continuation requests: Chart notes or medical record documentation supporting improvement in asthma control.

III. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with an allergist/immunologist or pulmonologist.

IV. CRITERIA FOR INITIAL APPROVAL

A. Authorization of 6 months may be granted for members 12 years of age or older who have previously received a biologic drug (e.g., Dupixent, Nucala) indicated for asthma.

B. Authorization of 6 months may be granted for treatment of severe asthma when all of the following criteria are met:
   1. Member is 12 years of age or older.

2. Member meets either of the following criteria:
   i. Member has a baseline blood eosinophil count of at least 150 cells per microliter
   ii. Member is dependent on systemic corticosteroids
3. Member has uncontrolled asthma as demonstrated by experiencing at least one of the following within the past year:
   i. Two or more asthma exacerbations requiring oral or injectable corticosteroid treatment.
   ii. One or more asthma exacerbation resulting in hospitalization or emergency medical care visit.
   iii. Poor symptom control (frequent symptoms or reliever use, activity limited by asthma, night waking due to asthma).
4. Member has inadequate asthma control despite current treatment with both of the following medications at optimized doses:
   i. High dose inhaled corticosteroid
   ii. Additional controller (i.e., long acting beta$_2$-agonist, long acting muscarinic antagonist, leukotriene modifier, or sustained-release theophylline)
5. Member will continue to use maintenance asthma treatments (e.g., inhaled corticosteroid, additional controller) in combination with the requested medication.

V. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for treatment of severe asthma when all of the following criteria are met:

A. Member is 12 years of age or older.
B. Asthma control has improved on the requested medication as demonstrated by at least one of the following:
   1. A reduction in the frequency and/or severity of symptoms and exacerbations
   2. A reduction in the daily maintenance oral corticosteroid dose
C. Member will continue to use maintenance asthma treatments (e.g., inhaled corticosteroid, additional controller) in combination with the requested medication.

VI. OTHER

Member cannot use the requested medication concomitantly with any other biologic drug or targeted synthetic drug for the same indication.

Note: If the member is a current smoker or vaper, they should be counseled on the harmful effects of smoking and vaping on pulmonary conditions and available smoking and vaping cessation options.

VII. REFERENCES

1. Fasenra [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; February 2021.
2. Nair P, Wenzel S, Rabe K, et al. Oral glucocorticoid-sparing effect of benralizumab in severe asthma. *N Engl J Med.* 2017;376:2448-2458.
3. Global Initiative for Asthma (GINA). Global Strategy for Asthma Management and Prevention. 2022 update. Available at: https://ginasthma.org/wp-content/uploads/2022/07/GINA-Main-Report-2022-FINAL-22-07-01-WMS.pdf. Accessed March 1, 2023.
4. American Academy of Allergy, Asthma & Immunology (AAAAI) 2020 Virtual Annual Meeting. Available at: https://annualmeeting.aaaai.org/. Accessed March 1, 2023.

5. Cloutier MM, Dixon AE, Krishnan JA, et al. Managing asthma in adolescents and adults: 2020 asthma guideline update from the National Asthma Education and Prevention Program. *JAMA.* 2020;324(22): 2301-2317.

1. FC2 Female Condom Leaflet. Miami, FL: Veru Inc.; September 2019. Available at: https://fc2.us.com/wp-content/uploads/2020/01/Female-Condom_USA-Leaflet_G0066_SEPT2019.pdf. Accessed March 15, 2022.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2022; Accessed March 15, 2022.
3. Colquitt CW, Martin TS. Contraceptive Methods: A Review of Nonbarrier and Barrier Products. *Journal of Pharmacy Practice*. 2017;30(1):130-135.
4. Eisenberg ML, Shindel AW, Smith JF, et al. Socioeconomic, Anthropomorphic, and Demographic Predictors of Adult Sexual Activity in the United States: Data from the National Survey of Family Growth. *J Sex Med.* 2010;7(1):50-58.
5. Twenge JM, Sherman RA, Wells BE. Declines in Sexual Frequency Among American Adults, 1989–2014. *Arch Sex Behav*. 2017;46(8):2389-2401.

Reference number(s)
1621-A

SPECIALTY GUIDELINE MANAGEMENT

FERRIPROX (deferiprone)
deferiprone (generic)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. **Transfusional Iron Overload due to Thalassemia Syndromes**
      a. Oral solution is indicated for treatment of transfusional iron overload in adult and pediatric patients 3 years of age and older with thalassemia syndromes.
      b. Tablets are indicated for treatment of transfusional iron overload in adult and pediatric patients 8 years of age and older with thalassemia syndromes.

   2. **Transfusional Iron Overload due to Sickle Cell Disease or Other Anemias**
      a. Ferriprox oral solution is indicated for the treatment of transfusional iron overload in adult and pediatric patients 3 years of age and older with sickle cell disease or other anemias.
      b. Ferriprox tablets are indicated for treatment of transfusional iron overload in adult and pediatric patients 8 years of age and older with sickle cell disease or other anemias.

B. Compendial Use
   Hereditary hemochromatosis

Limitations of Use
Safety and effectiveness have not been established for the treatment of transfusional iron overload in patients with myelodysplastic syndrome or in patients with Diamond Blackfan anemia.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

Transfusional Iron Overload:
A. Initial requests: pretreatment serum ferritin level
B. Continuation requests: current serum ferritin level

III. CRITERIA FOR INITIAL APPROVAL

A. Transfusional Iron Overload
Authorization of 6 months may be granted for treatment of transfusional iron overload when all of the following criteria are met:

1. Transfusional iron overload is due to either of the following:
   a. Thalassemia syndromes
   b. Sickle cell disease or other anemias
2. Member does not have transfusional iron overload due to myelodysplastic syndrome or Diamond Blackfan anemia
3. Pretreatment serum ferritin level is consistently greater than 1000 mcg/L.
4. Dose of Ferriprox will not exceed 99 mg/kg per day.

B. Hereditary Hemochromatosis

Authorization of 6 months may be granted for treatment of hereditary hemochromatosis when phlebotomy is not an option (e.g., poor candidate due to underlying medical disorders) or the member had an unsatisfactory response to phlebotomy.

IV. CONTINUATION OF THERAPY

A. Transfusional Iron Overload

Authorization of 6 months may be granted for continued treatment in members requesting reauthorization for transfusion iron overload when following criteria are met:

1. Member is experiencing benefit from therapy as evidenced by a decrease in serum ferritin levels as compared to pretreatment baseline.
2. Serum ferritin level is not consistently below 500 mcg/L.

B. Hereditary Hemochromatosis

Authorization of 6 months may be granted for continued treatment in members requesting reauthorization for hereditary hemochromatosis when member is experiencing benefit from therapy as evidenced by a decrease in serum ferritin levels as compared to pretreatment baseline

V. REFERENCES

1. Ferriprox tablets [package insert]. Cary, NC: Chiesi USA, Inc.; November 2021.
2. Ferriprox oral solution [package insert]. Cary, NC: Chiesi USA, Inc.; November 2021.
3. Deferiprone [package insert]. Hawthorne, NY: Taro Pharmaceuticals USA., Inc.; August 2022
4. Deferiprone [package insert]. Berkeley Heights, NJ:Hikma Pharmaceuticals USA Inc.; December 2021
5. Cappellini MD, Cohen A, Porter J, et al. Guidelines for the management of transfusion dependent thalassaemia (TDT) 4th Edition [Internet]. *Thalassaemia International Federation* 2021;20:1-351..
6. Hoffbrand AV, Taher A, Cappellini MD. How I treat transfusional iron overload. *Blood* 2012;120(18):3657-69
7. Kowdley, Kris V. MD, FACG1; Brown, Kyle E. MD, MSc2,3,4; Ahn, Joseph MD, MS, MBA, FACG (GRADE Methodologist)5; Sundaram, Vinay MD, MSc6 ACG Clinical Guideline: Hereditary Hemochromatosis, The American Journal of Gastroenterology: August 2019 - Volume 114 - Issue 8 - p 1202-1218

Reference number(s)
5791-A

SPECIALTY GUIDELINE MANAGEMENT

Filspari (sparsentan tablets)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Filspari is indicated to reduce proteinuria in adults with primary immunoglobulin A nephropathy (IgAN) at risk of rapid disease progression, generally a urine protein-to-creatinine ratio (UPCR) ≥ 1.5 g/g.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

A. Initial requests:
   1. Kidney biopsy confirming a diagnosis of primary immunoglobulin A nephropathy (IgAN).
   2. Laboratory report and/or chart note(s) indicating the member has proteinuria greater than or equal to 1 g/day or baseline UPCR greater than or equal to 0.8 g/g based on a 24-hour urine collection.

B. Continuation requests:
   1. Laboratory report and/or chart note(s) indicating the member has decreased levels of proteinuria or UPCR from baseline based on a 24-hour urine collection.

III. CRITERIA FOR INITIAL APPROVAL

Primary immunoglobulin A nephropathy (IgAN)
Authorization of up to 10 months may be granted when all of the following criteria are met:
A. Member has a diagnosis of primary immunoglobulin A nephropathy (IgAN) confirmed by kidney biopsy.
B. Member has proteinuria greater than or equal to 1 g/day or UPCR greater than or equal to 0.8 g/g based on a 24-hour urine collection.
C. Member has received a stable dose of maximally tolerated renin-angiotensin system (RAS) inhibitor therapy (e.g., angiotensin converting enzyme inhibitor [ACEI] or angiotensin II receptor blocker [ARB]) for at least 3 months prior to initiation of therapy, or member has an intolerance or contraindication to RAS inhibitors.
D. Member has experienced an intolerance to oral glucocorticoid (e.g., prednisone).

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in all members (including new members) who are currently receiving the requested medication and who are experiencing benefit from therapy as evidenced by either of the following:

A. Decreased levels of proteinuria from baseline on a 24-hour urine collection.
B. Decrease in UPCR from baseline based on a 24-hour urine collection.

V. REFERENCES

1. Filspari [package insert]. San Diego: Travere Therapeutics, Inc.; February 2023.
2. ClinicalTrial.gov. National Library of Medicine (US). Identifier NCT03762850 A Study of the Effect and Safety of Sparsentan in the Treatment of Patients With IgA Nephropathy (PROTECT). February 3, 2023. Available from: https://clinicaltrials.gov/ct2/show/study/NCT03762850.
3. Kidney Disease: Improving Global Outcomes (KDIGO) Glomerular Diseases Work Group. KDIGO 2021 Clinical Practice Guideline for the Management of Glomerular Diseases. Kidney Int. 2021 Oct; 100 (4S): S1-S276. doi: 10.1016/j.kint.2021.05.021.

Reference number(s)
1842-A

SPECIALTY GUIDELINE MANAGEMENT

GILENYA (fingolimod hydrochloride)
TASCENSO ODT (fingolimod lauryl sulfate)
fingolimod hydrochloride (generic)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in patients 10 years of age and older.

All other indications are considered experimental/investigational and not medically necessary.

II. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with a neurologist.

III. CRITERIA FOR INITIAL APPROVAL

A. Relapsing forms of multiple sclerosis
Authorization of 12 months may be granted to members who have been diagnosed with a relapsing form of multiple sclerosis (including relapsing-remitting and secondary progressive disease for those who continue to experience relapse).

B. Clinically isolated syndrome
Authorization of 12 months may be granted to members for the treatment of clinically isolated syndrome of multiple sclerosis.

IV. CONTINUATION OF THERAPY

For all indications: Authorization of 12 months may be granted to members who are experiencing disease stability or improvement while receiving the requested medication.

V. OTHER

Members will not use the requested medication concomitantly with other disease modifying multiple sclerosis agents (Note: Ampyra and Nuedexta are not disease modifying).

VI. REFERENCE

1. Gilenya [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; July 2022.
2. Fingolimod [package insert]. Weston, FL: Apotex Corporation; February 2023.
3. Tascenso ODT [package insert]. San Jose, CA: Handa Neuroscience, LLC; December 2022.

Reference number(s)
3982-A

SPECIALTY GUIDELINE MANAGEMENT

FINTEPLA (fenfluramine)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Fintepla is indicated for the treatment of seizures associated with Dravet syndrome (DS) and Lennox-Gastaut syndrome (LGS) in patients 2 years of age and older.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Seizures associated with Dravet syndrome
Authorization of 12 months may be granted for treatment of seizures associated with Dravet syndrome in members 2 years of age and older.

B. Seizures associated with Lennox-Gastaut syndrome
Authorization of 12 months may be granted for treatment of seizures associated with Lennox-Gastaut syndrome in members 2 years of age and older.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continuation of treatment in members (including new members) 2 years of age or older requesting reauthorization for an indication listed in Section II when the member has achieved or maintained a positive clinical response as evidenced by reduction in frequency or duration of seizures compared with seizure activity prior to initiating Fintepla.

IV. OTHER

Due to well documented potential for serious adverse effects, phentermine and fenfluramine are not recommended to be used concurrently. Member cannot use the requested medication concomitantly with phentermine.

V. REFERENCE

1. Fintepla [package insert]. Smyrna, GA: UCB, Inc.; March 2023.

Reference number(s)
2803-A

SPECIALTY GUIDELINE MANAGEMENT

FIRDAPSE (amifampridine)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Firdapse is indicated for the treatment of Lambert-Eaton myasthenic syndrome (LEMS) in adults and pediatric patients 6 years of age and older.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of either of the following diagnostic tests is necessary to initiate prior authorization review:
A. Electromyography (EMG)
B. Anti-P/Q type voltage-gated calcium channel antibody test

III. EXCLUSIONS

Coverage will not be provided for members with a history of seizures.

IV. CRITERIA FOR INITIAL APPROVAL

Lambert-Eaton Myasthenic Syndrome (LEMS)
Authorization of 6 months may be granted for treatment of Lambert-Eaton myasthenic syndrome (LEMS) when all of the following criteria are met:
A. Diagnosis is confirmed by either of the following:
    1. EMG showing compound muscle action potential (CMAP) that increased at least 2-fold after maximum voluntary contraction of the tested muscle
    2. A positive anti- P/Q type voltage-gated calcium channel antibody test
B. Member has proximal muscle weakness
C. For treatment-naïve members, the Quantitative Myasthenia Gravis (QMG) score is at least 5

V. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for LEMS who are responding to therapy (i.e., there is stability or improvement in symptoms relative to the natural course of LEMS).

VI. REFERENCES

1. Firdapse [package insert]. Coral Gables, FL: Catalyst Pharmaceuticals, Inc.; September 2022.
2. A Phase 3 Study of Amifampridine Phosphate in Patients with Lambert Eaton Myasthenic Syndrome (LEMS). (2018). Retrieved from https://clinicaltrials.gov/ct2 (Identification No. NCT01377922).

MEDICAL NECESSITY CRITERIA

DIABETIC TEST STRIPS (NON-PREFERRED)

Status: Client Requested Criteria

Type: Medical Necessity Criteria ***Ref # C15552-A***

CRITERIA FOR APPROVAL

1	Preferred products are available at a lower cost. Can your patient be switched to a preferred product? Available Formulary Alternatives: Accu-Chek and One Touch products [If yes, provide your patient with a new prescription for the preferred product.]	Yes	No
2	Does the patient have an insulin pump that is incompatible with Accu-Chek or One Touch products?	Yes	No

CVS caremark™

PRIOR AUTHORIZATION CRITERIA

BRAND NAME
(generic)

GLUMETZA
(metformin extended-release)

(metformin extended-release) (generic Fortamet)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

POLICY

FDA-APPROVED INDICATIONS

Glumetza
Glumetza is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Metformin Extended-Release (generic Fortamet)
Metformin hydrochloride extended-release tablets are indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has experienced an intolerance to generic Glucophage XR. The prescriber MUST submit chart notes or other documentation supporting date of trial and reason for intolerance to generic Glucophage XR.

AND

- Chart notes or other documentation supporting date of trial and reason for intolerance to generic Glucophage XR have been submitted to CVS Health

REFERENCES

1. Glumetza [package insert]. Bridgewater, NJ: Salix Pharmaceuticals; August 2019.
2. Metformin Extended-Release Tablets [package insert]. Morgantown, WV: Mylan Pharmaceuticals Inc.; November 2018.
3. Metformin Extended-Release Tablets [package insert]. East Brunswick, NJ: Unichem Pharmaceuticals (USA), Inc.; March 2022.
4. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2023; Accessed January 30, 2023.
5. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed January 30, 2023.

Reference number(s)
4619-A

SPECIALTY GUIDELINE MANAGEMENT

FOTIVDA (tivozanib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Fotivda is indicated for the treatment of adult patients with relapsed or refractory advanced renal cell carcinoma (RCC) following two or more prior systemic therapies.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Renal Cell Carcinoma (RCC)
Authorization of 12 months may be granted for treatment of relapsed or refractory advanced renal cell carcinoma in members who have received two or more prior systemic therapies, when the requested medication is used as a single agent.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

IV. REFERENCES

1. Fotivda [package insert]. Boston, MA: AVEO Pharmaceuticals, Inc.; March 2021.

Reference number(s)
2028-A

SPECIALTY GUIDELINE MANAGEMENT

FORTEO (teriparatide)
BONSITY (teriparatide)
TERIPARATIDE

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

A. Treatment of postmenopausal women with osteoporosis at high risk for fracture (defined herein as having a history of osteoporotic fracture or multiple risk factors for fracture) or who have failed or are intolerant to other available osteoporosis therapy.
B. Increase of bone mass in men with primary or hypogonadal osteoporosis at high risk for fracture or who have failed or are intolerant to other available osteoporosis therapy.
C. Treatment of men and women with osteoporosis associated with sustained glucocorticoid therapy (daily dosage equivalent to 5 mg or greater of prednisone) at high risk for fracture or who have failed or are intolerant to other available osteoporosis therapy.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: Supporting chart notes or medical record indicating a history of fractures, T-score, and FRAX fracture probability as applicable to Section III.

III. CRITERIA FOR INITIAL APPROVAL

A. Postmenopausal osteoporosis

Authorization of an initial total of 12 months may be granted to postmenopausal members with osteoporosis when ANY of the following criteria are met:

1. Member has a history of fragility fractures
2. Member has a pre-treatment T-score less than or equal to -2.5 OR member has osteopenia (i.e., pre-treatment T-score greater than -2.5 and less than -1) with a high pre-treatment FRAX fracture probability (See Appendix B) and meets ANY of the following criteria:
    a. Member has indicators of very high fracture risk (e.g., advanced age, frailty, glucocorticoid use, very low T-scores [less than or equal to -3], or increased fall risk)
    b. Member has failed prior treatment with or is intolerant to previous injectable osteoporosis therapy (e.g., zoledronic acid [Reclast], denosumab [Prolia], abaloparatide [Tymlos])
    c. Member has had an oral bisphosphonate trial of at least 1-year duration or there is a clinical reason to avoid treatment with an oral bisphosphonate (See Appendix A)

B. Primary or hypogonadal osteoporosis in men

Authorization of an initial total of 12 months may be granted to male members with primary or hypogonadal osteoporosis when ANY of the following criteria are met:

1. Member has a history of an osteoporotic vertebral or hip fracture
2. Member meets BOTH of the following criteria:
   a. Member has a pre-treatment T-score less than or equal to -2.5 OR member has osteopenia (i.e., pre-treatment T-score greater than -2.5 and less than -1) with a high pre-treatment FRAX fracture probability (See Appendix B)
   b. Member has had an oral OR injectable bisphosphonate trial of at least 1-year duration OR there is a clinical reason to avoid treatment with a bisphosphonate (See Appendix A)

C. Glucocorticoid-induced osteoporosis

Authorization of an initial total of 12 months may be granted to members with glucocorticoid-induced osteoporosis when ALL of the following criteria are met:

1. Member has had an oral OR injectable bisphosphonate trial of at least 1-year duration OR there is a clinical reason to avoid treatment with a bisphosphonate (See Appendix A)
2. Member is currently receiving or will be initiating glucocorticoid therapy at an equivalent prednisone dose of ≥ 2.5 mg/day for ≥ 3 months
3. Member meets ANY of the following criteria:
   a. Member has a history of a fragility fracture
   b. Member has a pre-treatment T-score less than or equal to -2.5
   c. Member has osteopenia (i.e., pre-treatment T-score greater than -2.5 and less than -1) with a high pre-treatment FRAX fracture probability (See Appendix B)

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for all members (including new members) who are currently receiving the requested medication through a previously authorized pharmacy or medical benefit, who meet one of the following:

A. Member has received less than 24 months of therapy and has not experienced clinically significant adverse events during therapy
B. Member has received 24 months of therapy or more and meets both of the following:
   1. Member has experienced clinical benefit (i.e., improvement or stabilization in T-score since the previous bone mass measurement)
   2. Member has not experienced any adverse effects

V. OTHER

The cumulative duration of parathyroid hormone analogs (e.g., teriparatide and abaloparatide) will not exceed a total of 24 months in the member's lifetime unless the member remains at or has returned to having a high risk for fracture.

VI. APPENDIX

Appendix A. Clinical reasons to avoid oral bisphosphonate therapy

- Presence of anatomic or functional esophageal abnormalities that might delay transit of the tablet (e.g., achalasia, stricture, or dysmotility)

- Active upper gastrointestinal problem (e.g., dysphagia, gastritis, duodenitis, erosive esophagitis, ulcers)
- Presence of documented or potential gastrointestinal malabsorption (e.g., gastric bypass procedures, celiac disease, Crohn's disease, infiltrative disorders, etc.)
- Inability to stand or sit upright for at least 30 to 60 minutes
- Inability to take oral bisphosphonate at least 30 to 60 minutes before first food, drink, or medication of the day
- Renal insufficiency (creatinine clearance < 35 mL/min)
- History of intolerance to an oral bisphosphonate

Appendix B. WHO Fracture Risk Assessment Tool

- High FRAX fracture probability: 10-year major osteoporotic fracture risk ≥ 20% or hip fracture risk ≥ 3%.
- 10-year probability; calculation tool available at: https://www.sheffield.ac.uk/FRAX/
- The estimated risk score generated with FRAX should be multiplied by 1.15 for major osteoporotic fracture (including fractures of the spine (clinical), hip, wrist, or humerus) and 1.2 for hip fracture if glucocorticoid treatment is greater than 7.5 mg (prednisone equivalent) per day.

VII. REFERENCES

1. Forteo [package insert]. Indianapolis, IN: Eli Lilly and Company; September 2021.
2. Bonsity [package insert]. San Diego, CA: Pfenex, Inc.; October 2019.
3. Teriparatide [package insert]. San Diego, CA: Alvogen, Inc.; November 2019.
4. Bisphosphonates. *Drug Facts and Comparisons.* Facts & Comparisons [database online]. St. Louis, MO: Wolters Kluwer Health Inc; October 24, 2019. Accessed October 10, 2022.
5. Cosman F, de Beur SJ, LeBoff MS, et al. National Osteoporosis Foundation. Clinician's guide to prevention and treatment of osteoporosis. *Osteoporos Int.* 2014;25(10): 2359-2381.
6. Jeremiah MP, Unwin BK, Greenwald MH, et al. Diagnosis and management of osteoporosis. *Am Fam Physician*. 2015;92(4):261-268.
7. Camacho PM, Petak SM, Binkley N, et al. American Association of Clinical Endocrinologists and American College of Endocrinology Clinical Practice Guidelines for the Diagnosis and Treatment of Postmenopausal Osteoporosis 2020. *Endocr Pract*. 2020;26 (Suppl 1):1-46.
8. National Institute for Health and Care Excellence. Osteoporosis Overview. Last updated February 2018. Available at: http://pathways.nice.org.uk/pathways/osteoporosis. Accessed April 10, 2019.
9. Treatment to prevent osteoporotic fractures: an update. Department of Health and Human Services, Agency for Healthcare Research and Quality. 2012; Publication No. 12-EHC023-EF. Available at www.effectivehealthcare.ahrq.gov/lbd.cfm.
10. Watts NB, Adler RA, Bilezikian JP, et al. Osteoporosis in men : an Endocrine Society clinical practice guideline. *J Clin Endocr Metab*. 2012;97(6):1802-1822.
11. Fink HA, Gordon G, Buckley L, et al. 2017 American College of Rheumatology Guidelines for the Prevention and Treatment of Glucocorticoid-Induced Osteoporosis. *Arthritis Care Res*. 2017;69:1521-1537.
12. FRAX® Fracture Risk Assessment Tool. © Centre for Metabolic Bone Diseases, University of Sheffield, UK. Available at: https://www.shef.ac.uk/FRAX. Accessed October 10, 2022.
13. Ensrud KE, Crandall CJ. Osteoporosis. *Ann Intern*. Med 2017;167(03):ITC17–ITC32.
14. Eastell R, Rosen CJ, Black DM, et al. Pharmacological Management of Osteoporosis in Postmenopausal Women: An Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab*. 2019;104:1595-1622.
15. Carey John. What is a 'failure' of bisphosphonate therapy for osteoporosis? Cleveland Clinic Journal of Medicine. Nov 2005, 72 (11) 1033-1039.

Reference number(s)
2028-A

Reference number(s)
3099-A

SPECIALTY GUIDELINE MANAGEMENT

FUZEON (enfuviride)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Fuzeon in combination with other antiretroviral agents is indicated for the treatment of human immunodeficiency virus (HIV)-1 infection in treatment-experienced patients with evidence of HIV-1 replication despite ongoing antiretroviral therapy.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Human immunodeficiency virus (HIV)-1
Authorization of 12 months may be granted for treatment of HIV-1 infection when either of the following criteria is met:

A. The member has viremia despite 3 or more prior months of therapy with at least one appropriate regimen used to treat HIV.
B. The member has viremia and documented resistance or intolerance to at least one appropriate regimen used to treat HIV.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for treatment of human immunodeficiency virus type 1 (HIV-1) infection when the member has had a positive or stable virologic response to Fuzeon.

IV. REFERENCES

1. Fuzeon [package insert]. South San Francisco, CA: Genentech USA, Inc.; December 2019.

Reference number
2650-A

SPECIALTY GUIDELINE MANAGEMENT

GALAFOLD (migalastat)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Galafold is indicated for the treatment of adults with a confirmed diagnosis of Fabry disease and an amenable galactosidase alpha gene (*GLA*) variant based on in vitro assay data.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
A. Initial requests: laboratory confirmation of an amenable galactosidase alpha (GLA) gene variant.
B. Continuation requests: lab results or chart notes documenting a positive response to therapy (e.g., reduction in plasma globotriaosylceramide [GL-3, Gb3] or GL-3/Gb3 inclusions, improvement and/or stabilization in renal function, pain reduction).

III. CRITERIA FOR INITIAL APPROVAL

Fabry disease with an amenable galactosidase alpha gene (*GLA*) variant
Authorization of 12 months may be granted for treatment of Fabry disease with an amenable galactosidase alpha gene (*GLA*) variant when both of the following criteria are met:
A. Member has an amenable galactosidase alpha gene *(GLA)* variant based on in vitro assay data; and
B. Galafold will not be used in combination with enzyme replacement therapy (ERT) for the treatment of Fabry disease.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III who are responding to therapy (e.g., reduction in plasma globotriaosylceramide [GL-3, Gb3] or GL-3/Gb3 inclusions, improvement and/or stabilization in renal function, pain reduction).

V. REFERENCES

1. Galafold [package insert]. Philadelphia, PA: Amicus Therapeutics US, LLC; December 2021.

2. Biegstraaten M, Arngrimsson R, Barbey F, et al. Recommendations for initiation and cessation of enzyme replacement therapy in patients with Fabry disease: the European Fabry Working Group consensus document. *Orphanet J Rare Dis.* 2015; 1036.
3. Ortiz A, Germain DP, Desnick RJ, et al. Fabry disease revisited: Management and treatment recommendations for adult patients. Mol Genet Metab. 2018;123(4):416-427.
4. Mehta A, Hughes DA. Fabry Disease. 2002 Aug 5 [Updated 2022 Jan 27]. In: Adam MP, Ardinger HH, Pagon RA, et al., editors. GeneReviews [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2022. Available from: https://www.ncbi.nlm.nih.gov/books/NBK1292/. Accessed May 18, 2022.

Reference number(s)
1838-A

SPECIALTY GUIDELINE MANAGEMENT

GATTEX (teduglutide)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Gattex is indicated for the treatment of adult and pediatric patients 1 year of age and older with short bowel syndrome (SBS) who are dependent on parenteral support.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

A. Initial requests
   1. Adult members (greater than or equal to 18 years of age): Chart notes supporting the use of parenteral nutrition/intravenous (IV) fluids at least 3 times a week for 12 months and current volume of parenteral support in liters per week.
   2. Pediatric members (less than 18 years of age): Chart notes supporting the use of parenteral nutrition/IV fluids to account for at least 30% of caloric and/or fluid/electrolyte needs.

B. Continuation requests
   1. Members who remain dependent on parenteral nutrition/IV fluids: Chart notes supporting the continued use of parenteral nutrition/IV fluids and current volume of parenteral support in liters per week.
   2. Members who were previously on parenteral nutrition and have been weaned off parenteral nutrition/IV fluids while on therapy with the requested drug: Chart notes supporting the volume of parenteral support in liters per week required at baseline.

III. CRITERIA FOR INITIAL APPROVAL

Short bowel syndrome (SBS)

A. Authorization of 6 months may be granted for treatment of short bowel syndrome in adult members greater than or equal to 18 years of age who have been dependent on parenteral nutrition and/or intravenous (IV) fluids for at least 12 months and receive parenteral nutrition and/or IV fluids at least 3 times a week.
B. Authorization of 6 months may be granted for treatment of short bowel syndrome in pediatric members less than 18 years of age who are receiving parenteral nutrition and/or IV fluids to account for at least 30% of caloric and/or fluid/electrolyte needs.

IV. CONTINUATION OF THERAPY

Short bowel syndrome (SBS)

A. Authorization of 6 months may be granted for continued treatment in members requesting reauthorization when the member remains dependent on parenteral nutrition and/or intravenous (IV) fluids and whose requirement for parenteral support has decreased by at least 20% from baseline while on therapy with the requested drug.
B. Authorization of 6 months may be granted for continued treatment in members requesting reauthorization when the member who was previously dependent on parenteral nutrition and/or IV fluids has been able to wean off the requirement for parenteral support while on therapy with the requested drug.

V. DOSAGE AND ADMINISTRATION

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

VI. REFERENCES

1. Gattex [package insert]. Lexington, MA: Shire-NPS Pharmaceuticals, Inc.; January 2021.
2. Jeppesen PB, Pertkiewicz M, Messing B, et al. Teduglutide reduces need for parenteral support among patients with short bowel syndrome with intestinal failure. *Gastroenterology*. 2012; 143(6):1473-1481.
3. Schwartz LK, O'Keefe SJD, Fujioka K, et al. Long-term teduglutide for the treatment of patients with intestinal failure associated with short bowel syndrome. *Clin Transl Gastroenerol*. 2016; 7(2):e142.

Reference number(s)
4206-A

SPECIALTY GUIDELINE MANAGEMENT

GAVRETO (pralsetinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
1. Gavreto is indicated for the treatment of adult patients with metastatic rearranged during transfection (*RET*) fusion-positive non-small cell lung cancer (NSCLC) as detected by an FDA approved test.
2. Gavreto is indicated for the treatment of adult and pediatric patients 12 years of age and older with advanced or metastatic *RET*-mutant medullary thyroid cancer (MTC) who require systemic therapy.
3. Gavreto is indicated for the treatment of adult and pediatric patients 12 years of age and older with advanced or metastatic *RET* fusion-positive thyroid cancer who require systemic therapy and who are radioactive iodine-refractory (if radioactive iodine is appropriate).

B. Compendial Uses
NSCLC with *RET* rearrangement-positive tumors

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: Documentation of the presence of a rearranged during transfection (*RET)* gene fusion (NSCLC or thyroid cancer) or a specific *RET* gene mutation (MTC) in tumor specimens or plasma.

III. CRITERIA FOR INITIAL APPROVAL

A. Non-Small Cell Lung Cancer
Authorization of 12 months may be granted as a single agent for treatment of advanced or metastatic non-small cell lung cancer when the tumors have a *RET* gene fusion.

B. Medullary Thyroid Cancer
Authorization of 12 months may be granted for treatment of members 12 years of age and older with advanced or metastatic medullary thyroid cancer with a *RET* gene mutation.

C. Anaplastic Thyroid Cancer
Authorization of 12 months may be granted for treatment of stage IV anaplastic thyroid cancer with a *RET* gene fusion when used as single agent.

D. Thyroid Cancer

Authorization of 12 months may be granted for treatment of members 12 years of age and older with advanced or metastatic thyroid cancer not amenable to radioactive iodine therapy (RAI) whose tumors have a *RET* gene fusion.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

V. REFERENCES

1. Gavreto [package insert]. South San Francisco, CA: Genentech, Inc.; February 2022.
2. The NCCN Drugs & Biologics Compendium® 2022 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed July 6, 2022.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME
(generic)

PROPECIA
(finasteride)

ROGAINE (OTC)
(minoxidil)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

POLICY

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for gender affirming treatment in a transgender or gender diverse (TGD) patient

AND

- The requested drug is medically necessary

REFERENCES

1. State of Washington SB 5313. November 2021.
2. State of Minnesota Administrative Bulletin 2021-3. December 2021.
3. State of Hawaii HB 2405. June 2022.
4. Coleman E, Radix AE, Bouman WP, et al. Standards of Care for the Health of Transgender and Gender Diverse People, Version 8. *Int J Transgend Health*. 2022;23(S1):S1-S258.
5. UCSF Gender Affirming Health Program, Department of Family and Community Medicine, University of California San Francisco. Guidelines for the Primary and Gender-Affirming Care of Transgender and Gender Nonbinary People; 2nd edition. Deutsch MB, ed. June 2016. Available at: transcare.ucsf.edu/guidelines.
6. Health Care for Transgender and Gender Diverse Individuals. ACOG Committee Opinion No. 823. American College of Obstetricians and Gynecologists. *Obstet Gynecol*. 2021;137:e75-88.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME
(generic)

PROPECIA
(finasteride)

ROGAINE (OTC)
(minoxidil)

Status: CVS Caremark® Criteria
Type: Initial Prior Authorization

POLICY

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for gender affirming treatment in a transgender or gender diverse (TGD) patient

AND

- The requested drug is medically necessary

Duration of Approval (DOA):

- 5134-A: DOA: 12 months

REFERENCES

1. State of Washington SB 5313. November 2021.
2. State of Minnesota Administrative Bulletin 2021-3. December 2021.
3. State of Hawaii HB 2405. June 2022.
4. State of Oregon HB 2002. July 2023.
5. Coleman E, Radix AE, Bouman WP, et al. Standards of Care for the Health of Transgender and Gender Diverse People, Version 8. *Int J Transgend Health*. 2022;23(S1):S1-S258.
6. UCSF Gender Affirming Health Program, Department of Family and Community Medicine, University of California San Francisco. Guidelines for the Primary and Gender-Affirming Care of Transgender and Gender Nonbinary People; 2nd edition. Deutsch MB, ed. June 2016. Available at: transcare.ucsf.edu/guidelines.
7. Health Care for Transgender and Gender Diverse Individuals. ACOG Committee Opinion No. 823. American College of Obstetricians and Gynecologists. *Obstet Gynecol*. 2021;137:e75-88.

QUANTITY LIMIT PRIOR AUTHORIZATION CRITERIA

BRAND NAME
(generic)

(gentamicin sulfate ophthalmic solution)

Status: CVS Caremark Criteria
Type: Quantity Limit; Post Limit Prior Authorization

POLICY

FDA-APPROVED INDICATIONS
Gentamicin Sulfate Ophthalmic Solution is indicated in the topical treatment of ocular bacterial infections, including conjunctivitis, keratitis, keratoconjunctivitis, corneal ulcers, blepharitis, blepharoconjunctivitis, acute meibomianitis, and dacryocystitis caused by susceptible strains of the following microorganisms:
Staphylococcus aureus, Staphylococcus epidermidis, Streptococcus pyogenes, Streptococcus pneumoniae, Enterobacter aerogenes, Escherichia coli, Haemophilus influenzae, Klebsiella pneumoniae, Neisseria gonorrhoeae, Pseudomonas aeruginosa, and Serratia marcescens.

INITIAL QUANTITY LIMIT**

LIMIT CRITERIA

Drug	1 Month Limit*	3 Month Limit*
gentamicin ophthalmic solution	20 mL (4 bottles, 5mL each) / 25 days	Does Not Apply*

**The duration of 25 days is used for a 30-day fill period to allow time for refill processing.*
**** These drugs are for short-term acute use; therefore, the mail limit will be the same as the retail limit. The intent is for prescriptions of the requested drug to be filled one month at a time, even if filled at mail order; there should be no 3 month supplies filled.***

**If the patient is requesting more than the initial quantity limit, the claim will reject with a message indicating that a prior authorization is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

COVERAGE CRITERIA
The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for the treatment of an ocular bacterial infection

AND

- The requested drug is not being used in a footbath

Quantity Limits apply.
40 mL per month*
3 month limit does not apply*
**The duration of 25 days is used for a 30-day fill period to allow time for refill processing.*
** These drugs are for short-term acute use; therefore, the mail limit will be the same as the retail limit. The intent is for prescriptions of the requested drug to be filled one month at a time, even if filled at mail order; there should be no 3 month supplies filled.*

REFERENCES
1. Gentamicin Sulfate Solution [package insert]. Bridgewater, NJ: Bausch Health US, LLC; February 2020.

2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2022; Accessed February 5, 2023.
3. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed February 5, 2023.
4. American Academy of Ophthalmology Conjunctivitis Preferred Practice Pattern 2018. Available at: https://www.aao.org/preferred-practice-pattern/conjunctivitis-ppp-2018. Accessed February 2023.
5. American Academy of Ophthalmology Bacterial Keratitis Preferred Practice Pattern 2018. Available at: https://www.aao.org/preferred-practice-pattern/bacterial-keratitis-ppp-2018. Accessed February 2023.
6. American Academy of Ophthalmology Blepharitis Preferred Practice Pattern 2018. Available at: https://www.aao.org/preferred-practice-pattern/blepharitis-ppp-2018. Accessed February 2023.
7. Pharmacy Auditing and Dispensing Job Aid: Billing Other Dosage Forms. Centers for Medicare and Medicaid Services. December 2015. Available at: https://www.cms.gov/Medicare-Medicaid-Coordination/Fraud-Prevention/Medicaid-Integrity-Program/Education/Pharmacy-Toolkits. Accessed February 2023.

QUANTITY LIMIT PRIOR AUTHORIZATION CRITERIA

BRAND NAME
(generic)

(gentamicin sulfate cream)

(gentamicin sulfate ointment)

Status: CVS Caremark Criteria
Type: Quantity Limit; Post Limit Prior Authorization

POLICY

FDA-APPROVED INDICATIONS
Primary skin infections: Impetigo contagiosa, superficial folliculitis, ecthyma, furunculosis, sycosis barbae, and pyoderma gangrenosum.
Secondary skin infections: Infectious eczematoid dermatitis, pustular acne, pustular psoriasis, infected seborrheic dermatitis, infected contact dermatitis (including poison ivy), infected excoriations, and bacterial super-infections of fungal or viral infections.
Please Note: Gentamicin Sulfate is a bactericidal agent that is not effective against viruses or fungi in skin infections. Gentamicin Sulfate is useful in the treatment of infected skin cysts and certain other skin abscesses when preceded by incision and drainage to permit adequate contact between the antibiotic and the infecting bacteria. Good results have been obtained in the treatment of infected stasis and other skin ulcers, infected superficial burns, paronychia, infected insect bites and stings, infected lacerations and abrasions, and wounds from minor surgery. Patients sensitive to neomycin can be treated with Gentamicin Sulfate, although regular observation of patients sensitive to topical antibiotics is advisable when such patients are treated with any topical antibiotic. Gentamicin Sulfate has been used successfully in infants over one year of age as well as in adults and children.
Gentamicin Sulfate Cream is recommended for wet, oozing primary infections, and greasy, secondary infections, such as pustular acne or infected seborrheic dermatitis. If a water-washable preparation is desired, the cream is preferable.
Gentamicin Sulfate Ointment helps retain moisture and has been useful in infection on dry eczematous or psoriatic skin.

INITIAL QUANTITY LIMIT**

LIMIT CRITERIA
Limits should accumulate across all drugs and strengths up to highest quantity listed depending on the order the claims are processed. Accumulation does not apply if limit is coded for daily dose.

PLEASE NOTE: Since manufacturer package sizes may vary, it is the discretion of the dispensing pharmacy to fill quantities per package size up to these quantity limits. In such cases the filling limit and day supply may be less than what is indicated.

Drug	1 Month Limit*	3 Month Limit*
gentamicin cream	120 gm / 25 days	Does Not Apply*
gentamicin ointment	120 gm / 25 days	Does Not Apply*

**The duration of 25 days is used for a 30-day fill period to allow time for refill processing.*
**** These drugs are for short-term acute use; therefore, the mail limit will be the same as the retail limit. The intent is for prescriptions of the requested drug to be filled one month at a time, even if filled at mail order; there should be no 3 month supplies filled.***

**If the patient is requesting more than the initial quantity limit, the claim will reject with a message indicating that a prior authorization is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for the treatment of a primary or secondary bacterial infection of the skin

AND

- The requested drug is not being used in a footbath

Quantity Limits apply.
240 grams per month*
3 month limit does not apply*

**The duration of 25 days is used for a 30-day fill period to allow time for refill processing.*
** These drugs are for short-term acute use; therefore, the mail limit will be the same as the retail limit. The intent is for prescriptions of the requested drug to be filled one month at a time, even if filled at mail order; there should be no 3 month supplies filled.*

REFERENCES

1. Gentamicin Sulfate Cream [package insert]. Allegan, MI: Perrigo; September 2017.
2. Gentamicin Sulfate Ointment [package insert]. South Plainfield, NJ: Cosette Pharmaceuticals, Inc.; February 2020.
3. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2022; Accessed February 5, 2023.
4. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed February 5, 2023.
5. Stevens D, Bisno A, Chambers H, et al. Practice Guidelines for the Diagnosis and Management of Skin and Soft Tissue Infections: 2014 Update by the Infectious Diseases Society of America. *Clinical Infectious Diseases* 2014; 59(2):e10–52.
6. Eichenfield L, Tom W, Berger T, et al. Guidelines of Care for the Management of Atopic Dermatitis Section 2. Management and Treatment of Atopic Dermatitis with Topical Therapies. *J Am Acad Dermatol* 2014; 71:116-32. https://www.aad.org/practicecenter/quality/clinical-guidelines/atopic-dermatitis. Accessed February 2022.
7. Burn Triage and Treatment - Thermal Injuries. Available at: https://chemm.nlm.nih.gov/burns.htm. Accessed February 2022.

Reference number(s)
1658-A

SPECIALTY GUIDELINE MANAGEMENT

GILOTRIF (afatinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. EGFR Mutation-Positive, Metastatic Non-Small Cell Lung Cancer
      Gilotrif is indicated for the first-line treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have non-resistant epidermal growth factor receptor (EGFR) mutations as detected by an FDA-approved test.
      Limitations of Use: Safety and efficacy of Gilotrif were not established in patients whose tumors have resistant EGFR mutations.
   2. Previously Treated, Metastatic Squamous NSCLC
      Gilotrif is indicated for the treatment of patients with metastatic squamous NSCLC progressing after platinum-based chemotherapy.

B. Compendial Uses
   NSCLC, recurrent, advanced or metastatic sensitizing EGFR mutation-positive as a single agent or as subsequent therapy in combination with cetuximab.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: For NSCLC, EGFR mutation testing results (where applicable).

III. CRITERIA FOR INITIAL APPROVAL

Non-Small Cell Lung Cancer (NSCLC)

A. Authorization of 12 months may be granted for treatment of recurrent, advanced or metastatic NSCLC when the member has sensitizing EGFR mutation-positive disease as a single agent or in combination with cetuximab.

B. Authorization of 12 months may be granted for treatment of metastatic squamous NSCLC progressing after platinum-based chemotherapy.

IV. CONTINUATION OF THERAPY

NSCLC

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for NSCLC when either of the following criteria are met:

1. There is no evidence of unacceptable toxicity or disease progression while on the current regimen.
2. Disease is T790M negative and there is no evidence of unacceptable toxicity.

V. REFERENCES

1. Gilotrif [package insert]. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc.; October 2019.
2. The NCCN Drugs & Biologics Compendium® © 2022 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed March 4, 2022.

Reference number(s)
1841-A

SPECIALTY GUIDELINE MANAGEMENT

COPAXONE (glatiramer acetate)
GLATOPA (glatiramer acetate)
glatiramer acetate

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Indicated for the treatment of patients with relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.

All other indications are considered experimental/investigational and not medically necessary.

II. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with a neurologist.

III. CRITERIA FOR INITIAL APPROVAL

A. Relapsing forms of multiple sclerosis
Authorization of 12 months may be granted to members who have been diagnosed with a relapsing form of multiple sclerosis (including relapsing-remitting and secondary progressive disease for those who continue to experience relapse).

B. Clinically isolated syndrome
Authorization of 12 months may be granted to members for the treatment of clinically isolated syndrome of multiple sclerosis.

IV. CONTINUATION OF THERAPY

For all indications: Authorization of 12 months may be granted for members who are experiencing disease stability or improvement while receiving Copaxone, Glatopa, or glatiramer acetate.

V. OTHER

Members will not use Copaxone, Glatopa, or glatiramer acetate concomitantly with other disease modifying multiple sclerosis agents (Note: Ampyra and Nuedexta are not disease modifying).

VI. REFERENCES

1. Copaxone [package insert]. Parsippany, NY: Teva Pharmaceuticals USA, Inc.; February 2023.
2. Glatopa [package insert]. Princeton, NJ: Sandoz Inc.; April 2022.
3. Glatiramer acetate 20mg/mL [package insert]. Morgantown, WV: Mylan Pharmaceuticals Inc.; May 2022.
4. Glatiramer acetate 40mg/mL [package insert]. Morgantown, WV: Mylan Pharmaceuticals Inc.; May 2022.
5. IBM Micromedex [database online]. Ann Arbor, MI: IBM Watson Health. Updated periodically. www.micromedexsolutions.com [available with subscription]. March 22, 2023.
6. AHFS DI (Adult and Pediatric) [database online]. Hudson, OH: Lexi-Comp, Inc.; http://online.lexi.com/lco/action/index/dataset/complete_ashp [available with subscription]. Accessed March 22, 2023.
7. The Multiple Sclerosis Coalition. *The use of disease-modifying therapies in multiple sclerosis: principles and current evidence.* http://www.nationalmssociety.org/getmedia/5ca284d3-fc7c-4ba5-b005-ab537d495c3c/DMT_Consensus_MS_Coalition_color. Accessed May 01, 2019.

QUANTITY LIMIT PRIOR AUTHORIZATION CRITERIA

BRAND NAME
(generic)

NEURONTIN
(gabapentin immediate-release capsules)

NEURONTIN
(gabapentin immediate-release tablets)

NEURONTIN
(gabapentin oral solution)

Status: CVS Caremark Criteria
Type: Quantity Limit; Post Limit Prior Authorization

POLICY

FDA-APPROVED INDICATIONS
Neurontin is indicated for:
- Management of postherpetic neuralgia in adults
- Adjunctive therapy in the treatment of partial onset seizures, with and without secondary generalization, in adults and pediatric patients 3 years and older with epilepsy

INITIAL QUANTITY LIMIT**

LIMIT CRITERIA
The limit is coded for daily dose. Limits do not accumulate together. Patient is allowed the maximum limit for each drug and strength.

Drug	Daily Limit
Gabapentin 100 mg	6 capsules/day
Gabapentin 300 mg	6 capsules/day
Gabapentin 400 mg	6 capsules/day
Gabapentin 600 mg	6 tablets/day
Gabapentin 800 mg	4 tablets/day
Gabapentin Oral solution 250 mg/5 mL	72 mL/day

**If the patient is requesting more than the initial quantity limit, the claim will reject with a message indicating that a prior authorization is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The patient is not taking more than 3600 mg per day of gabapentin

Quantity Limits apply.

The quantity limit is set at the maximum daily dosage of 3600 mg per day for gabapentin. All applicable strengths have been included on the limit criteria. Requested quantities that are greater than the initial limit for gabapentin oral solution 250 mg/5 mL, gabapentin 600 mg tablets or gabapentin 800 mg tablets would exceed the established maximum daily dose; therefore, no post limit quantities will be available for these strengths. A patient may receive up to 3600 mg per day on post limit approval for gabapentin 100 mg, 300 mg or 400 mg as follows:

- Gabapentin 100 mg: 1080 caps/25 days* or 3240 caps/75 days*
- Gabapentin 300mg: 360 caps/25 days* or 1080 caps/75 days*
- Gabapentin 400mg: 270 caps/25 days* or 810 caps/75 days*

**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*

REFERENCES

1. Neurontin [package insert]. New York, NY: Parke-Davis, Division of Pfizer Inc; December 2020.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2022; Accessed April 18, 2022.
3. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed April 18, 2022. .

QUANTITY LIMIT PRIOR AUTHORIZATION CRITERIA

BRAND NAME
(generic)

NEURONTIN
(gabapentin immediate-release capsules)

NEURONTIN
(gabapentin immediate-release tablets)

NEURONTIN
(gabapentin oral solution)

Status: CVS Caremark Criteria
Type: Quantity Limit; Post Limit Prior Authorization

POLICY

FDA-APPROVED INDICATIONS
Neurontin is indicated for:
- Management of postherpetic neuralgia in adults
- Adjunctive therapy in the treatment of partial onset seizures, with and without secondary generalization, in adults and pediatric patients 3 years and older with epilepsy

INITIAL QUANTITY LIMIT**

LIMIT CRITERIA
The limit is coded for daily dose. Limits do not accumulate together. Patient is allowed the maximum limit for each drug and strength.

Drug	Daily Limit
Gabapentin 100 mg	6 capsules/day
Gabapentin 300 mg	6 capsules/day
Gabapentin 400 mg	6 capsules/day
Gabapentin 600 mg	6 tablets/day
Gabapentin 800 mg	4 tablets/day
Gabapentin Oral solution 250 mg/5 mL	72 mL/day

**If the patient is requesting more than the initial quantity limit, the claim will reject with a message indicating that a prior authorization is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The patient is not taking more than 3600 mg per day of gabapentin

Quantity Limits apply.

The quantity limit is set at the maximum daily dosage of 3600 mg per day for gabapentin. All applicable strengths have been included on the limit criteria. Requested quantities that are greater than the initial limit for gabapentin oral solution 250 mg/5 mL, gabapentin 600 mg tablets or gabapentin 800 mg tablets would exceed the established maximum daily dose; therefore, no post limit quantities will be available for these strengths. A patient may receive up to 3600 mg per day on post limit approval for gabapentin 100 mg, 300 mg or 400 mg as follows:

- Gabapentin 100 mg: 1080 caps/25 days* or 3240 caps/75 days*
- Gabapentin 300mg: 360 caps/25 days* or 1080 caps/75 days*
- Gabapentin 400mg: 270 caps/25 days* or 810 caps/75 days*

**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*

REFERENCES

1. Neurontin [package insert]. New York, NY: Parke-Davis, Division of Pfizer Inc; December 2020.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2022; Accessed April 18, 2022.
3. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed April 18, 2022. .

QUANTITY LIMIT CRITERIA

BRAND NAME
(generic)

GRALISE
(gabapentin extended-release tablet)

HORIZANT
(gabapentin enacarbil extended-release tablet)

Status: CVS Caremark® Criteria
Type: Quantity Limit

POLICY

FDA-APPROVED INDICATIONS

Gralise
Gralise is indicated for the management of postherpetic neuralgia.

Gralise is not interchangeable with other gabapentin products because of differing pharmacokinetic profiles that affect the frequency of administration.

Horizant
Treatment of Restless Legs Syndrome
Horizant is indicated for the treatment of moderate-to-severe primary Restless Legs Syndrome (RLS) in adults.
Horizant is not recommended for patients who are required to sleep during the daytime and remain awake at night.
Management of Postherpetic Neuralgia
Horizant is indicated for the management of postherpetic neuralgia (PHN) in adults.

LIMIT CRITERIA

Limits do not accumulate together; patient is allowed the maximum limit for each drug and strength

Drug	1 Month Limit*	3 Month Limit*
Gralise 300 mg (gabapentin extended-release)	150 tablets / 25 days	450 tablets / 75 days
Gralise 450 mg (gabapentin extended-release)	90 tablets / 25 days	270 tablets / 75 days
Gralise 600 mg (gabapentin extended-release)	90 tablets / 25 days	270 tablets / 75 days
Gralise 750 mg (gabapentin extended-release)	60 tablets / 25 days	180 tablets / 75 days
Gralise 900 mg (gabapentin extended-release)	60 tablets / 25 days	180 tablets / 75 days
Horizant 300 mg (gabapentin enacarbil extended-release)	60 tablets / 25 days	180 tablets / 75 days
Horizant 600 mg (gabapentin enacarbil extended-release)	60 tablets / 25 days	180 tablets / 75 days

**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*

REFERENCES

1. Gralise [package insert]. Morristown, NJ: Almatica Pharma LLC.; March 2023.
2. Horizant [package insert]. Atlanta, GA: Arbor Pharmaceuticals, LLC; April 2020.
3. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. http://online.lexi.com/. Accessed April 18, 2022.
4. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. http://www.micromedexsolutions.com/. Accessed April 18, 2022.

QUANTITY LIMIT CRITERIA

DRUG CLASS	**ANTIEMETICS**
BRAND NAME* (generic)	**granisetron hydrochloride (ALL PRODUCTS)** **SANCUSO (granisetron transdermal system)** **SUSTOL (granisetron extended-release injection)**

Status: CVS Caremark Criteria
Type: Quantity Limit ***Ref # 121-H***

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Granisetron

Granisetron Tablets

Granisetron Hydrochloride Tablets are indicated for the prevention of:

- Nausea and vomiting associated with initial and repeat courses of emetogenic cancer therapy, including high-dose cisplatin.
- Nausea and vomiting associated with radiation, including total body irradiation and fractionated abdominal radiation.

Granisetron Injection:

Granisetron Hydrochloride Injection is indicated for:

- Prevention of nausea and/or vomiting associated with initial and repeat courses of emetogenic cancer therapy, including high-dose cisplatin.
- Prevention and treatment of postoperative nausea and vomiting in adults. As with other antiemetics, routine prophylaxis is not recommended in patients in whom there is little expectation that nausea and/or vomiting will occur postoperatively. In patients where nausea and/or vomiting must be avoided during the postoperative period, granisetron hydrochloride injection USP is recommended even where the incidence of postoperative nausea and/or vomiting is low.

Sancuso Transdermal System

Sancuso is indicated for the prevention of nausea and vomiting in adults receiving moderately and/or highly emetogenic chemotherapy regimens of up to 5 consecutive days duration.

Sustol Extended-Release Injection

Sustol is indicated in combination with other antiemetics in adults for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of moderately emetogenic chemotherapy (MEC) or anthracycline and cyclophosphamide (AC) combination chemotherapy regimens.

INITIAL LIMIT QUANTITY
Limits do not accumulate together; patient is allowed the maximum limit for each drug and strength

Drug	4 Week Limit*	12 Week Limit*
Granisetron Tablets	12 tablets / 21 days	Does Not Apply*
Granisetron Injection 1 mg/mL or 4mg/4mL	2 mL / 21 days	Does Not Apply*
Sancuso (granisetron transdermal system)	2 patches / 21 days	Does Not Apply*
Sustol (granisetron extended-release injection 10 mg/0.4 mL)	0.8 mL / 21 days	Does Not Apply*

** The duration of 21 days is used for a 28-day fill period to allow time for refill processing.*

** These drugs are for short-term acute use; therefore, the mail limit will be the same as the retail limit. The intent is for prescriptions of the requested drug to be filled one month at a time, even if filled at mail order; there should be no 3 month supplies filled.*

RATIONALE

Granisetron Tablets

Granisetron tablets are indicated for the prevention of nausea and vomiting associated with initial and repeat courses of emetogenic cancer therapy, including high-dose cisplatin. Granisetron tablets are also indicated for nausea and vomiting associated with radiation, including total body irradiation and fractionated abdominal radiation.

The recommended adult dosage of oral granisetron for emetogenic chemotherapy is 2 mg once daily or 1 mg twice daily. In the 2 mg once daily regimen, two 1 mg tablets are given up to one hour before chemotherapy. In the 1 mg twice-daily regimen, the first 1 mg tablet is given up to one hour before chemotherapy, and the second tablet is given 12 hours after the first tablet. Either regimen is administered only on the day(s) chemotherapy is given. Continued treatment, while not on chemotherapy, has not been found to be useful.

The recommended adult dosage of oral granisetron for either total body irradiation or fractionated abdominal radiation is 2 mg once daily. Two 1 mg tablets are taken within one hour of radiation.[1,5,6]

Patients need to be protected throughout the entire period of risk, which lasts for at least 3 days for high emetic risk and 2 days for moderate emetic risk agents after the last dose of chemotherapy. According to the National Comprehensive Cancer Network (NCCN) Antiemesis Guidelines for moderately emetogenic chemotherapy, repeated doses may be given on days 2 and 3 for dolasetron, granisetron and ondansetron.[7] Based on dosing recommendations, six tablets are sufficient for treatment through one chemotherapy cycle.

For granisetron tablets, the limits are designed to allow for treatment at the recommended doses on the day of chemotherapy or radiation plus additional doses one to two days post-chemotherapy or radiation as recommended based on exact treatment received. The limit allows a quantity sufficient for two chemotherapy cycles per 28 days (i.e., one chemotherapy cycle every 2 weeks). If the patient is requesting more than the initial quantity limit the claim will reject with a message indicating that a prior authorization is required.

Granisetron Injection

Granisetron injection is indicated for the prevention of nausea and/or vomiting associated with initial and repeat courses of emetogenic cancer therapy, including high-dose cisplatin.

The recommended adult dosage for granisetron injection is 10 mcg/kg administered intravenously within 30 minutes before initiation of chemotherapy, and only on the day(s) chemotherapy is given. The recommended dose in pediatric patients 2 to 16 years of age, is 10 mcg/kg.[2,5,6] The National Comprehensive Cancer Network (NCCN) Antiemesis Guideline indicates that the maximum daily dosage to be given is 1 mg. For moderately emetogenic chemotherapy, the same dose may be repeated on days 2 and 3.[7]

The recommended adult dosage for granisetron injection for the treatment of nausea and/or vomiting after surgery is 1 mg administered intravenously.

For granisetron injection, the limit is designed to allow for treatment at the recommended doses on the day of chemotherapy. Based on dosing recommendations, 1 mL (1 mg) is sufficient for treatment through one chemotherapy cycle. The limit allows a quantity sufficient for two chemotherapy cycles per 28 days (i.e., one chemotherapy cycle every 2 weeks). The dosing for treatment of postoperative nausea and vomiting falls within the limit. If the patient is requesting more than the initial quantity limit the claim will reject with a message indicating that a prior authorization is required.

Sancuso Transdermal System
Sancuso is indicated for the prevention of nausea and vomiting in adults receiving moderately and/or highly emetogenic chemotherapy regimens of up to 5 consecutive days duration.

For adults, the recommended dosage of Sancuso is one 3.1 mg patch applied to the upper outer arm a minimum of 24 hours before chemotherapy. The patch may be applied up to a maximum of 48 hours before chemotherapy as appropriate. Remove the patch a minimum of 24 hours after completion of chemotherapy. The patch can be worn for up to 7 days depending on the duration of the chemotherapy regimen.[3,5,6]

For Sancuso, the limit is designed to allow for treatment at the recommended doses 24-48 hours before the day of chemotherapy. Based on dosing recommendations, one patch is sufficient for treatment through one chemotherapy cycle. The limit allows a quantity sufficient for two chemotherapy cycles per 28 days (i.e., one chemotherapy cycle every 2 weeks). If the patient is requesting more than the initial quantity limit the claim will reject with a message indicating that a prior authorization is required.

Sustol Extended-Release Injection
Sustol is indicated in combination with other antiemetics in adults for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of moderately emetogenic chemotherapy (MEC) or anthracycline and cyclophosphamide (AC) combination chemotherapy regimens.

The recommended dosage of Sustol is 10 mg administered subcutaneously in combination with dexamethasone at least 30 minutes before the start of MEC or AC combination chemotherapy. Sustol is administered on Day 1 of chemotherapy and not more frequently than once every 7 days because of the extended-release properties of the formulation.[4,5,6] Sustol is intended for administration by a healthcare provider.[4]

For Sustol, the limit is designed to allow for treatment at the recommended doses on the day of chemotherapy. Based on dosing recommendations and the strength of Sustol injection (10 mg/0.4 mL), 0.4 mL (10 mg) is sufficient for treatment through one chemotherapy cycle. The limit allows a quantity sufficient for two chemotherapy cycles per 28 days (i.e., one chemotherapy cycle every 2 weeks). If the patient is requesting more than the initial quantity limit the claim will reject with a message indicating that a prior authorization is required.

REFERENCES

1. Granisetron Tablet [package insert]. Berlin, CT: Breckenridge Pharmaceutical, Inc.; October 2019.
2. Granisetron Injection [package insert]. E. Windsor, NJ: AuroMedics Pharma LLC; December 2021.
3. Sancuso Patch [package insert]. Bedminster, NJ: Kyowa Kirin, Inc.; July 2022.
4. Sustol Injection [package insert]. Chaska, MN: Lifecore Biomedical; May 2017.
5. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2022; Accessed November 14, 2022.
6. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed November 11, 2022.
7. National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology. Antiemesis. Version 2.2022. Available at: https://www.nccn.org/professionals/physician_gls/pdf/antiemesis.pdf. Accessed November 16, 2022.

Written by: UM Development (LS)
Date Written: 01/2000
Revised: (JG) 08/ 2002; (MG) 07/2003, 10/2004, 09/2005; (AK) 04/2006; (AM) 03/2007 (added 0.1 mg/mL injectable strength); (CT) 04/2007, 04/2008, 10/2008(2) (Sancuso added); (SE) 03/2009; (KD) 03/2010; (CY) 04/2011(Brand Kytril removed), 02/2012 (PONV removed for granisetron injectable, Sancuso limit reduced); (PL) 01/2013, (PL) 01/2014; (CF) 01/2015, 01/2016; (KM)

	01/2017 (added Sustol injection), (ME) 01/2018 (no clinical changes); (KC) 01/2019 (no clinical changes), (ME) 01/2020 (no clinical changes), 01/2021 (no clinical changes), (MRS) 01/2022 (no clinical changes), (TM/KJ) 12/2022 (no clinical changes)
Reviewed:	Medical Affairs 01/2000, 08/2002, 08/2003, 10/2004, 09/2005; (MM) 04/2006; (WLF) 03/2007, 04/2007, 04/2008, 10/2008, 03/2009, 03/2010; (KP) 04/2011, 02/2012; (LMS) 01/2013, (KP) 01/2014; (SES) 01/2015; (GAD) 01/2016; (JG) 02/2017; (CHART) 01/30/20, 01/28/21, 02/03/22, 12/29/2022
External Review:	10/2002, 08/2003, 11/2004, 08/2006, 08/2007, 08/2008, 10/2008, 08/2009, 08/2010, 08/2011, 04/2012, 06/2013, 04/2014, 04/2015, 04/2016, 04/2017, 04/2018, 04/2019, 04/2020, 04/2021, 04/2022, 04/2023

Reference number(s)
1741-A

SPECIALTY GUIDELINE MANAGEMENT

GENOTROPIN (somatropin)
HUMATROPE (somatropin)
NORDITROPIN (somatropin)
NUTROPIN AQ (somatropin)
OMNITROPE (somatropin)
SAIZEN (somatropin)
ZOMACTON (somatropin)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no contraindications or exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. Pediatric patients with growth failure due to any of the following:
      a. Growth hormone (GH) deficiency
      b. Turner syndrome
      c. Noonan syndrome
      d. Small for gestational age (SGA)
      e. Prader-Willi syndrome
      f. Chronic kidney disease (CKD)
      g. Short stature homeobox-containing gene (SHOX) deficiency
      h. Idiopathic short stature (ISS)*
   2. Adults with childhood-onset or adult-onset GH deficiency

** ISS may not be covered by some plans*

B. Compendial Uses
   1. Human immunodeficiency virus (HIV)-associated wasting/cachexia
   2. Short bowel syndrome (SBS)
   3. Growth failure associated with any of the following:
      a. Cerebral palsy
      b. Congenital adrenal hyperplasia
      c. Cystic fibrosis
      d. Russell-Silver syndrome

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review for both initial and continuation of therapy requests (where applicable):
A. Medical records supporting the diagnosis of neonatal GH deficiency

B. Pretreatment growth hormone provocative test result(s) (laboratory report or medical record documentation)
C. Growth chart
D. Pretreatment and/or current IGF-1 level (laboratory report or medical record documentation)*
E. The following laboratory test reports must be provided:
   1. Diagnostic karyotype results in Turner syndrome
   2. Diagnostic genetic test results in Prader-Willi syndrome
   3. Diagnostic molecular or genetic test results in SHOX deficiency
F. The following information must be provided for all continuation of therapy requests:
   1. Total duration of treatment (approximate duration is acceptable)
   2. Date of last dose administered
   3. Approving health plan/pharmacy benefit manager
   4. Date of prior authorization/approval
   5. Prior authorization approval letter

* IGF-1 levels vary based on the laboratory performing the analysis. Laboratory-specific values must be provided to determine whether the value is within the normal range.

III. CRITERIA FOR INITIAL APPROVAL

A. Pediatric GH Deficiency

Authorization of 12 months may be granted to members with pediatric GH deficiency when EITHER criteria 1. or 2. Below is met:

1. Member is a neonate or was diagnosed with GH deficiency as a neonate. Medical records must be available to support the diagnosis of neonatal GH deficiency (e.g., hypoglycemia with random GH level, evidence of multiple pituitary hormone deficiency, chart notes, or magnetic resonance imaging [MRI] results).
2. Member meets ALL of the following:
   i. Member has EITHER:
      a. Two pretreatment pharmacologic provocative GH tests with both results demonstrating a peak GH level < 10 ng/mL, OR
      b. A documented pituitary or CNS disorder (refer to Appendix A) and a pretreatment IGF-1 level > 2 standard deviations (SD) below the mean
   i. For members < 2.5 years of age at initiation of treatment, the pretreatment height is > 2 SD below the mean and growth velocity is slow
   ii. For members ≥ 2.5 years of age at initiation of treatment:
      a. Pretreatment height is > 2 SD below the mean and 1-year height velocity is > 1 SD below the mean, OR
      b. Pretreatment 1-year height velocity is > 2 SD below the mean
   iii. Epiphyses are open

B. Idiopathic Short Stature *(may not be covered by some plans)*

Authorization of 12 months may be granted to members with ISS when ALL of the following criteria are met:

1. Pretreatment height is > 2.25 SD below the mean
2. Predicted adult height is < 5'3" for boys and < 4'11" for girls
3. Pediatric GH deficiency has been ruled out with a provocative GH test (peak GH level ≥ 10 ng/mL)
4. Epiphyses are open

C. Small for Gestational Age

Authorization of 12 months may be granted to members born SGA when ALL of the following criteria are met:

1. Member meets at least one of the following:
   i. Birth weight < 2500 g at gestational age > 37 weeks
   ii. Birth weight or length less than 3rd percentile for gestational age
   iii. Birth weight or length ≥ 2 SD below the mean for gestational age
2. Pretreatment age is ≥ 2 years
3. Member failed to manifest catch-up growth by age 2 (i.e., pretreatment height > 2 SD below the mean)
4. Epiphyses are open

D. Turner Syndrome

Authorization of 12 months may be granted to members with Turner syndrome when ALL of the following criteria are met:

1. Diagnosis was confirmed by karyotyping
2. Patient's pretreatment height is less than the 5th percentile for age
3. Epiphyses are open

E. Growth Failure Associated with Chronic Kidney Disease (CKD), Cerebral Palsy, Congenital Adrenal Hyperplasia, Cystic Fibrosis, and Russell-Silver Syndrome

Authorization of 12 months may be granted to members with CKD, cerebral palsy, congenital adrenal hyperplasia, cystic fibrosis, or Russell-Silver syndrome when ALL of the following criteria are met:

1. For members < 2.5 years of age at initiation of treatment, the pretreatment height is > 2 SD below the mean and growth velocity is slow
2. For members ≥ 2.5 years of age at initiation of treatment:
   i. Pretreatment height is > 2 SD below the mean and 1-year height velocity is > 1 SD below the mean, OR
   ii. Pretreatment 1-year height velocity is > 2 SD below the mean
3. Epiphyses are open

F. Prader-Willi Syndrome

Authorization of 12 months may be granted to members with Prader-Willi syndrome when the diagnosis was confirmed by genetic testing demonstrating any of the following:

1. Deletion in the chromosomal 15q11.2-q13 region
2. Maternal uniparental disomy in chromosome 15
3. Imprinting defects, translocations, or inversions involving chromosome 15

G. Noonan Syndrome

Authorization of 12 months may be granted to members with Noonan syndrome when ALL of the following criteria are met:

1. Pretreatment height is > 2 SD below the mean and 1-year height velocity is > 1 SD below the mean OR pretreatment 1-year height velocity is > 2 SD below the mean
2. Epiphyses are open

H. Short Stature Homeobox-Containing Gene Deficiency

Authorization of 12 months may be granted to members with SHOX deficiency when ALL of the following criteria are met:

1. The diagnosis of SHOX deficiency was confirmed by molecular or genetic analyses
2. Pretreatment height is > 2 SD below the mean and 1-year height velocity is > 1 SD below the mean OR pretreatment 1-year height velocity is > 2 SD below the mean
3. Epiphyses are open

I. Adult GH Deficiency

Authorization of 12 months may be granted to members with adult GH deficiency when ANY of the following criteria is met:

1. Member meets both of the following:
   i. Member has had 2 pretreatment pharmacologic provocative GH tests and both results demonstrated deficient GH responses defined as the following:
      a. Insulin tolerance test (ITT) with a peak GH level ≤ 5 ng/mL
      b. Macrilen with a peak GH level of less than 2.8 ng/mL
      c. Glucagon stimulation test with a peak GH level ≤ 3.0 ng/mL in patients with a body mass index (BMI) ≤ 30 kg/m^2 and a high pretest probability of GHD (e.g., acquired structural abnormalities) OR a BMI < 25 kg/m^2
      d. Glucagon stimulation test with a peak GH level ≤ 1.0 ng/mL in patients with a BMI of ≥ 25 kg/m^2 and a low pretest probability of GHD (e.g., acquired structural abnormalities) OR a BMI > 30 kg/m^2
   ii. Member has a low pre-treatment IGF-1 (between 0 to 2 SD below the mean for age and gender)
2. Member meets both of the following:
   i. Member has had 1 pretreatment pharmacologic provocative GH test that demonstrated deficient GH responses defined as one of the following:
      a. Insulin tolerance test (ITT) with a peak GH level ≤ 5 ng/mL
      b. Macrilen with a peak GH level of less than 2.8 ng/mL
      c. Glucagon stimulation test with a peak GH level ≤ 3.0 ng/mL in patients with a body mass index (BMI) ≤ 30 kg/m^2 and a high pretest probability of GHD (e.g., acquired structural abnormalities) OR a BMI < 25 kg/m^2
      d. Glucagon stimulation test with a peak GH level ≤ 1.0 ng/mL in patients with a BMI of ≥ 25 kg/m^2 and a low pretest probability of GHD (e.g., acquired structural abnormalities) OR a BMI > 30 kg/m^2
   ii. Member has a pretreatment IGF-1 level that is more than 2 SD below the mean for age and gender
3. Member has organic hypothalamic-pituitary disease (e.g., suprasellar mass with previous surgery and cranial irradiation) with ≥ 3 documented pituitary hormone deficiencies (refer to Appendix B) and a low pre-treatment IGF-1 more than 2 standard deviations below the mean for age and gender
4. Member has genetic or structural hypothalamic-pituitary defects (refer to Appendix C)
5. Member has childhood-onset GH deficiency and a congenital abnormality of the CNS, hypothalamus or pituitary (refer to Appendix C)

J. HIV-Associated Wasting/Cachexia

Authorization of 12 weeks may be granted to members with HIV-associated wasting or cachexia when ALL of the following criteria are met:

1. Member trialed and experienced a suboptimal response to alternative therapies (e.g., cyproheptadine, dronabinol, megestrol acetate or testosterone if hypogonadal) or contraindication or intolerance to alternative therapies
2. Member is currently on antiretroviral therapy
3. BMI was less than 18.5 kg/m^2 prior to initiating therapy with growth hormone (see Appendix D)

K. Short Bowel Syndrome

Authorization of a lifetime total of 8 weeks may be granted to members with short bowel syndrome who depend on intravenous parenteral nutrition for nutritional support when GH will be used in conjunction with optimal management of SBS.

IV. CONTINUATION OF THERAPY

A. Pediatric GH Deficiency, Turner Syndrome, Noonan Syndrome, CKD, SGA, ISS, SHOX deficiency, Congenital Adrenal Hyperplasia, Cerebral Palsy, Cystic Fibrosis, and Russell-Silver Syndrome
Authorization of 12 months may be granted for continuation of therapy when ALL of the following criteria are met:
1. Epiphyses are open (confirmed by X-ray or X-ray is not available)
2. Member's growth rate is > 2 cm/year unless there is a documented clinical reason for lack of efficacy (e.g., on treatment less than 1 year, nearing final adult height/late stages of puberty)

B. Prader-Willi Syndrome
Authorization of 12 months may be granted for continuation of therapy when the member's body composition and psychomotor function have improved or stabilized in response to GH therapy.

C. Adult GH Deficiency
Authorization of 12 months may be granted for continuation of therapy when ANY of the following criteria is met:
1. Member meets all of the following:
    i. Member has had 2 pretreatment pharmacologic provocative GH tests and both results demonstrated deficient GH responses defined as the following:
        a. Insulin tolerance test (ITT) or another provocative GH test with a peak GH level ≤ 5 ng/mL
        b. Macrilen with a peak GH level of less than 2.8 ng/mL
        c. Glucagon stimulation test with a peak GH level ≤ 3.0 ng/mL in patients with a body mass index (BMI) ≤ 30 kg/m^2 and a high pretest probability of GHD (e.g., acquired structural abnormalities) OR a BMI < 25 kg/m^2
        d. Glucagon stimulation test with a peak GH level ≤ 1.0 ng/mL in patients with a BMI of ≥ 25 kg/m^2 and a low pretest probability of GHD (e.g., acquired structural abnormalities) OR a BMI > 30 kg/m^2
    ii. Member has a low pre-treatment IGF-1 (between 0 to 2 SD below the mean for age and gender)
    iii. Current IGF-1 level is not elevated for age and gender
2. Member meets all of the following:
    i. Member has had 1 pretreatment pharmacologic provocative GH test that demonstrated deficient GH responses defined as one of the following:
        a. Insulin tolerance test (ITT) or another provocative GH test with a peak GH level ≤ 5 ng/mL
        b. Macrilen with a peak GH level of less than 2.8 ng/mL
        c. Glucagon stimulation test with a peak GH level ≤ 3.0 ng/mL in patients with a body mass index (BMI) ≤ 30 kg/m^2 and a high pretest probability of GHD (e.g., acquired structural abnormalities) OR a BMI < 25 kg/m^2
        d. Glucagon stimulation test with a peak GH level ≤ 1.0 ng/mL in patients with a BMI of ≥ 25 kg/m^2 and a low pretest probability of GHD (e.g., acquired structural abnormalities) OR a BMI > 30 kg/m^2
    ii. Member has a pretreatment IGF-1 level that is more than 2 SD below the mean for age and gender
    iii. Current IGF-1 level is not elevated for age and gender
3. Member meets both of the following:
    i. Member has organic hypothalamic-pituitary disease (e.g., suprasellar mass with previous surgery and cranial irradiation) with ≥ 3 documented pituitary hormone deficiencies (refer to Appendix B) and a low pre-treatment IGF-1 more than 2 standard deviations below the mean for age and gender
    ii. Current IGF-1 level is not elevated for age and gender
4. Member has genetic or structural hypothalamic-pituitary defects (refer to Appendix C) and current IGF-1 level is not elevated for age and gender
5. Member has childhood-onset GH deficiency and a congenital abnormality of the CNS, hypothalamus or pituitary (refer to Appendix C) and current IGF-1 level is not elevated for age and gender

D. HIV-Associated Wasting/Cachexia

Authorization of 12 weeks may be granted for continuation of therapy when ALL of the following criteria are met:

1. Member is diagnosed with HIV-associated wasting/cachexia
2. Member is currently on antiretroviral therapy.
3. Member is currently receiving treatment with growth hormone excluding obtainment as samples or via manufacturer's patient assistance programs
4. Current BMI is less than 27 kg/m^2 (see Appendix D).

V. APPENDICES

A. Appendix A: Examples of Hypothalamic/Pituitary/CNS Disorders

1. Congenital genetic abnormalities
   a. Transcription factor defects (PIT-1, PROP-1, LHX3/4, HESX-1, PITX-2)
   b. Growth hormone releasing hormone (GHRH) receptor gene defects
   c. GH secretagogue receptor gene defects
   d. GH gene defects
   e. GH receptor/post receptor defects
2. Congenital structural abnormalities
   a. Optic nerve hypoplasia/septo-optic dysplasia
   b. Agenesis of corpus callosum
   c. Empty sella syndrome
   d. Ectopic posterior pituitary
   e. Pituitary aplasia/hypoplasia
   f. Pituitary stalk defect
   g. Holoprosencephaly
   h. Encephalocele
   i. Hydrocephalus
   j. Anencephaly or prosencephaly
   k. Arachnoid cyst
   l. Other mid-line facial defects (e.g., single central incisor, cleft lip/palate)
   m. Vascular malformations
3. Acquired structural abnormalities (or causes of hypothalamic/pituitary damage)
   a. CNS tumors/neoplasms (e.g., craniopharyngioma, glioma/astrocytoma, pituitary adenoma, germinoma)
   b. Cysts (Rathke cleft cyst or arachnoid cleft cyst)
   c. Surgery
   d. Radiation
   e. Chemotherapy
   f. CNS infections
   g. CNS infarction (e.g., Sheehan's syndrome)
   h. Inflammatory processes (e.g., autoimmune hypophysitis)
   i. Infiltrative processes (e.g., sarcoidosis, histiocytosis, hemochromatosis)
   j. Head trauma/traumatic brain injury
   k. Aneurysmal subarachnoid hemorrhage
   l. Perinatal or postnatal trauma
   m. Surgery of the pituitary or hypothalamus

B. Appendix B: Pituitary Hormones (Other than Growth Hormone)

1. Adrenocorticotropic hormone (ACTH)

2. Antidiuretic hormone (ADH)
3. Follicle stimulating hormone (FSH)
4. Luteinizing hormone (LH)
5. Thyroid stimulating hormone (TSH)
6. Prolactin

C. Appendix C: Requirements for GH-Stimulation Testing in Adults

1. Testing for adult GHD is not required
   a. Three or more pituitary hormone deficiencies and low IGF-1
   b. Congenital structural abnormalities
      i. Transcription factor defects (PIT-1, PROP-1, LHX3/4, HESX-1, PITX-2)
      ii. GHRH receptor-gene defects
      iii. GH-receptor/post-receptor defects
      iv. GH-gene defects associated with brain structural defects
      v. Single central incisor
      vi. Cleft lip/palate
   c. Acquired causes such as perinatal insults
2. Testing for adult GHD is required
   a. Acquired
      i. Skull-base lesions
      ii. Pituitary adenoma
      iii. Craniopharyngioma
      iv. Rathke's cleft cyst
      v. Meningioma
      vi. Glioma/astrocytoma
      vii. Neoplastic sellar and parasellar lesions
      viii. Chordoma
      ix. Hamartoma
      x. Lymphoma
      xi. Metastases
      xii. Other brain injury
      xiii. Traumatic brain injury
      xiv. Sports-related head trauma
      xv. Blast injury
      xvi. Infiltrative/granulomatous disease
      xvii. Langerhans cell histiocytosis
      xviii. Autoimmune hypophsitis (primary or secondary)
      xix. Sarcoidosis
      xx. Tuberculosus
      xxi. Amyloidosis
   b. Surgery to the sella, suprasellar, and parasellar region
   c. Cranial irradiation
   d. Central nervous system infections (bacteria, viruses, fungi, parasites)
   e. Infarction/hemorrhage (e.g., apoplexy, Sheehan's syndrome, subarachnoid hemorrhage, ischemic stroke, snake bite)
   f. Empty sella
   g. Hydrocephalus
   h. Idiopathic

D. Appendix D: Calculation of BMI

$$\frac{\text{Weight (pounds)} \times 703}{\text{Weight (kg)}}$$

BMI = $\frac{\text{---------- OR ----------}}{\text{[Height (inches)]}^2 \qquad \text{[Height (m)]}^2}$

BMI classification:		
	Underweight	< 18.5 kg/m^2
	Normal weight	18.5 – 24.9 kg/m^2
	Overweight	25 – 29.9 kg/m^2
	Obesity (class 1)	30 – 34.9 kg/m^2
	Obesity (class 2)	35 – 39.9 kg/m^2
	Extreme obesity (class 3)	≥ 40 kg/m^2

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Reference number(s)
2100-A

SPECIALTY GUIDELINE MANAGEMENT

HAEGARDA (C1 Esterase Inhibitor Subcutaneous [Human])

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Haegarda is indicated for routine prophylaxis to prevent Hereditary Angioedema (HAE) attacks in patients 6 years of age and older.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
A. For initial authorization, the following should be documented:
   1. C1 inhibitor functional and antigenic protein levels
   2. F12, angiopoietin-1, plasminogen, kininogen-1 (KNG1), heparan sulfate-glucosamine 3-O-sulfotransferase 6 (HS3ST6), or myoferlin (MYOF) gene mutation testing, if applicable
   3. Chart notes confirming family history of angioedema and the angioedema was refractory to a trial of high-dose antihistamine therapy, if applicable
B. For continuation of therapy, chart notes demonstrating a reduction in frequency of attacks

III. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with a prescriber who specializes in the management of HAE.

IV. CRITERIA FOR APPROVAL

Hereditary angioedema (HAE)
Authorization of 6 months may be granted for prevention of hereditary angioedema attacks when the requested medication will not be used in combination with any other medication used for prophylaxis of HAE attacks and either of the following criteria is met at the time of diagnosis:
A. Member has C1 inhibitor deficiency or dysfunction as confirmed by laboratory testing and meets one of the following criteria:
   1. C1 inhibitor (C1-INH) antigenic level below the lower limit of normal as defined by the laboratory performing the test, or

2. Normal C1-INH antigenic level and a low C1-INH functional level (functional C1-INH less than 50% or C1-INH functional level below the lower limit of normal as defined by the laboratory performing the test).

B. Member has normal C1 inhibitor as confirmed by laboratory testing and meets one of the following criteria:
1. Member has an F12, angiopoietin-1, plasminogen, kininogen-1 (KNG1), heparan sulfate-glucosamine 3-O-sulfotransferase 6 (HS3ST6), or myoferlin (MYOF) gene mutation as confirmed by genetic testing, or
2. Member has a documented family history of angioedema and the angioedema was refractory to a trial of high-dose antihistamine therapy (i.e., cetirizine at 40 mg per day or the equivalent) for at least one month.

V. CONTINUATION OF THERAPY

Authorization of 6 months may be granted for continuation of therapy when all of the following criteria are met:
A. Member meets the criteria for initial approval.
B. Member has experienced a significant reduction in frequency of attacks (e.g., ≥ 50%) since starting treatment.
C. Member has reduced the use of medications to treat acute attacks since starting treatment.

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Reference number(s)
2134-A, 2677-A

SPECIALTY GUIDELINE MANAGEMENT

HARVONI (ledipasvir and sofosbuvir)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Harvoni is indicated for the treatment of adults and pediatric patients 3 years of age and older with chronic hepatitis C virus (HCV):

A. genotype 1, 4, 5, or 6 infection without cirrhosis or with compensated cirrhosis
B. genotype 1 infection with decompensated cirrhosis, for use in combination with ribavirin
C. genotype 1 or 4 infection who are liver transplant recipients without cirrhosis or with compensated cirrhosis, for use in combination with ribavirin

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Hepatitis C virus infection, without ribavirin

1. Genotype 1 infection

i. Authorization of up to 12 weeks total may be granted for treatment-naïve members with compensated cirrhosis.
ii. Authorization of up to 12 weeks total may be granted for treatment-naïve members without cirrhosis who have any of the following: HIV co-infection, or are less than 18 years of age, or have pre-treatment HCV RNA greater than or equal to 6 million IU/mL.
iii. Authorization of up to 8 weeks total may be granted for treatment-naive members without cirrhosis who have pre-treatment HCV RNA below 6 million IU/mL and are HIV-uninfected.
iv. Authorization of up to 12 weeks total may be granted for members without cirrhosis who failed prior treatment with peginterferon alfa (PEG-IFN) with or without ribavirin (RBV) with or without an HCV protease inhibitor (telaprevir, boceprevir, or simeprevir).
v. Authorization of up to 24 weeks total may be granted for members with compensated cirrhosis who failed prior treatment with PEG-IFN with or without RBV with or without an HCV protease inhibitor.

2. Genotype 4 or 5

Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who are treatment-naïve or who failed prior treatment with PEG-IFN with or without RBV with or without an HCV protease inhibitor.

3. Genotype 6 infection

Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis when either of the following criteria are met:

i. Member is treatment-naïve and does not have genotype 6e subtype

ii. Member has failed prior treatment with PEG-IFN with or without RBV with or without an HCV protease inhibitor

4. Decompensated cirrhosis (CTP class B or C)
Authorization of up to 24 weeks total may be granted for members with HCV genotype 1, 4, 5 or 6 infection and documented anemia (baseline Hgb below 10 g/dL) or RBV ineligibility (see Section IV).

5. Recurrent HCV infection post liver transplantation
Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis and recurrent HCV genotype 1, 4, 5 or 6 infection post liver transplantation.

6. Kidney transplant recipients
Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who have HCV genotype 1, 4, 5 or 6 infection and are treatment-naïve or who have not failed prior treatment with a direct-acting antiviral.

B. Hepatitis C virus infection, in combination with ribavirin

1. Genotype 1 infection
Authorization of up to 12 weeks total may be granted for members with compensated cirrhosis who failed prior treatment with PEG-IFN with or without RBV with or without an HCV protease inhibitor.

2. Genotype 4 infection
Authorization of up to 12 weeks total may be granted for members with compensated cirrhosis who failed prior treatment with PEG-IFN with or without RBV with or without an HCV protease inhibitor.

3. Decompensated cirrhosis (CTP class B or C)
i. Authorization of up to 12 weeks total may be granted for members with HCV genotype 1, 4, 5 or 6 infection.
ii. Authorization of up to 24 weeks total may be granted for members with HCV genotype 1, 4, 5 or 6 infection who failed prior treatment with a sofosbuvir-based regimen (eg, sofosbuvir and RBV, sofosbuvir plus PEG-IFN and RBV, sofosbuvir plus simeprevir with or without RBV).

4. Recurrent HCV infection post liver transplantation
i. Authorization of up to 12 weeks total may be granted for treatment-naïve members with recurrent HCV genotype 1, 4, 5 or 6 infection post liver transplantation and decompensated cirrhosis.
ii. Authorization of up to 24 weeks total may be granted for treatment experienced members with recurrent HCV genotype 1, 4, 5 or 6 infection post liver transplantation and decompensated cirrhosis.

C. HCV and HIV coinfection
Authorization may be granted for members with HCV and HIV coinfection when the criteria for approval of the requested regimen in Section A or B above are met.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. APPENDIX: RIBAVIRIN INELIGIBILITY

RBV ineligibility is defined as one or more of the below:

- Intolerance to RBV
- Pregnant female or male whose female partner is pregnant
- Hemoglobinopathy
- Coadministration with didanosine
- History of significant or unstable cardiac disease

V. REFERENCES

1. Harvoni [package insert]. Foster City, CA: Gilead Sciences; March 2020.
2. AASLD/IDSA/IAS–USA. Recommendations for testing, managing, and treating hepatitis C. https://www.hcvguidelines.org. Last changes made September 29, 2021. Accessed October 15, 2021.

Reference number(s)
1925-A, 1926-A

SPECIALTY GUIDELINE MANAGEMENT

NOVAREL (chorionic gonadotropin)
PREGNYL (chorionic gonadotropin)
OVIDREL (choriogonadotropin alfa)
chorionic gonadotropin

*Hereafter, hCG will be used to describe all products

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
Novarel and Pregnyl are indicated for:
1. Prepubertal cryptorchidism not due to anatomic obstruction
2. Selected cases of hypogonadotropic hypogonadism (hypogonadism secondary to a pituitary deficiency) in males
3. Induction of ovulation and pregnancy in the anovulatory, infertile woman in whom the cause of anovulation is secondary and not due to primary ovarian failure, and who has been appropriately pretreated with human menotropins

Ovidrel is indicated for:
1. Induction of final follicular maturation and early luteinization in infertile women who have undergone pituitary desensitization and who have been appropriately pretreated with follicle stimulating hormones as part of an assisted reproductive technology (ART) program such as in vitro fertilization and embryo transfer
2. Induction of ovulation and pregnancy in anovulatory infertile patients in whom the cause of infertility is functional and not due to primary ovarian failure

B. Compendial Use
Infertility, luteal phase support

All other indications are considered experimental/investigational and not medically necessary.

II. MEDICAL BENEFIT ALIGNMENT

Specialty Guideline Management coverage review will be bypassed for drug(s) being requested for a procedure that has been approved under a member's medical benefit plan. Such members will be exempt from the requirements in Sections IV and V. A medical authorization number and confirmation of the approved procedure(s) will be required.

NOTE: Some plans may opt-out of medical benefit alignment. Members receiving coverage under such plans must meet the requirements in Sections IV and V.

III. REQUIRED DOCUMENTATION

The following information is necessary to initiate the prior authorization review for hypogonadotropic hypogonadism: testosterone, FSH, and LH levels.

IV. CRITERIA FOR INITIAL APPROVAL

A. Induction of oocyte maturation and/or release
Authorization of 12 months may be granted for members undergoing ovulation induction or assisted reproductive technology (ART).

B. Prepubertal cryptorchidism
Authorization of 6 months may be granted for treatment of prepubertal cryptorchidism.

C. Hypogonadotropic hypogonadism
Authorization of 12 months may be granted for treatment of hypogonadotropic hypogonadism in members who meet both of the following criteria:
1. Low pretreatment testosterone levels
2. Low or low-normal follicle stimulating hormone (FSH) or luteinizing hormone (LH) levels

V. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

VI. REFERENCES

1. Novarel [package insert]. Parsippany, NJ: Ferring Pharmaceuticals Inc.; May 2018.
2. Pregnyl [package insert]. Whitehouse Station, NJ: Merck & Co., Inc.; January 2015.
3. Ovidrel [package insert]. Rockland, MA: EMD Serono, Inc.; June 2018.
4. Chorionic Gonadotropin for Injection [package insert]. Lake Zurich, IL: Fresenius Kabi; February 2016.
5. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, CO. Available at: http://www.micromedexsolutions.com Accessed May 2, 2022.
6. Nosarka S, Kruger T, Siebert I, et al. Luteal phase support in in vitro fertilization: meta-analysis of randomized trials. *Gynecol Obstet Invest*. 2005;60:67-74.
7. American Association of Clinical Endocrinologists. Medical guidelines for clinical practice for the evaluation and treatment of hypogonadism in adult male patients – 2002 Update. *Endocr Pract*. 2002:8:439-456.

Reference number(s)
2417-A, 3536-A

SPECIALTY GUIDELINE MANAGEMENT

HEMLIBRA (emicizumab-kxwh)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Hemlibra is indicated for routine prophylaxis to prevent or reduce the frequency of bleeding episodes in adult and pediatric patients ages newborn and older with hemophilia A (congenital factor VIII deficiency) with or without factor VIII inhibitors.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
For continuation requests: Chart notes documenting benefit from therapy (e.g., reduced frequency or severity of bleeds).

III. PRESCRIBER SPECIALTIES

Must be prescribed by or in consultation with a hematologist.

IV. CRITERIA FOR INITIAL APPROVAL

Hemophilia A (congenital factor VIII deficiency)
Authorization of 12 months may be granted for treatment of hemophilia A (congenital factor VIII deficiency) when all of the following criteria is met:

A. Member must be using the requested medication for routine prophylaxis to prevent or reduce the frequency of bleeding episodes.
B. Member meets one of the following criteria:
    1. Member has mild disease (See Appendix A) and has had an insufficient response to desmopressin or a documented clinical reason for not using desmopressin (See Appendix B).
    2. Member has moderate or severe disease (See Appendix A).
C. Prophylactic use of factor VIII products (e.g., Advate, Adynovate, Eloctate) will be discontinued after the first week of starting therapy with the requested medication.

V. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section IV when the member is experiencing benefit from therapy (e.g., reduced frequency or severity of bleeds) and member is not using the requested medication in combination with factor VIII products (e.g., Advate, Adynovate, Eloctate, etc.) for prophylactic use.

VI. DOSAGE AND ADMINISTRATION

For initial and continuation requests, dosing does not exceed the following:
A. Induction: 3mg/kg subcutaneously once weekly for the first 4 weeks.
B. Maintenance: 1.5mg/kg once weekly, or 3mg/kg once every 2 weeks, or 6mg/kg once every 4 weeks.

VII. APPENDICES

Appendix A: Classification of Hemophilia by Clotting Factor Level (% Activity) and Bleeding Episodes

Severity	Clotting Factor Level % activity*	Bleeding Episodes
Severe	<1%	Spontaneous bleeding episodes, predominantly into joints and muscles Severe bleeding with trauma, injury or surgery
Moderate	1% to 5%	Occasional spontaneous bleeding episodes Severe bleeding with trauma, injury or surgery
Mild	6% to 40%	Severe bleeding with serious injury, trauma or surgery

Appendix B: Clinical Reasons For Not Utilizing Desmopressin in Patients with Hemophilia A
a. Age < 2 years
b. Pregnancy
c. Fluid/electrolyte imbalance
d. High risk for cardiovascular or cerebrovascular disease (especially the elderly)
e. Predisposition to thrombus formation
f. Trauma requiring surgery
g. Life-threatening bleed
h. Contraindication or intolerance to desmopressin
i. Stimate Nasal Spray is unavailable due to backorder/shortage issues (where applicable)

VIII. REFERENCES

1. Hemlibra [package insert]. South San Francisco, CA: Genentech, Inc.; June 2022.
2. Srivastava A, Santagostino E, Dougall A, et al. WFH Guidelines for the Management of Hemophilia, 3rd edition. *Haemophilia*. 2020;26 Suppl 6:1-158. doi:10.1111/hae.14046.
3. National Hemophilia Foundation. MASAC recommendations concerning products licensed for the treatment of hemophilia and other bleeding disorders. Revised March 2022. MASAC Document #272. https://www.hemophilia.org/sites/default/files/document/files/272_Treatment.pdf. Accessed December 2, 2022.
4. National Hemophilia Foundation. Hemophilia A (Factor VIII Deficiency). Available at: http://www.hemophilia.org/NHFWeb/MainPgs/MainNHF.aspx?menuid=180&contentid=45&rptname=bleeding. Accessed December 2, 2022.

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6. Leissinger C, Carcao M, Gill JC, et al. Desmopressin (DDAVP) in the management of patients with congenital bleeding disorders. *Haemophilia*. 2014;20:158-167.

Reference number(s)
2426-A

SPECIALTY GUIDELINE MANAGEMENT

HETLIOZ (tasimelteon) capsules
HETLIOZ LQ (tasimelteon) oral suspension

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

A. Non-24-Hour Sleep-Wake Disorder (Non-24):
Hetlioz capsules are indicated for the treatment of Non-24 in adults.

B. Nighttime Sleep Disturbances in Smith-Magenis Syndrome (SMS):
1. Hetlioz capsules are indicated for treatment of nighttime sleep disturbances in SMS in patients 16 years of age and older.
2. Hetlioz LQ oral suspension is indicated for the treatment of nighttime sleep disturbances in SMS in pediatric patients 3 to 15 years of age.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

The following information is necessary to initiate the prior authorization review:

A. For initial therapy, chart notes or test results to support one of the following:
1. Total blindness in both eyes, OR
2. Smith-Magenis Syndrome.

B. For continuation of therapy, documentation to support one of the following:
1. For Non-24-Hour Sleep-Wake Disorder, both of the following:
   i. Chart notes or test results confirming total blindness in both eyes
   ii. An increased total nighttime sleep and/or decreased daytime nap duration, OR
2. For nighttime sleep disturbances in Smith-Magenis syndrome:
   i. Chart notes or test results confirming Smith-Magenis Syndrome
   ii. Improvement in quality of sleep such as improvement in sleep efficiency, sleep onset and final sleep offset, or waking after sleep onset.

III. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with a sleep specialist (e.g., neurologist experienced with sleep disorders, physician certified in sleep medicine) or psychiatrist.

IV. CRITERIA FOR INITIAL APPROVAL

A. Non-24-Hour Sleep-Wake Disorder
Authorization of 6 months may be granted for treatment of Non-24-Hour Sleep-Wake Disorder when all of the following criteria are met:
1. The member has a diagnosis of total blindness in both eyes (e.g., nonfunctioning retinas).
2. The member is not able to perceive light in either eye.
3. The member is experiencing difficulty initiating sleep, difficulty awakening in the morning, or excessive daytime sleepiness.

B. Nighttime Sleep Disturbances in Smith-Magenis Syndrome (SMS)
Authorization of 6 months may be granted for the treatment of nighttime sleep disturbances in Smith-Magenis Syndrome (SMS) when all of the following criteria are met:
1. The member has a confirmed clinical diagnosis of Smith-Magenis syndrome.
2. The member has a history of sleep disturbances.

V. CONTINUATION OF THERAPY

A. Non-24-Hour Sleep-Wake Disorder
Authorization of 12 months may be granted for treatment of Non-24-Hour Sleep-Wake Disorder when all of the following criteria are met:
1. The member has a diagnosis of total blindness in both eyes (e.g., nonfunctioning retinas).
2. The member is not able to perceive light in either eye.
3. The member is experiencing increased total nighttime sleep and/or decreased daytime nap duration.

B. Nighttime Sleep Disturbances in Smith-Magenis Syndrome (SMS)
Authorization of 12 months may be granted for the treatment of nighttime sleep disturbances in Smith-Magenis syndrome if the member experiences improvement in the quality of sleep since starting therapy with Hetlioz.

VI. REFERENCES

1. Hetlioz [package insert]. Washington, D.C.: Vanda Pharmaceuticals, Inc.; January 2023.
2. Auger, Robert R, Burgess, Helen J, et al. Clinical Practice Guideline for the Treatment of Intrinsic Circadian Rhythm Sleep-Wake Disorders: Advanced Sleep-Wake Phase Disorder (ASWPD), Delayed Sleep-Wake Phase Disorder (DSWPD), Non-24-Hour Sleep-Wake Rhythm Disorder (N24SWD), and Irregular Sleep-Wake Rhythm Disorder (ISWRD). An Update for 2015: An American Academy of Sleep Medicine Clinical Practice Guideline. *J Clin Sleep Med.* 2015 Oct;11(10):1199-236.

PRIOR AUTHORIZATION CRITERIA

DRUG CLASS	HIGH RISK MEDICATIONS (HRM) CRITERIA
Prior Authorization applies only to patients 70 years of age or older.	
DESCRIPTION	
ANTIARRHYTHMIC	**disopyramide** **disopyramide extended release**
ANTIDEPRESSANT	**amitriptyline** **clomipramine** **doxepin capsules, tablets, solution *(applies to greater than 6mg daily)*** **imipramine hydrochloride** **imipramine pamoate** **trimipramine**
ANTIEMETIC	**scopolamine patch**
ANTIHISTAMINE	**carbinoxamine maleate** **clemastine fumarate** **cyproheptadine hydrochloride** **dexchlorpheniramine maleate** **diphenhydramine oral** **hydroxyzine hydrochloride** **hydroxyzine pamoate** **promethazine hydrochloride** **promethazine/phenylephrine**
ANTI-INFECTIVE	**nitrofurantoin**
ANTINEOPLASTIC	**megestrol acetate** **Megace ES oral suspension**
ANTIPARKINSON	**benztropine mesylate (oral dosage form only)** **trihexyphenidyl hydrochloride**
ANTIPSYCHOTIC-ANTIDEPRESSANT COMBINATION	**perphenazine-amitriptyline**
ANTISPASMODIC	**methscopolamine**

BARBITURATE	**phenobarbital**
BARBITURATE-ANALGESIC	**butalbital-apap** **butalbital-apap-caffeine** **butalbital-asa-caffeine** **butalbital-apap-caffeine w/codeine** **butalbital-asa-caffeine w/codeine**
CARDIOVASCULAR	**digoxin tablets, oral solution (*applies to greater than 0.125mg daily)*** **guanfacine** **methyldopa, methyldopa/hctz**
CNS/ADHD	**guanfacine extended release**
ESTROGEN (ORAL) (includes combination drugs)	**conjugated estrogens** **conjugated estrogen synthetic A and B** **conjugated estrogen-medroxyprogesterone acetate** **esterified estrogens** **estradiol** **estradiol-drospirenone, estradiol- norethindrone, estradiol-estradiol norgestimate, estropipate, conjugated estrogens/bazedoxifene (Duavee)**
ESTROGEN (TOPICAL)	**estradiol, estradiol-levonorgestrel, estradiol-norethindrone**
HYPOGLYCEMIC (ORAL)	**glyburide, glyburide-metformin, glyburide micronized**
NON-BENZODIAZEPINE SEDATIVE - HYPNOTIC	**eszopiclone** **zaleplon** **zolpidem immediate-release** **zolpidem extended-release** **zolpidem sublingual** **zolpidem spray**
NON-STEROIDAL ANTI-INFLAMMATORY	**ketorolac tromethamine tablets**
SKELETAL MUSCLE RELAXANT (includes combination drugs)	**carisoprodol** **carisoprodol/asa/codeine** **chlorzoxazone** **cyclobenzaprine hydrochloride** **metaxalone** **methocarbamol** **orphenadrine citrate extended release** **orphenadrine/asa/caffeine**

VASODILATOR **dipyridamole (oral dosage form only)**

Status: CVS Caremark Criteria
Type: Initial Prior Authorization with Age

POLICY

COVERAGE CRITERIA
The requested drug will be covered with prior authorization when the following criteria are met:

- The American Geriatrics Society identifies the use of this medication as potentially inappropriate in older adults, meaning it is best avoided, prescribed at reduced dosage, or used with caution or carefully monitored. The prescriber must acknowledge that the benefit of therapy with this prescribed medication outweighs the potential risks for this patient

REFERENCES

1. Barclay, L. New Criteria Define Inappropriate Meds in Older Inpatients. Medscape Medical News (online). June 2011; http://www.medscape.com/viewarticle/744559. Accessed January 12, 2023.
2. NCQA.2019. (online) https://www.ncqa.org/hedis/measures/hedis-2019-ndc-license/hedis-2019-final-ndc-lists/. Accessed January 12, 2023.
3. Steven, A., Colombi, A., et al. Potentially Inappropriate Medications and Risk of Hospitalization in Retirees. Drugs Aging 2010 May; 27(5):407-415.
4. Patient Safety Analysis: HRM Measures – Report User Guide. August 2018. Acumen LLC.
5. The American Geriatrics Society 2019 Beers Criteria Update Expert Panel. American Geriatrics Society Updated Beers Criteria for Potentially Inappropriate Medication Use in Older Adults. American Geriatrics Society. 2019.
6. Hanlon, Joseph T, PharmD, MS, Semla, Todd P. MS, PharmD and Schmader, Kenneth E. MD. Alternative Medications for Medications in the Use of High-Risk Medications in the Elderly and Potentially Harmful Drug–Disease Interactions in the Elderly Quality Measures. Journal of American Geriatrics Society.2015.
7. Pharmacy Quality Alliance. 2022 PQA Measure Manual. Pharmacy Quality Alliance. April 2022.
8. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, Ohio: UpToDate, Inc.; 2023; Accessed January 12, 2023.
9. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. https://www.micromedexsolutions.com. Accessed January 12, 2023.

Reference number(s)
1659-A

SPECIALTY GUIDELINE MANAGEMENT

HYCAMTIN CAPSULES (topotecan)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication
Hycamtin capsules are indicated for the treatment of relapsed small cell lung cancer (SCLC) in patients with a prior complete or partial response and who are at least 45 days from the end of first-line chemotherapy.

B. Compendial Uses
1. Small Cell Lung Cancer (SCLC)
2. Merkel Cell Carcinoma (MCC)

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Small Cell Lung Cancer (SCLC)
Authorization of 12 months may be granted for treatment of small cell lung cancer.

B. Merkel Cell Carcinoma (MCC)
Authorization of 12 months may be granted for treatment of Merkel cell carcinoma when all of the following criteria are met:
1. Member has primary or recurrent metastatic disseminated disease.
2. Member has contraindications to checkpoint immunotherapy [e.g., Bavencio (avelumab), Keytruda (pembrolizumab)].

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

IV. REFERENCES

1. Hycamtin Capsules [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corp.; September 2018.
2. The NCCN Drugs & Biologics Compendium® © 2022 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed February 17, 2022.

Reference number(s)
2008-A

SPECIALTY GUIDELINE MANAGEMENT

HUMIRA (adalimumab)
ABRILADA (adalimumab-afzb)
AMJEVITA (adalimumab-atto)
CYLTEZO (adalimumab-adbm)
HADLIMA (adalimumab-bwwd)
HULIO (adalimumab-fkjp)
HYRIMOZ (adalimumab-adaz)
IDACIO (adalimumab-aacf)
YUFLYMA (adalimumab-aaty)
YUSIMRY (adalimumab-aqvh)
adalimumab-adaz
adalimumab-fkjp

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
1. Reducing signs and symptoms, inducing major clinical response, inhibiting the progression of structural damage, and improving physical function in adult patients with moderately to severely active rheumatoid arthritis (RA).
2. Reducing signs and symptoms of moderately to severely active polyarticular juvenile idiopathic arthritis (JIA) in patients 2 years of age and older.
3. Reducing signs and symptoms, inhibiting the progression of structural damage, and improving physical function in adult patients with active psoriatic arthritis (PsA).
4. Reducing signs and symptoms in adult patients with active ankylosing spondylitis (AS).
5. The treatment of moderately to severely active Crohn's disease (CD) in adult and pediatric patients 6 years of age and older.
6. The treatment of moderately to severely active ulcerative colitis (UC) in adults and pediatric patients 5 years of age and older.
   Limitations of Use: The effectiveness of Humira has not been established in patients who have lost response to or were intolerant to tumor necrosis factor (TNF) blockers.
7. The treatment of adult patients with moderate to severe chronic plaque psoriasis (PsO) who are candidates for systemic therapy or phototherapy, and when other systemic therapies are medically less appropriate.
8. The treatment of moderate to severe hidradenitis suppurativa in patients 12 years of age and older.
9. The treatment of non-infectious intermediate, posterior, and panuveitis in adults and pediatric patients 2 years of age and older.

B. Compendial Uses
1. Axial spondyloarthritis

2. Non-radiographic axial spondyloarthritis
3. Behcet's disease
4. Pyoderma gangrenosum
5. Oligoarticular juvenile idiopathic arthritis
6. Immunotherapy-related inflammatory arthritis

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

A. Rheumatoid arthritis (RA)
   1. Initial requests:
      i. Chart notes, medical record documentation, or claims history supporting previous medications tried (if applicable), including response to therapy. If therapy is not advisable, documentation of clinical reason to avoid therapy.
      ii. Laboratory results, chart notes, or medical record documentation of biomarker testing (i.e., rheumatoid factor [RF], anti-cyclic citrullinated peptide [anti-CCP], and C-reactive protein [CRP] and/or erythrocyte sedimentation rate [ESR]) (if applicable).
   2. Continuation requests: Chart notes or medical record documentation supporting positive clinical response.

B. Articular juvenile idiopathic arthritis (JIA)
   1. Initial requests: Chart notes, medical record documentation, or claims history supporting previous medications tried (if applicable), including response to therapy.
   2. Continuation requests: Chart notes or medical record documentation supporting positive clinical response.

C. Ankylosing spondylitis (AS), non-radiographic axial spondyloarthritis (nr-axSpA), psoriatic arthritis (PsA), hidradenitis suppurativa, and uveitis (non-infectious intermediate, posterior and panuveitis)
   1. Initial requests: Chart notes, medical record documentation, or claims history supporting previous medications tried (if applicable), including response to therapy. If therapy is not advisable, documentation of clinical reason to avoid therapy.
   2. Continuation requests: Chart notes or medical record documentation supporting positive clinical response.

D. Crohn’s disease (CD)
   Continuation requests: Chart notes or medical record documentation supporting positive clinical response to therapy or remission.

E. Ulcerative colitis (UC)
   Continuation requests: Chart notes or medical record documentation supporting positive clinical response to therapy or remission.

F. Plaque psoriasis (PsO)
   1. Initial requests:
      i. Chart notes or medical record documentation of affected area(s) and body surface area (BSA) affected (if applicable).

ii. Chart notes, medical record documentation, or claims history supporting previous medications tried (if applicable), including response to therapy. If therapy is not advisable, documentation of clinical reason to avoid therapy.

2. Continuation requests: Chart notes or medical record documentation of decreased body surface area (BSA) affected and/or improvement in signs and symptoms.

G. Behcet's disease and immunotherapy-related inflammatory arthritis (initial requests only): Chart notes, medical record documentation, or claims history supporting previous medications tried, including response to therapy (if applicable).

H. Pyoderma gangrenosum (initial requests only): Chart notes, medical record documentation, or claims history supporting previous medications tried (if applicable), including response to therapy. If therapy is not advisable, documentation of clinical reason to avoid therapy.

III. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with one of the following:

A. Rheumatoid arthritis, articular juvenile idiopathic arthritis, ankylosing spondylitis, non-radiographic axial spondyloarthritis, and Behcet's disease: rheumatologist
B. Psoriatic arthritis and hidradenitis suppurativa: rheumatologist or dermatologist
C. Crohn's disease and ulcerative colitis: gastroenterologist
D. Plaque psoriasis and pyoderma gangrenosum: dermatologist
E. Uveitis: ophthalmologist or rheumatologist
F. Immunotherapy-related inflammatory arthritis: oncologist, hematologist, or rheumatologist

IV. CRITERIA FOR INITIAL APPROVAL

A. Rheumatoid arthritis (RA)

1. Authorization of 12 months may be granted for adult members who have previously received a biologic or targeted synthetic drug (e.g., Rinvoq, Xeljanz) indicated for moderately to severely active rheumatoid arthritis.

2. Authorization of 12 months may be granted for adult members for treatment of moderately to severely active RA when all of the following are criteria are met:
   i. Member meets either of the following criteria:
      a. Member has been tested for either of the following biomarkers and the test was positive:
         1. Rheumatoid factor (RF)
         2. Anti-cyclic citrullinated peptide (anti-CCP)
      b. Member has been tested for ALL of the following biomarkers:
         1. RF
         2. Anti-CCP
         3. C-reactive protein (CRP) and/or erythrocyte sedimentation rate (ESR)
   ii. Member meets either of the following criteria:
      a. Member has experienced an inadequate response to at least a 3-month trial of methotrexate despite adequate dosing (i.e., titrated to at least 15 mg/week).
      b. Member has an intolerance or contraindication to methotrexate (see Appendix A).

B. Articular juvenile idiopathic arthritis (JIA)

1. Authorization of 12 months may be granted for members 2 years of age or older who have previously received a biologic or targeted synthetic drug (e.g., Xeljanz) indicated for moderately to severely active articular juvenile idiopathic arthritis.

2. Authorization of 12 months may be granted for members 2 years of age or older for treatment of moderately to severely active articular juvenile idiopathic arthritis when any of the following criteria is met:
   i. Member has had an inadequate response to methotrexate or another conventional synthetic drug (e.g., leflunomide, sulfasalazine, hydroxychloroquine) administered at an adequate dose and duration.
   ii. Member has had an inadequate response to a trial of scheduled non-steroidal anti-inflammatory drugs (NSAIDs) and/or intra-articular glucocorticoids (e.g., triamcinolone hexacetonide) and one of the following risk factors for poor outcome:
      a. Involvement of ankle, wrist, hip, sacroiliac joint, and/or temporomandibular joint (TMJ)
      b. Presence of erosive disease or enthesitis
      c. Delay in diagnosis
      d. Elevated levels of inflammation markers
      e. Symmetric disease
   iii. Member has risk factors for disease severity and potentially a more refractory disease course (see Appendix B) and the member also meets one of the following:
      a. High-risk joints are involved (e.g., cervical spine, wrist, or hip).
      b. High disease activity.
      c. Is judged to be at high risk for disabling joint disease.

C. Psoriatic arthritis (PsA)

1. Authorization of 12 months may be granted for adult members who have previously received a biologic or targeted synthetic drug (e.g., Rinvoq, Otezla) indicated for active psoriatic arthritis.

2. Authorization of 12 months may be granted for adult members for treatment of active psoriatic arthritis when either of the following criteria is met:
   i. Member has mild to moderate disease and meets one of the following criteria:
      a. Member has had an inadequate response to methotrexate, leflunomide, or another conventional synthetic drug (e.g., sulfasalazine) administered at an adequate dose and duration.
      b. Member has an intolerance or contraindication to methotrexate or leflunomide (see Appendix A), or another conventional synthetic drug (e.g., sulfasalazine).
      c. Member has enthesitis or predominantly axial disease.
   ii. Member has severe disease.

D. Ankylosing spondylitis (AS) and non-radiographic axial spondyloarthritis (nr-axSpA)

1. Authorization of 12 months may be granted for adult members who have previously received a biologic or targeted synthetic drug (e.g., Rinvoq, Xeljanz) indicated for active ankylosing spondylitis or active non-radiographic axial spondyloarthritis.

2. Authorization of 12 months may be granted for adult members for treatment of active ankylosing spondylitis or active non-radiographic axial spondyloarthritis when either of the following criteria is met:
   i. Member has experienced an inadequate response to at least two non-steroidal anti-inflammatory drugs (NSAIDs).
   ii. Member has an intolerance or contraindication to two or more NSAIDs.

E. Crohn's disease (CD)

Authorization of 12 months may be granted for members 6 years of age or older for treatment of moderately to severely active CD.

F. Ulcerative colitis (UC)

Authorization of 12 months may be granted for members 5 years of age or older for treatment of moderately to severely active ulcerative colitis.

G. Plaque psoriasis (PsO)

1. Authorization of 12 months may be granted for adult members who have previously received a biologic or targeted synthetic drug (e.g., Sotyktu, Otezla) indicated for treatment of moderate to severe plaque psoriasis.

2. Authorization of 12 months may be granted for adult members for treatment of moderate to severe plaque psoriasis when any of the following criteria is met:
   i. Crucial body areas (e.g., hands, feet, face, neck, scalp, genitals/groin, intertriginous areas) are affected.
   ii. At least 10% of body surface area (BSA) is affected.
   iii. At least 3% of body surface area (BSA) is affected and the member meets either of the following criteria:
      a. Member has had an inadequate response or intolerance to either phototherapy (e.g., UVB, PUVA) or pharmacologic treatment with methotrexate, cyclosporine, or acitretin.
      b. Member has a clinical reason to avoid pharmacologic treatment with methotrexate, cyclosporine, and acitretin (see Appendix A).

H. Hidradenitis suppurativa

1. Authorization of 12 months may be granted for members 12 years of age or older who have previously received a biologic indicated for treatment of moderate to severe hidradenitis suppurativa.

2. Authorization of 12 months may be granted for member 12 years of age or older for treatment of moderate to severe hidradenitis suppurativa when either of the following is met:
   i. Member has experienced an inadequate response to an oral antibiotic for at least 90 days.
   ii. Member has an intolerance or contraindication to oral antibiotics.

I. Uveitis (non-infectious intermediate, posterior and panuveitis)

1. Authorization of 12 months may be granted for members 2 years of age or older who have previously received a biologic indicated for non-infectious intermediate, posterior, and panuveitis.

2. Authorization of 12 months may be granted for members 2 years of age or older for treatment of non-infectious intermediate, posterior and panuveitis when either of the following is met:
   i. Member has experienced an inadequate response to corticosteroids or immunosuppressive therapy (e.g., azathioprine, cyclosporine, methotrexate).
   ii. Member has an intolerance or contraindication to corticosteroids and immunosuppressive therapy (e.g., azathioprine, cyclosporine, methotrexate).

J. Behcet's disease

1. Authorization of 12 months may be granted for members who have previously received Otezla or a biologic indicated for the treatment of Behcet's disease.

2. Authorization of 12 months may be granted for the treatment of Behcet's disease when the member has had an inadequate response to at least one non-biologic medication for Behcet's disease (e.g., apremilast, colchicine, systemic glucocorticoids, azathioprine).

K. Pyoderma gangrenosum

1. Authorization of 12 months may be granted for members who have previously received a biologic indicated for treatment of pyoderma gangrenosum.

2. Authorization of 12 months may be granted for treatment of pyoderma gangrenosum when either of the following is met:
   i. Member has experienced an inadequate response to corticosteroids or immunosuppressive therapy (e.g., cyclosporine or mycophenolate mofetil).
   ii. Member has an intolerance or contraindication to corticosteroids and immunosuppressive therapy (e.g., cyclosporine, mycophenolate mofetil).

L. Immunotherapy-related inflammatory arthritis

Authorization of 12 months may be granted for treatment of severe/refractory immunotherapy-related inflammatory arthritis that is not responding to corticosteroids and anti-inflammatory agents.

V. CONTINUATION OF THERAPY

A. Rheumatoid arthritis (RA)

Authorization of 12 months may be granted for all adult members (including new members) who are using the requested medication for moderately to severely active rheumatoid arthritis and who achieve or maintain a positive clinical response as evidenced by disease activity improvement of at least 20% from baseline in tender joint count, swollen joint count, pain, or disability.

B. Articular juvenile idiopathic arthritis (JIA)

Authorization of 12 months may be granted for all members 2 years of age or older (including new members) who are using the requested medication for moderately to severely active articular juvenile idiopathic arthritis and who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition when there is improvement in any of the following from baseline:

1. Number of joints with active arthritis (e.g., swelling, pain, limitation of motion)
2. Number of joints with limitation of movement
3. Functional ability

C. Psoriatic arthritis (PsA)

Authorization of 12 months may be granted for all adult members (including new members) who are using the requested medication for psoriatic arthritis and who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition when there is improvement in any of the following from baseline:

1. Number of swollen joints
2. Number of tender joints
3. Dactylitis
4. Enthesitis
5. Axial disease
6. Skin and/or nail involvement

D. Ankylosing spondylitis (AS) and non-radiographic axial spondyloarthritis (nr-axSpA)

Authorization of 12 months may be granted for all adult members (including new members) who are using the requested medication for active ankylosing spondylitis or active non-radiographic axial spondyloarthritis and who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition when there is improvement in any of the following from baseline:

1. Functional status
2. Total spinal pain
3. Inflammation (e.g., morning stiffness)

E. Crohn's disease (CD)

1. Authorization of 12 months may be granted for all members 6 years of age or older (including new members) who are using the requested medication for moderately to severely active Crohn's disease and who achieve or maintain remission.

2. Authorization of 12 months may be granted for all members 6 years of age or older (including new members) who are using the requested medication for moderately to severely active Crohn's disease and who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition when there is improvement in any of the following from baseline:
   i. Abdominal pain or tenderness
   ii. Diarrhea
   iii. Body weight
   iv. Abdominal mass
   v. Hematocrit
   vi. Appearance of the mucosa on endoscopy, computed tomography enterography (CTE), magnetic resonance enterography (MRE), or intestinal ultrasound
   vii. Improvement on a disease activity scoring tool (e.g., Crohn's Disease Activity Index [CDAI] score)

F. Ulcerative colitis (UC)

1. Authorization of 12 months may be granted for all members 5 years of age and older (including new members) who are using the requested medication for moderately to severely active ulcerative colitis and who achieve or maintain remission.

2. Authorization of 12 months may be granted for all members 5 years of age and older (including new members) who are using the requested medication for moderately to severely active ulcerative colitis and who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition when there is improvement in any of the following from baseline:
   i. Stool frequency
   ii. Rectal bleeding
   iii. Urgency of defecation
   iv. C-reactive protein (CRP)
   v. Fecal calprotectin (FC)
   vi. Appearance of the mucosa on endoscopy, computed tomography enterography (CTE), magnetic resonance enterography (MRE), or intestinal ultrasound
   vii. Improvement on a disease activity scoring tool (e.g., Ulcerative Colitis Endoscopic Index of Severity [UCEIS], Mayo score)

G. Plaque psoriasis (PsO)

Authorization of 12 months may be granted for all adult members (including new members) who are using the requested medication for moderate to severe plaque psoriasis and who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition when either of the following is met:

1. Reduction in body surface area (BSA) affected from baseline
2. Improvement in signs and symptoms from baseline (e.g., itching, redness, flaking, scaling, burning, cracking, pain)

H. Hidradenitis suppurativa

Authorization of 12 months may be granted for all members 12 years of age and older (including new members) who are using the requested medication for moderate to severe hidradenitis suppurativa and who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition when any of the following is met:

1. Reduction in abscess and inflammatory nodule count from baseline
2. Reduced formation of new sinus tracts and scarring
3. Decrease in frequency of inflammatory lesions from baseline
4. Reduction in pain from baseline
5. Reduction in suppuration from baseline
6. Improvement in frequency of relapses from baseline
7. Improvement in quality of life from baseline
8. Improvement on a disease severity assessment tool from baseline

I. Uveitis (non-infectious intermediate, posterior and panuveitis)

Authorization of 12 months may be granted for all members 2 years of age and older (including new members) who are using the requested medication for non-infectious intermediate, posterior, and panuveitis and who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition when the patient meets any of the following:

1. Reduced frequency of disease flares compared to baseline
2. Stability or improvement in anterior chamber (AC) cell grade compared to baseline
3. Stability or improvement in vitreous haze (VH) grade compared to baseline
4. Stability or improvement in visual acuity compared to baseline
5. Reduction in glucocorticoid requirements from baseline
6. No new active inflammatory chorioretinal and/or inflammatory retinal vascular lesions relative to baseline

J. Immunotherapy-related inflammatory arthritis

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

K. All other indications

Authorization of 12 months may be granted for all members (including new members) who are using the requested medication for an indication outlined in Section IV and who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition.

VI. OTHER

For all indications: Member has had a documented negative tuberculosis (TB) test (which can include a tuberculosis skin test [PPD], an interferon-release assay [IGRA], or a chest x-ray)* within 6 months of initiating therapy for persons who are naïve to biologic drugs or targeted synthetic drugs associated with an increased risk of TB.

* If the screening testing for TB is positive, there must be further testing to confirm there is no active disease. Do not administer the requested medication to members with active TB infection. If there is latent disease, TB treatment must be started before initiation of the requested medication.

For all indications: Member cannot use the requested medication concomitantly with any other biologic drug or targeted synthetic drug.

VII. DOSAGE AND ADMINISTRATION

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. For rheumatoid arthritis, member must initiate treatment with every other week dosing.

VIII. APPENDICES

Appendix A: Examples of Clinical Reasons to Avoid Pharmacologic Treatment with Methotrexate, Cyclosporine, Acitretin, or Leflunomide

1. Clinical diagnosis of alcohol use disorder, alcoholic liver disease, or other chronic liver disease
2. Drug interaction
3. Risk of treatment-related toxicity
4. Pregnancy or currently planning pregnancy
5. Breastfeeding
6. Significant comorbidity prohibits use of systemic agents (e.g., liver or kidney disease, blood dyscrasias, uncontrolled hypertension)
7. Hypersensitivity
8. History of intolerance or adverse event

Appendix B: Risk Factors for Articular Juvenile Idiopathic Arthritis

1. Positive rheumatoid factor
2. Positive anti-cyclic citrullinated peptide antibodies
3. Pre-existing joint damage

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Reference number(s)
1726-A

SPECIALTY GUIDELINE MANAGEMENT

IBRANCE (palbociclib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
Ibrance is indicated for the treatment of hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer in combination with:
1. an aromatase inhibitor as initial endocrine based therapy in postmenopausal women or in men, or
2. fulvestrant in patients with disease progression following endocrine therapy.

B. Compendial Uses
1. Breast cancer: Therapy for recurrent HR-positive, HER2-negative disease
2. Soft tissue sarcoma: Single-agent therapy for unresectable well-differentiated/dedifferentiated liposarcoma of the retroperitoneum.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of hormone receptor (HR) and human epidermal growth factor receptor 2 (HER2) status is necessary to initiate the prior authorization review, where applicable.

III. CRITERIA FOR INITIAL APPROVAL

A. Breast cancer
Authorization of 12 months may be granted for treatment of HR-positive, HER2-negative recurrent, advanced, or metastatic breast cancer when one of the following criteria is met:
1. Ibrance is used in combination with an aromatase inhibitor (e.g., anastrozole, exemestane, letrozole).
2. Ibrance is used in combination with fulvestrant.

B. Soft tissue sarcoma
Authorization of 12 months may be granted for treatment of unresectable well-differentiated/dedifferentiated liposarcoma of the retroperitoneum when used as a single agent.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication outlined in section III when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

V. REFERENCES

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Reference number(s)
1606-A

SPECIALTY GUIDELINE MANAGEMENT

FIRAZYR (icatibant)
Sajazir (icatibant)
icatibant

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Treatment of acute attacks of hereditary angioedema (HAE) in adults 18 years of age and older.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
A. For initial authorization, the following should be documented:
   1. C1 inhibitor functional and antigenic protein levels
   2. F12, angiopoietin-1, plasminogen, kininogen-1 (KNG1), heparan sulfate-glucosamine 3-O-sulfotransferase 6 (HS3ST6), or myoferlin (MYOF) gene mutation testing, if applicable
   3. Chart notes confirming family history of angioedema and the angioedema was refractory to a trial of high-dose antihistamine therapy, if applicable
B. For continuation of therapy, chart notes demonstrating a reduction in severity and/or duration of attacks

III. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with a prescriber who specializes in the management of HAE.

IV. CRITERIA FOR INITIAL APPROVAL

Hereditary angioedema (HAE)
Authorization of 6 months may be granted for treatment of acute HAE attacks when the requested medication will not be used in combination with any other medication used for the treatment of acute HAE attacks and either of the following criteria is met at the time of diagnosis:
A. Member has C1 inhibitor deficiency or dysfunction as confirmed by laboratory testing and meets one of the following criteria:
   1. C1 inhibitor (C1-INH) antigenic level below the lower limit of normal as defined by the laboratory performing the test, or

2. Normal C1-INH antigenic level and a low C1-INH functional level (functional C1-INH less than 50% or C1-INH functional level below the lower limit of normal as defined by the laboratory performing the test).

B. Member has normal C1 inhibitor as confirmed by laboratory testing and meets one of the following criteria:
   1. Member has an F12, angiopoietin-1, plasminogen, kininogen-1 (KNG1), heparan sulfate-glucosamine 3-O-sulfotransferase 6 (HS3ST6), or myoferlin (MYOF) gene mutation as confirmed by genetic testing, or
   2. Member has a documented family history of angioedema and the angioedema was refractory to a trial of high-dose antihistamine therapy (i.e., cetirizine at 40 mg per day or the equivalent) for at least one month.

V. CONTINUATION OF THERAPY

Authorization of 6 months may be granted for continuation of therapy when all of the following criteria are met:
A. Member meets the criteria for initial approval.
B. Member has experienced a reduction in severity and/or duration of acute attacks.
C. Prophylaxis should be considered based on the attack frequency, attack severity, comorbid conditions, and member's quality of life.

VI. REFERENCES

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Reference number(s)
2173-A

SPECIALTY GUIDELINE MANAGEMENT

ICLUSIG (ponatinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. Adult patients with chronic phase (CP) chronic myeloid leukemia (CML) with resistance or intolerance to at least two prior kinase inhibitors
   2. Adult patients with accelerated phase (AP) or blast phase (BP) chronic myeloid leukemia (CML) or Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ ALL) for whom no other kinase inhibitors are indicated
   3. Adult patients with T315I-positive CML (chronic phase, accelerated phase, or blast phase) or T315I-positive Ph+ ALL

   Limitation of use: Iclusig is not indicated and is not recommended for the treatment of patients with newly diagnosed CP-CML.

B. Compendial Uses
   1. Follow-up therapy for CML patients after hematopoietic stem cell transplant (HSCT)
   2. Ph+ B-cell acute lymphoblastic leukemia or lymphoblastic lymphoma (Ph+ B-ALL/LL)
   3. Maintenance therapy for Ph+ B-ALL/LL patients after hematopoietic stem cell transplant (HSCT)
   4. Myeloid/lymphoid neoplasms with eosinophilia and FGFR1 or ABL1 rearrangements in chronic phase
   5. Lymphoid, myeloid or mixed lineage neoplasms with eosinophilia and FGFR1 or ABL1 rearrangements in blast phase

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

The following information is necessary to initiate the prior authorization review:
A. Prior to initiation of therapy for treatment of CML or Ph+ ALL/LL: results of cytogenetic and/or molecular testing for detection of the Ph chromosome or the BCR-ABL gene
B. For members requesting initiation of therapy with the requested medication for treatment of T315I-positive CML or Ph+ ALL/LL: results of BCR-ABL1 mutation testing for T315I mutation
C. For members requesting initiation of therapy with the requested medication for treatment of myeloid and/or lymphoid neoplasms with eosinophilia: results of testing or analysis confirming FGFR1 or ABL1 rearrangement

III. CRITERIA FOR INITIAL APPROVAL

A. Chronic Myeloid Leukemia (CML)

Authorization of 12 months may be granted for treatment of CML that has been confirmed by detection of the Ph chromosome or BCR-ABL gene by cytogenetic and/or molecular testing when any of the following criteria are met:

1. Member has T315I-positive CML
2. Member has chronic phase (CP) chronic myeloid leukemia (CML) with resistance or intolerance to at least two prior kinase inhibitors (e.g., bosutinib, dasatinib, imatinib, nilotinib)
3. Member has accelerated phase (AP) or blast phase (BP) CML and treatment with any other kinase inhibitors (e.g., bosutinib, dasatinib, imatinib, nilotinib) is not indicated

B. Ph+ Acute Lymphoblastic Leukemia (ALL)/Lymphoblastic Lymphoma (LL)

Authorization of 12 months may be granted for treatment of Ph+ ALL/LL that has been confirmed by detection of the Ph chromosome or BCR-ABL gene by cytogenetic and/or molecular testing when any of the following criteria are met:

1. Member has T315I-positive mutation
2. Treatment with any other kinase inhibitors (e.g., bosutinib, dasatinib, imatinib, nilotinib) is not indicated

C. Myeloid/Lymphoid Neoplasms with Eosinophilia

Authorization of 12 months may be granted for treatment of myeloid and/or lymphoid neoplasms with eosinophilia and FGFR1 or ABL1 rearrangement in the chronic phase or blast phase.

IV. CONTINUATION OF THERAPY

A. CML

Authorization of 12 months may be granted for continued treatment of CML when there is no evidence of unacceptable toxicity or disease progression while on the current regimen and either of the following is met:

1. Member has CML that has been confirmed by detection of Ph chromosome or BCR-ABL gene by cytogenetic and/ or molecular testing
2. Member has received HSCT for CML

B. Ph+ ALL/LL

Authorization of 12 months may be granted for continued treatment of ALL/LL when there is no evidence of unacceptable toxicity or disease progression while on the current regimen and either of the following criteria is met:

1. Member has Ph+ ALL/LL that has been confirmed by detection of Ph chromosome or BCR-ABL gene by cytogenetic and/ or molecular testing
2. Member has received HSCT for ALL/LL

C. Myeloid/Lymphoid Neoplasms with Eosinophilia

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

V. REFERENCES

1. Iclusig [package insert]. Lexington, MA: Takeda Pharmaceuticals America, Inc.; February 2022.
2. The NCCN Drugs & Biologics Compendium® © 2022 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed April 5, 2022.
3. NCCN Clinical Practice Guidelines in Oncology® Chronic Myeloid Leukemia (Version 3.2022). © 2022 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed April 5, 2022.

4. NCCN Clinical Practice Guidelines in Oncology® Acute Lymphoblastic Leukemia (Version 1.2022). © 2022 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed April 5, 2022.

Reference number(s)
2238-A

SPECIALTY GUIDELINE MANAGEMENT

IDHIFA (enasidenib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication
Idhifa is indicated for the treatment of adult patients with relapsed or refractory acute myeloid leukemia (AML) with an isocitrate dehydrogenase-2 (IDH-2) mutation as detected by an FDA-approved test.

B. Compendial Uses
As a single agent in patients 60 years of age or older with IDH2-mutated AML in the following settings:
1. Treatment induction when not a candidate for intensive remission induction therapy or declines intensive therapy
2. Post-induction therapy following response to previous lower intensity therapy with the same regimen

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: medical record documentation of isocitrate dehydrogenase-2 (IDH2) mutation

III. CRITERIA FOR INITIAL APPROVAL

Acute Myeloid Leukemia (AML)

A. Authorization of 12 months may be granted for treatment induction of newly diagnosed AML with a susceptible IDH2 mutation when all of the following criteria is met:
1. The requested medication will be used as a single-agent
2. Member is age 60 years or older
3. Member has comorbidities that preclude the use of intensive induction chemotherapy or declines intensive induction chemotherapy

B. Authorization of 12 months may be granted for post-induction therapy for AML with a susceptible IDH2 mutation when all of the following criteria is met:
1. The requested medication will be used as a single-agent
2. Member is age 60 years or older
3. Member has experienced response to Idhifa therapy.

C. Authorization of 12 months may be granted for treatment of relapsed or refractory AML with a susceptible IDH2 mutation.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

V. REFERENCES

1. Idhifa [package insert]. Summit, NJ: Celgene Corporation; November 2020.
2. The NCCN Drugs & Biologics Compendium® © 2022 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed January 7, 2022.

Reference number(s)
2172-A

SPECIALTY GUIDELINE MANAGEMENT

GLEEVEC (imatinib mesylate)
imatinib mesylate (generic)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
1. Newly diagnosed adult and pediatric patients with Philadelphia chromosome positive chronic myeloid leukemia (Ph+ CML) in chronic phase
2. Patients with Ph+ CML in blast crisis, accelerated phase, or in chronic phase after failure of interferon-alpha therapy
3. Adult patients with relapsed or refractory Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ ALL)
4. Pediatric patients with newly diagnosed Ph+ ALL in combination with chemotherapy
5. Adult patients with myelodysplastic/myeloproliferative diseases (MDS/MPD) associated with PDGFR (platelet-derived growth factor receptor) gene re-arrangements
6. Adult patients with aggressive systemic mastocytosis without the D816V c-Kit mutation or with c-Kit mutational status unknown
7. Adult patients with hypereosinophilic syndrome (HES) and/or chronic eosinophilic leukemia (CEL) who have the FIP1L1-PDGFRα fusion kinase (mutational analysis or FISH demonstration of CHIC2 allele deletion) and for patients with HES and/or CEL who are FIP1L1-PDGFRα fusion kinase negative or unknown
8. Adult patients with unresectable, recurrent and/or metastatic dermatofibrosarcoma protuberans (DFSP)
9. Patients with Kit (CD117) positive unresectable and/or metastatic malignant gastrointestinal stromal tumors (GIST)
10. Adjuvant treatment of adult patients following complete gross resection of Kit (CD117) positive GIST

B. Compendial Uses
1. Primary treatment of advanced phase CML (accelerated phase or blast phase)
2. Follow-up therapy for CML patients after hematopoietic stem cell transplant (HSCT)
3. Ph+ B-cell acute lymphoblastic leukemia or lymphoblastic lymphoma (Ph+ B-ALL/LL)
4. Maintenance therapy for Ph+ B-ALL/LL patients after HSCT
5. GIST
6. Desmoid tumors
7. Pigmented villonodular synovitis/tenosynovial giant cell tumor
8. Recurrent chordoma
9. Metastatic or unresectable C-Kit mutated melanoma as subsequent therapy
10. Kaposi sarcoma that has progressed on or not responded to first-line systemic therapy
11. Chronic myelomonocytic leukemia
12. Chronic graft versus host disease
13. Relapsed or refractory pediatric T-cell ALL/LL with ABL-class translocation

14. Myeloid/lymphoid neoplasms with eosinophilia and the ABL1, FIP1L1-PDGFRA, or PDGFRB rearrangement in chronic phase or blast phase
15. Aggressive Systemic Mastocytosis (ASM)
16. Dermatofibrosarcoma Protuberans (DFSP)

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

The following information is necessary to initiate the prior authorization review:
1. For treatment of CML or Ph+ ALL/LL: results of cytogenetic and/or molecular testing for detection of the Ph chromosome or the BCR-ABL gene.
2. For treatment of T-cell ALL/LL: results of cytogenetic and/or molecular testing confirming ABL-class translocation
3. For treatment of MDS/MPD and CMML: results of molecular testing or analysis confirming PDGFR gene rearrangement
4. For the treatment of ASM: results of molecular testing or analysis for D816V c-KIT mutation and FIP1L1-PDGFRA fusion gene (where applicable)
5. For treatment of melanoma: results of molecular testing or analysis confirming c-KIT mutation
6. For treatment of myeloid and/or lymphoid neoplasms with eosinophilia: results of testing or analysis confirming ABL1, FIP1L1-PDGFRA, or PDGFRB rearrangement

III. CRITERIA FOR INITIAL APPROVAL

A. Chronic Myeloid Leukemia (CML)
Authorization of 7 months may be granted for treatment of CML that has been confirmed by detection of the Ph chromosome or BCR-ABL gene by cytogenetic and/or molecular testing when the member did not fail (other than due to intolerance) prior therapy with a TKI (e.g., dasatinib, nilotinib, bosutinib, ponatinib).

B. Acute Lymphoblastic Leukemia (ALL)/Lymphoblastic Lymphoma (LL)
Authorization of 12 months may be granted for treatment of ALL/LL when any of the following criteria is met:
1. Member has Ph+ ALL/LL that has been confirmed by detection of the Ph chromosome or BCR-ABL gene by cytogenetic and/or molecular testing
2. Member has T-cell ALL/LL with ABL-class translocation that has been confirmed by cytogenetic and/or molecular testing and the disease is relapsed or refractory
3. Member has received HSCT for Ph+ ALL/LL

C. Gastrointestinal Stromal Tumor (GIST), Desmoid Tumors, Pigmented Villonodular Synovitis/Tenosynovial Giant Cell Tumor (PVNS/TGCT), Hypereosinophilic Syndrome/Chronic Eosinophilic Leukemia (HES/CEL), Dermatofibrosarcoma Protuberans (DFSP), Chordoma
Authorization of 12 months may be granted for treatment of GIST, desmoid tumors, PVNS/TGCT, HES/CEL, DFSP, or recurrent chordoma.

D. Myelodysplastic Syndromes/Myeloproliferative Diseases (MDS/MPD) and Chronic Myelomonocytic Leukemia (CMML)
Authorization of 12 months may be granted for treatment of MDS/MPD or CMML when the member's disease is associated with PDGFR (platelet-derived growth factor receptor) gene rearrangements

E. Aggressive Systemic Mastocytosis (ASM)
Authorization of 12 months may be granted for treatment of ASM when any of the following criteria is met:
1. D816V c-KIT mutation is negative
2. D816V c-KIT mutation status is unknown
3. Well-differentiated systemic mastocytosis (WDSM)
4. Eosinophilia is present with FIP1L1-PDGFRA fusion gene

F. Melanoma
Authorization of 12 months may be granted for treatment of metastatic or unresectable c-KIT mutation-positive melanoma when the requested medication is used as a single agent and as subsequent therapy.

G. Kaposi Sarcoma
Authorization of 12 months may be granted for treatment of Kaposi sarcoma when the requested medication is used as subsequent therapy as a single agent or in combination with antiretroviral therapy.

H. Chronic Graft-Versus-Host Disease (cGVHD)
Authorization of 12 months may be granted for treatment of cGVHD when the requested medication is used as subsequent therapy in combination with systemic corticosteroids.

I. Myeloid/Lymphoid Neoplasms with Eosinophilia
Authorization of 12 months may be granted for treatment of myeloid and/or lymphoid neoplasms with eosinophilia and ABL1, FIP1L1-PDGFRA, or PDGFRB rearrangement in the chronic phase or blast phase.

IV. CONTINUATION OF THERAPY

A. CML
Authorization may be granted for continued treatment of CML that has been confirmed by detection of Ph chromosome or BCR-ABL gene by cytogenetic and/ or molecular testing when either of the following criteria is met:
1. Authorization of 12 months may be granted when any of the following criteria is met:
   a. BCR-ABL1 is less than or equal to 10% and there is no evidence of disease progression or unacceptable toxicity while on the current regimen for members who have been receiving the requested medication for 6 months or greater
   b. Member has received HSCT and there is no evidence of disease progression or unacceptable toxicity while on the current regimen
2. Authorization of up to 7 months may be granted when the member has completed less than 6 months of therapy with the requested medication.

B. Acute Lymphoblastic Leukemia or Lymphoblastic Lymphoma (ALL/LL)
Authorization of 12 months may be granted for continued treatment of ALL/LL when there is no evidence of unacceptable toxicity or disease progression while on the current regimen and any of the following criteria is met:
1. Member has Ph+ ALL/LL that has been confirmed by detection of Ph chromosome or BCR-ABL gene by cytogenetic and/ or molecular testing.
2. Member has T-cell ALL/LL with ABL-class translocation that has been confirmed by cytogenetic and/or molecular testing.
3. Member has received HSCT for ALL/LL

C. Desmoid Tumors, PVNS/TGCT, HES/CEL, DFSP, Chordoma, MDS/MPD, CMML, ASM, Melanoma, Kaposi sarcoma, cGVHD, or Myeloid/Lymphoid Neoplasms with Eosinophilia
Authorization of 12 months may be granted for continued treatment of desmoid tumors, PVNS/TGCT, HES/CEL, DFSP, chordoma, MDS/MPD, CMML, ASM, melanoma, Kaposi sarcoma, cGVHD, or myeloid/lymphoid neoplasms with eosinophilia when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

D. GIST
Authorization of 12 months may be granted for continued treatment of GIST when the member is receiving clinical benefit and there is no evidence of unacceptable toxicity while on the current regimen.

V. REFERENCES

1. Gleevec [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; March 2022.
2. imatinib [package insert]. Cranbury, NJ: Sun Pharmaceuticals Industries, Inc.; August 2020.
3. The NCCN Drugs & Biologics Compendium® © 2022 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed April 14, 2022.
4. NCCN Clinical Practice Guidelines in Oncology® Acute Lymphoblastic Leukemia (Version 1.2022). © 2022 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed April 14, 2022.
5. NCCN Clinical Practice Guidelines in Oncology® Pediatric Acute Lymphoblastic Leukemia (ALL) (Version 1.2022). © 2022 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed April 14, 2022.

Reference number
1997-A

SPECIALTY GUIDELINE MANAGEMENT

IMBRUVICA (ibrutinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
1. Mantle Cell Lymphoma (MCL)
   Imbruvica is indicated for the treatment of adult patients with MCL who have received at least one prior therapy.

2. Chronic Lymphocytic Leukemia (CLL)/Small Lymphocytic Lymphoma (SLL)
   i. Imbruvica is indicated for the treatment of adult patients with CLL/SLL.
   ii. Imbruvica is indicated for the treatment of adult patients with CLL/SLL with 17p deletion.

3. Waldenström's Macroglobulinemia (WM)
   Imbruvica is indicated for the treatment of adult patients with WM.

4. Marginal Zone Lymphoma (MZL)
   Imbruvica is indicated for the treatment of adult patients with MZL who require systemic therapy and have received at least one prior anti-CD20-based therapy.

5. Chronic Graft versus Host Disease (cGVHD)
   Imbruvica is indicated for the treatment of adult and pediatric patients age 1 year and older with cGVHD after failure of one or more lines of systemic therapy.

B. Compendial Use
1. Mantle cell lymphoma
2. Marginal zone lymphomas
   a. Gastric mucosa associated lymphoid tissue (MALT) lymphoma
   b. Nongastric MALT lymphoma
   c. Nodal marginal zone lymphoma
   d. Splenic marginal zone lymphoma
3. Hairy cell leukemia
4. Waldenström's macroglobulinemia/lymphoplasmacytic lymphoma (WM/LPL)
5. Primary central nervous system lymphoma
6. Diffuse large B-cell lymphoma
7. High-grade B-cell lymphoma (including high-grade B-cell lymphoma with translocations of MYC and BCL2 and/or BCL6 [double/triple hit lymphoma], high-grade B-cell lymphoma, not otherwise specified)
8. AIDS-related B-cell lymphoma
9. Monomorphic post-transplant lymphoproliferative disorders (PTLD)
10. Chronic Lymphocytic Leukemia (CLL)/Small Lymphocytic Lymphoma (SLL)

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Mantle Cell Lymphoma (MCL)
Authorization of 12 months may be granted for the treatment of MCL when any of the following criteria is met:
1. The member has received at least one prior therapy when the requested medication is used as a single agent or in combination with rituximab or venetoclax.
2. The requested medication will be used in combination with rituximab as pretreatment to induction therapy with RHyperCVAD (rituximab, cyclophosphamide, vincristine, doxorubicin, and dexamethasone) regimen.
3. The requested medication will be used in combination with rituximab for members aged 65 years and older.

B. Chronic Lymphocytic Leukemia (CLL) and Small Lymphocytic Lymphoma (SLL)
Authorization of 12 months may be granted for the treatment of CLL/SLL as a single agent or in combination with rituximab or obinutuzumab.

C. Waldenström's Macroglobulinemia/lymphoplasmacytic lymphoma (WM/LPL)
Authorization of 12 months may be granted for the treatment of WM/LPL when the requested medication is used as a single agent or in combination with rituximab.

D. Marginal Zone Lymphoma (MZL)
Authorization of 12 months may be granted for the treatment of MZL, such as gastric or non-gastric MALT lymphoma, nodal marginal zone lymphoma, or splenic marginal zone lymphoma, when the member has received at least one prior therapy.

E. Chronic Graft-Versus-Host Disease (cGVHD)
Authorization of 12 months may be granted for the treatment of cGVHD when the member has failed one or more lines of therapy.

F. Hairy Cell Leukemia
Authorization of 12 months may be granted for the treatment of hairy cell leukemia when the requested medication is used as a single agent for disease progression.

G. Primary central nervous system lymphoma
Authorization of 12 months may be granted for treatment of primary central nervous system lymphoma when any of the following criteria is met:
1. The requested medication is used for relapsed or refractory disease as either a single agent, or in combination with high-dose methotrexate and rituximab.
2. The requested medication is used for induction therapy as a single agent.

H. Diffuse large B-cell lymphoma
Authorization of 12 months may be granted for single agent subsequent treatment of diffuse large B-cell lymphoma in members who are non-candidates for transplant.

I. High-grade B-cell lymphoma (including high-grade B-cell lymphoma with translocations of MYC and BCL2 and/or BCL6 [double/triple hit lymphoma], high-grade B-cell lymphoma, not otherwise specified)
Authorization of 12 months may be granted for single agent subsequent treatment of high-grade B-cell lymphoma (including high-grade B-cell lymphoma with translocations of MYC and BCL2 and/or BCL6 [double/triple hit lymphoma], high-grade B-cell lymphoma, not otherwise specified) in members who are non-candidates for transplant.

J. AIDS-related B-cell lymphomas
Authorization of 12 months may be granted for single agent subsequent treatment of AIDS-related B-cell lymphomas in members who are non-candidates for transplant.

K. Monomorphic post-transplant lymphoproliferative disorders
Authorization of 12 months may be granted for single agent subsequent treatment of monomorphic post-transplant lymphoproliferative disorders in members who are non-candidates for transplant.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

IV. REFERENCES

1. Imbruvica [package insert]. South San Francisco, CA: Pharmacyclics LLC; August 2022.
2. The NCCN Drugs & Biologics Compendium® © 2022 National Comprehensive Cancer Network. The NCCN Drugs & Biologics Compendium. http://www.nccn.org. Accessed May 25, 2022.
3. Jain P, Zhao S, Lee HJ, et al Ibrutinib with rituximab in first-line treatment of older patients with mantle cell lymphoma. *J Clin Oncol.* 2022;40(2):202-212.
4. Wang ML, Jurczak W, Jerkeman M, et al. Ibrutinib plus bendamustine and rituximab in untreated mantle-cell lymphoma. *N Engl J Med.* 2022;386:2482-2494.

Reference number(s)
2860-A

SPECIALTY GUIDELINE MANAGEMENT

INBRIJA (levodopa inhalation powder)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Inbrija is indicated for the intermittent treatment of OFF episodes in patients with Parkinson's disease treated with carbidopa/levodopa.

All other indications are considered experimental/investigational and not medically necessary.

II. EXCLUSIONS

Coverage will not be provided for members with any of the following exclusions:
A. Asthma
B. Chronic obstructive pulmonary disease (COPD)
C. Other chronic underlying lung disease
D. Members who are receiving concomitant treatment with nonselective monoamine oxidase (MAO) inhibitors (e.g. phenelzine, tranylcypromine)

III. CRITERIA FOR INITIAL APPROVAL

Parkinson's disease
Authorization of 6 months may be granted for intermittent treatment of "off" episodes in members with Parkinson's disease when all of the following criteria are met:
A. The member experiences at least 2 hours per day of off time
B. The member is currently being treated with oral carbidopa/levodopa
C. Attempts to manage off episodes by adjusting the dosing or formulation of carbidopa/levodopa were ineffective
D. Treatment with carbidopa/levodopa plus one of the following therapies was ineffective at managing off episodes:
   1. Dopamine agonist (e.g., pramipexole, ropinirole)
   2. Monoamine oxidase B (MAO-B) inhibitor (e.g., selegiline, rasagiline)
   3. Catechol-O-methyl transferase (COMT) inhibitor (e.g., entacapone, tolcapone)

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for intermittent treatment of "off" episodes in members with Parkinson's disease when all of the following criteria are met:
A. The member is currently being treated with oral carbidopa/levodopa

B. The member is experiencing improvement on Inbrija therapy (e.g., reduction in daily off time, improvement in motor function post-administration)

V. REFERENCES

1. Inbrija [package insert]. Ardsley, NY: Acorda Therapeutics, Inc.; August 2020.
2. Miyasaki JM, Martin W, Suchowersky O, et al. Practice parameter: Initiation of treatment for Parkinson's disease: An evidence-based review. *Neurology* Jan 2002, 58 (1) 11-17.
3. National Institute for Clinical Excellence: Parkinson's disease in adults. July 2017. https://www.nice.org.uk/guidance/ng71/resources/parkinsons-disease-in-adults-pdf-1837629189061. Accessed August 1, 2021.
4. Fox SH, Katzenschlager R, Lim SY, et al. International Parkinson and movement disorder society evidence-based medicine review: update on treatments for the motor symptoms of Parkinson's disease. *Mov Disord*. 2018; 33(8):1248-1266.

Reference number(s)
1740-A

SPECIALTY GUIDELINE MANAGEMENT

INCRELEX (mecasermin)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no contraindications or exclusions to the prescribed therapy.

FDA-Approved Indications
Increlex is indicated for the treatment of growth failure in pediatric patients 2 years of age and older with severe primary insulin-like growth factor-1 (IGF-1) deficiency or with growth hormone (GH) gene deletion who have developed neutralizing antibodies to GH.

Severe primary IGF-1 deficiency is defined by:
- Height standard deviation (SD) score ≤ –3.0 and
- Basal IGF-1 SD score ≤ –3.0 and
- Normal or elevated GH.

Limitations of use: Increlex is not a substitute to GH for approved GH indications. Increlex is not indicated for use in patients with secondary forms of IGF-1 deficiency, such as GH deficiency, malnutrition, hypothyroidism, or chronic treatment with pharmacologic doses of anti-inflammatory corticosteroids.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review for continuation of therapy requests:
A. Total duration of treatment (approximate duration is acceptable)
B. Date of last dose administered
C. Approving health plan/pharmacy benefit manager
D. Date of prior authorization/approval
E. Prior authorization approval letter

III. CRITERIA FOR INITIAL APPROVAL

Severe Primary IGF-1 Deficiency
Authorization of 12 months may be granted to members with severe primary IGF-1 deficiency or GH gene deletion with neutralizing antibodies to GH when ALL of the following criteria are met:
A. Pretreatment height is ≥ 3 standard deviations (SD) below the mean for age and gender
B. Pretreatment basal IGF-1 level is ≥ 3 SD below the mean for age and gender
C. Pediatric GH deficiency has been ruled out with a provocative GH test (i.e., peak GH level ≥ 10 ng/mL)
D. Epiphyses are open

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continuation of therapy for severe primary IGF-1 deficiency or GH gene deletion with neutralizing antibodies to GH when ALL of the following criteria are met:

A. The member's growth rate is > 2 cm/year [2] or there is a documented clinical reason for lack of efficacy (e.g., on treatment less than 1 year, nearing final adult height/late stages of puberty).
B. Epiphyses are open (confirmed by X-ray or X-ray is not available).

V. REFERENCES

1. Increlex [package insert]. Cambridge, MA: Ipsen Biopharmaceuticals, Inc.; December 2019.

QUANTITY LIMIT CRITERIA

DRUG CLASS	**INFLUENZA TREATMENT & PREVENTION**
BRAND NAME* **(generic)**	**RELENZA (zanamivir)** **TAMIFLU (oseltamivir)** **XOFLUZA (baloxavir)**

Status: CVS Caremark Criteria
Type: Quantity Limit ***Ref # 110-H***

**Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA APPROVED INDICATIONS

Relenza

Treatment of Influenza

Relenza (zanamivir) inhalation powder is indicated for treatment of uncomplicated acute illness due to influenza A and B virus in adults and pediatric patients aged 7 years and older who have been symptomatic for no more than 2 days.

Prophylaxis of Influenza

Relenza is indicated for prophylaxis of influenza in adults and pediatric patients aged 5 years and older.

Important Limitations of Use

Relenza is not recommended for treatment or prophylaxis of influenza in individuals with underlying airways disease (such as asthma or chronic obstructive pulmonary disease) due to risk of serious bronchospasm.

Relenza has not been proven effective for treatment of influenza in individuals with underlying airways disease.

Relenza has not been proven effective for prophylaxis of influenza in the nursing home setting.

Relenza is not a substitute for early influenza vaccination on an annual basis as recommended by the Centers for Disease Control's Immunization Practices Advisory Committee.

Influenza viruses change over time. Emergence of resistance mutations could decrease drug effectiveness. Other factors (for example, changes in viral virulence) might also diminish clinical benefit of antiviral drugs. Prescribers should consider available information on influenza drug susceptibility patterns and treatment effects when deciding whether to use Relenza.

There is no evidence for efficacy of zanamivir in any illness caused by agents other than influenza virus A and B.

Patients should be advised that the use of Relenza for treatment of influenza has not been shown to reduce the risk of transmission of influenza to others.

Compendial Uses

Treatment of influenza A or B viral infection when administered after 48 hours in patients aged 7 years and older who are at higher risk for influenza complications or in patients aged 7 years and older with severe, complicated, or progressive illness[4-8]

Tamiflu

Treatment of Influenza

Tamiflu is indicated for the treatment of acute, uncomplicated illness due to influenza A and B infection in patients 2 weeks of age and older who have been symptomatic for no more than 48 hours.

Prophylaxis of Influenza

Tamiflu is indicated for the prophylaxis of influenza A and B in patients 1 year and older.
Limitations of Use
Tamiflu is not a substitute for early influenza vaccination on an annual basis as recommended by the Centers for Disease Control and Prevention Advisory Committee on Immunization Practices.
Influenza viruses change over time. Emergence of resistance substitutions could decrease drug effectiveness. Other factors (for example, changes in viral virulence) might also diminish clinical benefit of antiviral drugs. Prescribers should consider available information on influenza drug susceptibility patterns and treatment effects when deciding whether to use Tamiflu.
Tamiflu is not recommended for patients with end-stage renal disease not undergoing dialysis.

Compendial Uses
Treatment of influenza A or B viral infection when administered after 48 hours in patients who are at higher risk for influenza complications or in patients with severe, complicated, or progressive illness[4-8]
Prophylaxis of influenza A or B viral infection in patients 3 months to 1 year of age if necessary after exposure to another person with influenza[4-8]

Xofluza
Treatment of Influenza
Xofluza is indicated for the treatment of acute uncomplicated influenza in patients 12 years of age and older who have been symptomatic for no more than 48 hours and who are: otherwise healthy, or at high risk of developing influenza-related complications.
Post-Exposure Prophylaxis of Influenza
Xofluza is indicated for post-exposure prophylaxis of influenza in persons 12 years of age and older following contact with an individual who has influenza.
Limitations of Use
Influenza viruses change over time, and factors such as the virus type or subtype, emergence of resistance, or changes in viral virulence could diminish the clinical benefit of antiviral drugs. Consider available information on drug susceptibility patterns for circulating influenza virus strains when deciding whether to use Xofluza.

RATIONALE
The limits for Relenza and Tamiflu are based on the Center for Disease Control and Prevention (CDC) recommendation to allow a quantity to accommodate at least 2 weeks of community setting prophylaxis, at least 14 doses up to 20 doses (due to packaging), once every 90 days. The limits for Relenza and Tamiflu are also based on the recommended dosing regimen for the treatment or household prevention of influenza, providing quantity sufficient for 5 days of treatment or 10 days of household prevention, twice every 90 days, (10 doses each course for 2 courses, for a total of 40 blisters of Relenza, 20 capsules of Tamiflu 75mg or 45 mg, 40 capsules of Tamiflu 30mg [two capsules for 60mg dosing], or 6 bottles of Tamiflu suspension). The limits for Xofluza are based on the recommended dosing regimen for the treatment or post-exposure prophylaxis of influenza providing quantity sufficient for 1 day of therapy, twice every 90 days (1 dose each course for 2 courses, for a total of 2 tablets of the Xofluza 40mg (1 tablet per blister pack) or Xofluza 80mg (1 tablet per blister pack) or 4 tablets of Xofluza 20mg (2 tablets per blister pack) or Xofluza 40mg (2 tablets per blister pack) or 4 bottles of suspension).

If the patient is requesting more than the initial quantity limit, then the system will reject with a message indicating that a prior authorization is required. Quantities for extended community setting prophylaxis (Tamiflu, Relenza), or for another course of therapy for treatment (Tamiflu, Relenza, Xofluza), or household prevention/post-exposure prophylaxis (Tamiflu, Relenza, Xofluza) may be covered through the prior authorization.

The CDC states that influenza activity often begins to increase in October. Most of the time flu activity peaks between December and February, although activity can last as late as May.[6-8] When indicated, antiviral treatment should be started as soon as possible after illness onset, ideally within 48 hours of symptom onset.[6-8] The CDC states that antiviral treatment might have some benefits in patients with severe, complicated or progressive illness, and in patients at higher risk for influenza complications when started after 48 hours of illness onset.[4-8]

The CDC does not recommend widespread or routine use of antiviral medications for chemoprophylaxis so as to limit the possibilities that antiviral resistant viruses could emerge. To be effective as chemoprophylaxis, an antiviral medication must be taken each day for the duration of potential exposure to a person with influenza and continued for 7 days after the

last known exposure. For persons taking antiviral chemoprophylaxis after inactivated influenza vaccination, the recommended duration is until immunity after vaccination develops (antibody development after vaccination takes about two weeks in adults and can take longer in children depending on age and vaccination history). For control of outbreaks in institutional settings (e.g. long-term care facilities for elderly persons and children) and hospitals, the CDC recommends antiviral chemoprophylaxis for a minimum of 2 weeks and continuing up to 1 week after the last known case was identified.[4-8]

Relenza (zanamivir)

Treatment

The recommended dose of Relenza for treatment of influenza in adults and pediatric patients aged 7 years and older is 10mg twice daily for 5 days.

Prophylaxis – Household

The recommended dose of Relenza for prophylaxis of influenza in adults and pediatric patients aged 5 years and older in a household setting is 10mg once daily for 10 days. There are no data on the effectiveness of prophylaxis with Relenza in a household setting when initiated more than 1.5 days after the onset of signs or symptoms in the index case.

Prophylaxis – Community

The recommended dose of Relenza for prophylaxis of influenza in adults and adolescents in a community setting is 10mg once daily for 28 days. There are no data on the effectiveness of prophylaxis with Relenza in a community outbreak when initiated more than 5 days after the outbreak was identified in the community. The safety and effectiveness of prophylaxis with Relenza have not been evaluated for longer than 28 days' duration.

The Relenza 10-mg dose is provided by 2 inhalations (one 5-mg blister per inhalation). Relenza is supplied in five Rotadisks each containing 4 blisters of the drug (20 blisters), packaged in a carton with 1 Diskhaler inhalation device.

Each dose of Relenza is provided by 2 inhalations, which is 2 blisters. Therefore, the initial limit will be 40 blisters, which allows for 20 doses of 2 inhalations per dose accommodating at least 14 doses up to 20 doses (due to packaging) for community prophylaxis, or 2 courses of therapy of 10 doses each for treatment or household prophylaxis, per 90 days.

Tamiflu (oseltamivir)

Treatment

The recommended oral dosage of Tamiflu for treatment of influenza in adults and adolescents 13 years and older is 75mg (one 75mg capsule or 12.5mL of oral suspension) twice daily for 5 days.

The recommended oral dosage of Tamiflu for treatment of influenza in pediatric patients 2 weeks of age through 12 years of age is based on body weight, see table. Although not part of the FDA-approved indications, use of oral oseltamivir (Tamiflu) for treatment in infants less than 2 weeks of age if necessary is recommended by the CDC and the American Academy of Pediatrics.[4-8]

Prophylaxis - Household

Initiate post-exposure prophylaxis with Tamiflu within 48 hours following close contact with an infected individual. The recommended dosage of Tamiflu for prophylaxis of influenza in adults and adolescents 13 years and older is 75mg (one 75mg capsule or 12.5mL of oral suspension) orally once daily for at least 10 days following close contact with an infected individual.

Prophylaxis in pediatric patients is recommended for 10 days following close contact with an infected individual. The recommended oral dosage of Tamiflu for prophylaxis of influenza in pediatric patients 1 year to 12 years of age is based on body weight, see table. Although not part of the FDA-approved indications, use of oral oseltamivir (Tamiflu) for chemoprophylaxis in infants 3 months to 1 year of age if necessary is recommended by the CDC and the American Academy of Pediatrics.[4-8]

Prophylaxis - Community

The recommended dosage of Tamiflu for prophylaxis of influenza in adults and adolescents 13 years and older is 75mg (one 75mg capsule or 12.5mL of oral suspension) orally once daily for up to 6 weeks during a community outbreak. In immunocompromised patients, Tamiflu may be continued for up to 12 weeks.

Prophylaxis in pediatric patients is recommended up to 6 weeks during a community outbreak. The recommended oral dosage of Tamiflu for prophylaxis of influenza in pediatric patients 1 year to 12 years of age is based on body weight, see table. Although not part of the FDA-approved indications, use of oral oseltamivir (Tamiflu) for chemoprophylaxis in infants 3 months to 1 year of age if necessary is recommended by the CDC and the American Academy of Pediatrics.[4-8]

Weight	Treatment Dosage for 5 days	Prophylaxis Dosage	Oral Suspension (6 mg/mL)	Bottles to Dispense	Capsules to Dispense (Strength)

		for 10 days	for each Dose		
Patients from 2 Weeks to less than 1 Year of Age					
Any weight	3mg/kg twice daily	Not applicable	0.5mL/kg	1 bottle	Not applicable
Patients 1 to 12 Years of Age Based on Body Weight					
15kg or less	30mg twice daily	30mg once daily	5mL	1 bottle	10 capsules (30mg)
15.1kg to 23kg	45mg twice daily	45mg once daily	7.5mL	2 bottles	10 capsules (45mg)
23.1kg to 40kg	60mg twice daily*	60mg once daily*	10mL	2 bottles	20 capsules (30mg)
40.1kg or more	75mg twice daily	75mg once daily	12.5mL	3 bottles	10 capsules (75mg)

*Two 30mg capsules should be used for the 60mg dose.

The Tamiflu dose is provided by 1 to 2 capsules or up to 12.5mL oral suspension based on age or body weight. Tamiflu capsules are available in 30mg, 45mg, and 75mg strengths in blister packs of 10. Tamiflu is also available as an oral suspension for constitution delivering 360mg/60mL (6mg/mL). Constituted oral suspension can be stored under refrigeration for up to 17 days or for up to 10 days at controlled room temperature.

Each dose of Tamiflu is provided by 1 to 2 capsules or up to 12.5mL oral suspension. Therefore, the initial limit will be 20 capsules of 45mg or 75mg, 40 capsules of 30mg (two capsules for 60mg dose), or 360mL of oral suspension, which allows for 20 doses, accommodating at least 14 doses up to 20 doses (due to packaging) for community prophylaxis, or 2 courses of therapy of 10 doses each for treatment or household prophylaxis, per 90 days.

Xofluza (baloxavir marboxil)

Treatment or Post-Exposure Prophylaxis

Xofluza should be taken as a single dose as soon as possible and within 48 hours of influenza symptom onset for treatment of acute uncomplicated influenza or following contact with an individual who has influenza. The recommended dosage of Xofluza in patients 12 years of age or older is a single weight-based dose as follows:

Recommended Xofluza Dosage in Adults and Adolescents 12 Years and Older	
Patient Body Weight (kg)	Recommended Oral Dose
Less than 80 kg	One 40mg tablet (blister card contains one 40mg tablet) 40 mg/20 mL (1 bottle) taken as a single dose
At least 80 kg	One 80mg tablet (blister card contains one 80mg tablet) 80mg/40 mL (2 bottles) taken as a single dose

Per the prescribing information, Xofluza is available as 1 x 40mg tablet per blister card and 1 x 80mg tablet per blister card.[3] According to the compendia, Xofluza is also still available as 2 x 20mg tablets per blister card, and 2 x 40mg tablets per blister card.[5] Xofluza is also available as an oral suspension for constitution containing 40mg/20mL (2mg/mL). This dosage form can be used for oral or enteral use. Constituted oral suspension can be stored at room temperature. Xofluza for oral suspension contains no preservative and must be administered within 10 hours after constitution.[3]

Each dose of Xofluza is provided by 1 or 2 tablets (depending on tablet strength), or the maximum of 2 bottles based on body weight. Therefore, the initial limit will be 4 tablets of 20mg (2 tablets per blister card), 4 tablets of 40mg (2 tablets per blister card), 2 tablets of 40mg (1 tablet per blister card), 2 tablets of 80mg (1 tablet per blister card), or 80mL (4 bottles of 40mg/20mL) which allows for 2 doses, accommodating 2 courses of therapy of 1 dose each for treatment or post-exposure prophylaxis, per 90 days.

REFERENCES

1. Relenza [package insert]. Research Triangle Park, NC: GlaxoSmithKline; June 2018.
2. Tamiflu [package insert]. South San Francisco, CA: Genentech, Inc.; August 2019.
3. Xofluza [package insert]. South San Francisco, CA: Genentech USA, Inc. March 2021.
4. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2021; Accessed August 10, 2021.
5. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed August 10, 2021.

6. Centers for Disease Control and Prevention Seasonal Influenza (Flu) – Health Professionals – Antiviral Drugs. Available at: https://www.cdc.gov/flu/professionals/antivirals/index.htm. Accessed August 2020.
7. American Academy of Pediatrics Committee on Infectious Diseases. Recommendations for Prevention and Control of Influenza in Children, 2019–2020. *Pediatrics*. 2019;144(4).
8. Uyeki T, Bernstein H, Bradley J, et al. Clinical Practice Guidelines by the Infectious Diseases Society of America: 2018 Update on Diagnosis, Treatment, Chemoprophylaxis, and Institutional Outbreak Management of Seasonal Influenza. *Clinical Infectious Diseases*. 2019; 68(6), e1–e47.

Written by:	UM Development (LS)
Date Written:	09/1999
Revised:	12/1999, 11/2000, 01/2001; (MG) 12/2002, 10/2003; (NB) 10/2004; (MG) 08/2005, 01/2006; (CT) (new indication) 04/2006, 02/2007, 07/2007 (new dosages), 03/2008, 03/2009; (MS) 01/2010; (CY) 12/2010, 07/2011 (updated Tamiflu new strength 6mg/ml 12/2010(2)), 12/2011; (PL) 12/2012; (CF) 12/2013, 12/2014, 12/2015 (no clinical changes), (TM) 12/2016 (no clinical changes), (TM) 12/2017, (TM) 10/2018 (add Xofluza), (TM) 12/2018 (susp 360mL), (TM) 09/2019 (no clinical changes), (TM) 10/2019 (update Xofluza PI), (TM) 08/2020 (no clinical changes), (TM) 11/2020 (add Xofluza susp), (DFW/AW) 08/2021 (off-cycle – added limit for new Xofluza 40mg/80mg 1 tablet per blister card), 08/2021 (annual review – no clinical changes)
Reviewed:	Medical Affairs 09/1999, 12/1999, 12/2000, 01/2001, 12/2002, 11/2003, 10/2004, 08/2005; (MM) 01/2006, 04/2006; (WF) 02/2007, 07/2007, 03/2008, 03/2009; (KP) 01/2010, 12/2010, 07/2011, 01/2012; (LMS) 12/2012; (LMS) 12/2013; (LCB) 12/2014, (JG) 12/2016, (ME) 12/2017, (SD) 11/2018, (EPA) 12/2018, CHART: 09/2019, (CHART) 12/03/2020, (CHART) 08/26/2021
External Review:	05/2002, 03/2003, 12/2003, 11/2004, 08/2005, 04/2006, 06/2007, 06/2008, 05/2009, 06/2009, 02/2010, 05/2011, 03/2012, 4/2013, 3/2014, 04/2014, 02/2015, 04/2015, 04/2016, 04/2017, 02/2018, 11/2018, 04/2019, 12/2019, 12/2020, 12/2021

LIMIT CRITERIA

Limits should accumulate across all drugs and strengths up to highest quantity listed depending on the order the claims are processed. Accumulation does not apply if limit is coded for daily dose.

Medication	Strength	Limit*
Relenza (zanamivir)	5 mg blister per inhalation	40 blisters / 90 days
Tamiflu (oseltamivir)	6 mg/mL suspension	360 mL / 90 days
	30 mg per capsule	40 capsules / 90 days
	45 mg per capsule	20 capsules / 90 days
	75 mg per capsule	20 capsules / 90 days
Xofluza (baloxavir marboxil)	20 mg per tablet (2 tablets per blister card)	4 tablets / 90 days
	40 mg per tablet (1 tablet per blister card)	2 tablets / 90 days
	40 mg per tablet (2 tablets per blister card)	4 tablets / 90 days
	80 mg per tablet (1 tablet per blister card)	2 tablets / 90 days
	40 mg/20mL suspension	80 mL / 90 days

**These drugs are for short-term acute use; therefore the 3 month limit will be the same as the 1 month limit.*

Reference number(s)
1750-A

SPECIALTY GUIDELINE MANAGEMENT

INGREZZA (valbenazine)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Treatment of adults with tardive dyskinesia

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary for both initial approval and continuation of therapy prior authorization reviews: Documentation of score of items 1 to 7 of the Abnormal Involuntary Movement Scale (AIMS).

III. CRITERIA FOR INITIAL APPROVAL

Tardive dyskinesia
Authorization of 6 months may be granted for treatment of tardive dyskinesia when the baseline AIMS score for items 1 to 7 is obtained.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for treatment of tardive dyskinesia when the member's tardive dyskinesia symptoms have improved as indicated by a decreased AIMS score (items 1 to 7) from baseline.

V. REFERENCES

1. Ingrezza [package insert]. San Diego, CA: Neurocrine Biosciences, Inc.; August 2022.
2. Hauser, Robert, et al. KINECT-3: A Phase 3 Randomized, Double-Blind, Placebo-Controlled Trial of Valbenazine for Tardive Dyskinesia. *American Journal of Psychiatry.* 2017 Mar 21: 1-9.
3. American Psychiatric Association. (2021). *Practice Guideline for the Treatment of Patients With Schizophrenia, third edition.* https://doi.org/10.1176/appi.books.9780890424841

Reference number(s)
4002-A

SPECIALTY GUIDELINE MANAGEMENT

INQOVI (decitabine and cedazuridine)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Inqovi is indicated for treatment of adult patients with myelodysplastic syndromes (MDS), including previously treated and untreated, *de novo* and secondary MDS with the following French-American-British subtypes (refractory anemia, refractory anemia with ringed sideroblasts, refractory anemia with excess blasts, and chronic myelomonocytic leukemia [CMML]) and intermediate-1, intermediate-2, and high-risk International Prognostic Scoring System groups.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Myelodysplastic syndromes (MDS)/Chronic myelomonocytic leukemia (CMML)
Authorization of 12 months may be granted for the treatment of myelodysplastic syndromes (MDS), including chronic myelomonocytic leukemia (CMML).

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

IV. REFERENCES

1. Inqovi [package insert]. Japan: Otsuka Pharmaceutical Co, Ltd; July 2020.

Reference number
3161-A

SPECIALTY GUIDELINE MANAGEMENT

INREBIC (fedratinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
Inrebic is indicated for the treatment of adult patients with intermediate-2 or high-risk primary or secondary (post-polycythemia vera or post-essential thrombocythemia) myelofibrosis (MF).

B. Compendial Uses
1. Treatment for myeloid/lymphoid neoplasms with eosinophilia and JAK2 rearrangement in chronic phase
2. Treatment for myeloid, lymphoid, or mixed lineage neoplasms with eosinophilia and JAK2 rearrangement in blast phase
3. Treatment for myelofibrosis in accelerated phase or blast phase/acute myeloid leukemia

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: Testing or analysis confirming JAK2 rearrangement (if applicable).

III. CRITERIA FOR INITIAL APPROVAL

A. Myelofibrosis/Acute Myeloid Leukemia
Authorization of 12 months may be granted for the treatment of intermediate-2 or high-risk primary or secondary (post-polycythemia vera or post-essential thrombocythemia) myelofibrosis (MF), accelerated phase myelofibrosis (MF) or blast phase myelofibrosis (MF)/acute myeloid leukemia.

B. Myeloid/Lymphoid Neoplasms
Authorization of 12 months may be granted for the treatment of myeloid and/or lymphoid neoplasms with eosinophilia and JAK2 rearrangement in the chronic phase or blast phase.

IV. CONTINUATION OF THERAPY

A. Myelofibrosis
Authorization of 12 months may be granted for continued treatment in members requesting reauthorization when there is no evidence of unacceptable toxicity and there has been an improvement in symptoms.

B. Myeloid/Lymphoid Neoplasms
Authorization of 12 months may be granted for continued treatment in members requesting reauthorization when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

V. REFERENCES

1. Inrebic [package insert]. Summit, NJ: Celgene Corporation; December 2021.
2. National Comprehensive Cancer Network. The NCCN Drugs & Biologics Compendium. http://www.nccn.org. Accessed March 14, 2022.

QUANTITY LIMIT CRITERIA

DRUG CLASS	**INSOMNIA AGENTS***
BRAND NAME (generic)	
	AMBIEN (zolpidem)
	AMBIEN CR (zolpidem extended-release)
	DORAL (quazepam)
	(estazolam)
	(flurazepam)
	HALCION (triazolam)
	LUNESTA (eszopiclone)
	RESTORIL (temazepam)
	ROZEREM (ramelteon)
	(zaleplon)
	(zolpidem tartrate capsules)

Status: CVS Caremark Criteria
Type: Quantity Limit

** Edluar, Intermezzo, ZolpiMist, Belsomra, Dayvigo, and Quviviq are not included in these criteria. Refer to Insomnia (Edluar, Intermezzo, ZolpiMist) or Insomnia (Belsomra, Dayvigo, Quviviq) Prior Authorization criteria.*

POLICY

FDA-APPROVED INDICATIONS

Ambien

Ambien (zolpidem tartrate) is indicated for the short-term treatment of insomnia characterized by difficulties with sleep initiation. Ambien has been shown to decrease sleep latency for up to 35 days in controlled clinical studies.

The clinical trials performed in support of efficacy were 4–5 weeks in duration with the final formal assessments of sleep latency performed at the end of treatment.

Ambien CR
Ambien CR (zolpidem tartrate extended-release tablets) is indicated for the treatment of insomnia characterized by difficulties with sleep onset and/or sleep maintenance (as measured by wake time after sleep onset).
The clinical trials performed in support of efficacy were up to 3 weeks (using polysomnography measurement up to 2 weeks in both adult and elderly patients) and 24 weeks (using patient-reported assessment in adult patients only) in duration.

Doral
Doral is indicated for the treatment of insomnia characterized by difficulty in falling asleep, frequent nocturnal awakenings, and/or early morning awakenings. The effectiveness of Doral has been established in placebo-controlled clinical studies of 5 nights duration in acute and chronic insomnia.
The sustained effectiveness of Doral has been established in chronic insomnia in a sleep lab (polysomnographic) study of 28 nights duration. Because insomnia is often transient and intermittent, the prolonged administration of Doral Tablets is generally not necessary or recommended. Since insomnia may be a symptom of several other disorders, the possibility that the complaint may be related to a condition for which there is a more specific treatment should be considered.

Estazolam
Estazolam is indicated for the short-term management of insomnia characterized by difficulty in falling asleep, frequent nocturnal awakenings, and/or early morning awakenings. Both outpatient studies and a sleep laboratory study have shown that estazolam administered at bedtime improved sleep induction and sleep maintenance.
Because insomnia is often transient and intermittent, the prolonged administration of estazolam is generally neither necessary nor recommended. Since insomnia may be a symptom of several other disorders, the possibility that the complaint may be related to a condition for which there is a more specific treatment should be considered.
There is evidence to support the ability of estazolam to enhance the duration and quality of sleep for intervals up to 12 weeks.

Flurazepam
Flurazepam hydrochloride capsules are indicated for the treatment of insomnia characterized by difficulty in falling asleep, frequent nocturnal awakenings, and/or early morning awakenings.
Since insomnia is often transient and intermittent, short-term use is usually sufficient. Prolonged use of hypnotics is usually not indicated and should only be undertaken concomitantly with appropriate evaluation of the patient.

Halcion
Halcion is indicated for the short-term treatment of insomnia (generally 7 to 10 days) in adults.

Lunesta
Lunesta (eszopiclone) is indicated for the treatment of insomnia. In controlled outpatient and sleep laboratory studies, Lunesta administered at bedtime decreased sleep latency and improved sleep maintenance.
The clinical trials performed in support of efficacy were up to 6 months in duration. The final formal assessments of sleep latency and maintenance were performed at 4 weeks in the 6-week study (adults only), at the end of both 2-week studies (elderly only) and at the end of the 6-month study (adults only).

Restoril
Restoril (temazepam) is indicated for the short-term treatment of insomnia (generally 7 to 10 days).
For patients with short-term insomnia, instructions in the prescription should indicate that Restoril (temazepam) should be used for short periods of time (7 to 10 days).
The clinical trials performed in support of efficacy were 2 weeks in duration with the final formal assessment of sleep latency performed at the end of treatment.

Rozerem
Rozerem is indicated for the treatment of insomnia characterized by difficulty with sleep onset.
The clinical trials performed in support of efficacy were up to six months in duration. The final formal assessments of sleep latency were performed after two days of treatment during the crossover study (elderly only), at five weeks in the six-week studies (adults and elderly), and at the end of the six-month study (adults and elderly).

Zaleplon
Zaleplon capsules are indicated for the short-term treatment of insomnia. Zaleplon capsules have been shown to decrease the time to sleep onset for up to 30 days in controlled clinical studies. It has not been shown to increase total sleep time or decrease the number of awakenings.
The clinical trials performed in support of efficacy ranged from a single night to 5 weeks in duration. The final formal assessments of sleep latency were performed at the end of treatment.

Zolpidem Tartrate Capsules
Zolpidem Tartrate Capsules are indicated for the short-term treatment of transient insomnia characterized by difficulties with sleep initiation in adults younger than 65 years of age.

INITIAL LIMIT QUANTITY
Limits should accumulate across all drugs and strengths up to highest quantity listed depending on the order the claims are processed.

Drug	1 Month Limit*	3 Month Limit*
Ambien all strengths (zolpidem)	15 tablets / 25 days	45 tablets / 75 days
Ambien CR all strengths (zolpidem extended-release)	15 tablets / 25 days	45 tablets / 75 days
Doral all strengths (quazepam)	15 tablets / 25 days	45 tablets / 75 days
estazolam all strengths	15 tablets / 25 days	45 tablets / 75 days
flurazepam all strengths	15 capsules / 25 days	45 capsules / 75 days
Halcion all strengths (triazolam)	10 tablets / 25 days	30 tablets / 75 days
Lunesta all strengths (eszopiclone)	15 tablets / 25 days	45 tablets / 75 days
Restoril all strengths (temazepam)	15 capsules / 25 days	45 capsules / 75 days
Rozerem all strengths (ramelteon)	15 tablets / 25 days	45 tablets / 75 days
zaleplon all strengths	15 capsules / 25 days	45 capsules / 75 days
zolpidem tartrate capsules all strengths	15 capsules / 25 days	45 capsules / 75 days

**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*

REFERENCES

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9. Rozerem [package insert]. Deerfield, Illinois: Takeda Pharmaceuticals America, Inc.; November 2021.
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14. Sateia MJ, Buysse DJ, Krystal AD, Neubauer DN, Heald JL. Clinical practice guideline for the pharmacologic treatment of chronic insomnia in adults: An American Academy of Sleep Medicine clinical practice guideline. *J Clin Sleep Med.* 2017;13(2):307-349.
15. Qaseem A, Kansagara D, Forciea MA, Cooke M, Denberg TD, Management of chronic insomnia disorder in adults: A clinical practice guideline from the American College of Physicians. *Ann Intern Med*. Epub, 2016. 165(2):125-33. doi: 10.7326/M15-2175. Epub 2016 May 3.
16. Schutte-Rodin S, Broch L, Buysse D, Dorsey C, Sateia M. Clinical guideline for the evaluation and management of chronic insomnia in adults. *J Clin Sleep Med* 2008*;* 4(5):487-504.

PRIOR AUTHORIZATION CRITERIA

DRUG CLASS	**INSOMNIA AGENTS***
BRAND NAME (generic)	
	AMBIEN (zolpidem)
	AMBIEN CR (zolpidem extended-release)
	DORAL (quazepam)
	(estazolam)
	(flurazepam)
	HALCION (triazolam)
	LUNESTA (eszopiclone)
	RESTORIL (temazepam)
	ROZEREM (ramelteon)
	(zaleplon)
	(zolpidem tartrate capsules)

Status: CVS Caremark Criteria
Type: Post Limit Prior Authorization

** Edluar, Intermezzo, ZolpiMist, Belsomra, Dayvigo and Quviviq are not included in these criteria. Refer to Insomnia (Edluar, Intermezzo, ZolpiMist) or Insomnia (Belsomra, Dayvigo, Quviviq) Prior Authorization criteria.*

POLICY

FDA-APPROVED INDICATIONS

Ambien

Ambien (zolpidem tartrate) is indicated for the short-term treatment of insomnia characterized by difficulties with sleep initiation. Ambien has been shown to decrease sleep latency for up to 35 days in controlled clinical studies.

The clinical trials performed in support of efficacy were 4–5 weeks in duration with the final formal assessments of sleep latency performed at the end of treatment.

Ambien CR
Ambien CR (zolpidem tartrate extended-release tablets) is indicated for the short-term treatment of insomnia characterized by difficulties with sleep onset and/or sleep maintenance (as measured by wake time after sleep onset).
The clinical trials performed in support of efficacy were up to 3 weeks (using polysomnography measurement up to 2 weeks in both adult and elderly patients) and 24 weeks (using patient-reported assessment in adult patients only) in duration.

Doral
Doral is indicated for the treatment of insomnia characterized by difficulty in falling asleep, frequent nocturnal awakenings, and/or early morning awakenings. The effectiveness of Doral has been established in placebo-controlled clinical studies of 5 nights duration in acute and chronic insomnia.
The sustained effectiveness of Doral has been established in chronic insomnia in a sleep lab (polysomnographic) study of 28 nights duration. Because insomnia is often transient and intermittent, the prolonged administration of Doral Tablets is generally not necessary or recommended. Since insomnia may be a symptom of several other disorders, the possibility that the complaint may be related to a condition for which there is a more specific treatment should be considered.

Estazolam
Estazolam is indicated for the short-term management of insomnia characterized by difficulty in falling asleep, frequent nocturnal awakenings, and/or early morning awakenings. Both outpatient studies and a sleep laboratory study have shown that estazolam administered at bedtime improved sleep induction and sleep maintenance.
Because insomnia is often transient and intermittent, the prolonged administration of estazolam is generally neither necessary nor recommended. Since insomnia may be a symptom of several other disorders, the possibility that the complaint may be related to a condition for which there is a more specific treatment should be considered.
There is evidence to support the ability of estazolam to enhance the duration and quality of sleep for intervals up to 12 weeks.

Flurazepam
Flurazepam hydrochloride capsules are indicated for the treatment of insomnia characterized by difficulty in falling asleep, frequent nocturnal awakenings, and/or early morning awakenings.
Since insomnia is often transient and intermittent, short-term use is usually sufficient. Prolonged use of hypnotics is usually not indicated and should only be undertaken concomitantly with appropriate evaluation of the patient.

Halcion
Halcion is indicated for the short-term treatment of insomnia (generally 7 to 10 days) in adults.

Lunesta
Lunesta (eszopiclone) is indicated for the treatment of insomnia. In controlled outpatient and sleep laboratory studies, Lunesta administered at bedtime decreased sleep latency and improved sleep maintenance.
The clinical trials performed in support of efficacy were up to 6 months in duration. The final formal assessments of sleep latency and maintenance were performed at 4 weeks in the 6-week study (adults only), at the end of both 2-week studies (elderly only) and at the end of the 6-month study (adults only).

Restoril
Restoril (temazepam) is indicated for the short-term treatment of insomnia (generally 7 to 10 days).
For patients with short-term insomnia, instructions in the prescription should indicate that Restoril (temazepam) should be used for short periods of time (7 to 10 days).
The clinical trials performed in support of efficacy were 2 weeks in duration with the final formal assessment of sleep latency performed at the end of treatment.

Rozerem
Rozerem is indicated for the treatment of insomnia characterized by difficulty with sleep onset.
The clinical trials performed in support of efficacy were up to six months in duration. The final formal assessments of sleep latency were performed after two days of treatment during the crossover study (elderly only), at five weeks in the six-week studies (adults and elderly), and at the end of the six-month study (adults and elderly).

Zaleplon
Zaleplon capsules are indicated for the short-term treatment of insomnia. Zaleplon capsules have been shown to decrease the time to sleep onset for up to 30 days in controlled clinical studies. It has not been shown to increase total sleep time or decrease the number of awakenings.
The clinical trials performed in support of efficacy ranged from a single night to 5 weeks in duration. The final formal assessments of sleep latency were performed at the end of treatment.

Zolpidem Tartrate Capsules
Zolpidem Tartrate Capsules are indicated for the short-term treatment of transient insomnia characterized by difficulties with sleep initiation in adults younger than 65 years of age.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for insomnia

AND

- Potential causes of sleep disturbances have been addressed or are currently being addressed (e.g., inappropriate sleep hygiene and sleep environment issues or treatable medical/psychological causes of chronic insomnia)

Quantity Limits apply.
Ambien, Ambien CR, Lunesta, Rozerem: 30 tablets per 25 days* or 90 tablets per 75 days*
Zolpidem tartrate capsules: 30 capsules per 25 days* or 90 capsules per 75 days*
Zaleplon: 60 capsules per 25 days* or 180 capsules per 75 days*
**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*

REFERENCES

1. Ambien [package insert]. Bridgewater, New Jersey: sanofi-aventis U.S. LLC; February 2022.
2. Ambien CR [package insert]. Bridgewater, New Jersey: sanofi-aventis U.S. LLC; February 2022.
3. Doral [package insert]. Atlanta, Georgia: Galt Pharmaceuticals LLC; January 2021.
4. Estazolam [package insert]. East Windsor, New Jersey: Novitium Pharma LLC; April 2021.
5. Flurazepam [package insert]. Morgantown, West Virginia: Mylan Pharmaceuticals, Inc.; February 2021.
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7. Lunesta [package insert]. Marlborough, Massachusetts: Sunovion Pharmaceuticals Inc.; August 2019.
8. Restoril [package insert]. Webster Groves, Missouri: SpecGx LLC; February 2021.
9. Rozerem [package insert]. Deerfield, Illinois: Takeda Pharmaceuticals America, Inc.; November 2021.
10. Zaleplon [package insert]. Princeton, New Jersey: OrchidPharma Inc.; September 2019.
11. Zolpidem Tartrate Capsules [package insert]. Morristown, NJ: Almatica Pharma LLC; May 2023.
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15. Qaseem A, Kansagara D, Forciea MA, Cooke M, Denberg TD, Management of chronic insomnia disorder in adults: A clinical practice guideline from the American College of Physicians. *Ann Intern Med*. Epub, 2016. 165(2):125-33. doi: 10.7326/M15-2175. Epub 2016 May 3.
16. Schutte-Rodin S, Broch L, Buysse D, Dorsey C, Sateia M. Clinical guideline for the evaluation and management of chronic insomnia in adults. *J Clin Sleep Med* 2008*;* 4(5):487-504.

Reference number(s)
1703-A

SPECIALTY GUIDELINE MANAGEMENT

INTRON A (interferon alfa-2b)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
1. Malignant melanoma
2. Condylomata acuminata
3. Hairy cell leukemia
4. AIDS-related Kaposi sarcoma
5. Chronic hepatitis B virus infection
6. Chronic hepatitis C virus infection
7. Follicular non-Hodgkin's lymphoma

B. Compendial Uses
1. Adult T-cell leukemia/lymphoma (ATLL)
2. Mycosis fungoides (MF)/Sezary syndrome (SS)
3. Renal cell carcinoma
4. Chronic myeloid leukemia (CML)
5. Giant cell tumor of the bone
6. Ocular surface neoplasia (conjunctival and corneal neoplasm)

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Malignant melanoma
Authorization of 12 months may be granted for treatment of malignant melanoma.

B. Adult T-cell leukemia/lymphoma (ATLL)
Authorization of 12 months may be granted for treatment of adult T-cell leukemia/lymphoma (ATLL) when the requested medication is used in combination with zidovudine.

C. Mycosis fungoides (MF)/Sezary syndrome (SS)
Authorization of 12 months may be granted for treatment of mycosis fungoides (MF)/Sezary syndrome (SS).

D. Hairy cell leukemia
Authorization of 12 months may be granted for treatment of hairy cell leukemia.

E. Follicular lymphoma

Authorization of 12 months may be granted for treatment of follicular lymphoma (clinically aggressive).

F. Renal cell carcinoma
Authorization of 12 months may be granted for treatment of renal cell carcinoma when the requested medication will be used in combination with bevacizumab.

G. Condylomata acuminata
Authorization of 12 months may be granted for treatment of condylomata acuminata.

H. AIDS-related Kaposi sarcoma
Authorization of 12 months may be granted for treatment of AIDS-related Kaposi sarcoma

I. Chronic myeloid leukemia (CML)
Authorization of 6 months may be granted for treatment of CML.

J. Giant cell tumor of the bone
Authorization of 12 months may be granted for treatment of giant cell tumor of the bone.

K. Chronic hepatitis C virus infection
Authorization of 16 weeks may be granted for treatment of chronic hepatitis C virus infection.

L. Chronic hepatitis B (including hepatitis D virus co-infection) virus infection
Authorization of 16 weeks may be granted for treatment of chronic hepatitis B (including hepatitis D virus co-infection) virus infection.

M. Ocular surface neoplasia (conjunctival and corneal neoplasm)
Authorization of 12 months may be granted for treatment of ocular surface neoplasia (conjunctival and corneal neoplasm).

III. CONTINUATION OF THERAPY

A. Chronic Hepatitis C
Authorization of 52 weeks, up to a total of 96 weeks, may be granted for continued treatment of chronic hepatitis C when the member is receiving clinical benefit and there is no evidence of unacceptable toxicity while on the current regimen.

B. Chronic Hepatitis B
Authorization of up to a total of 24 weeks may be granted for continued of chronic hepatitis B when the member is receiving clinical benefit and there is no evidence of unacceptable toxicity while on the current regimen.

C. All Other Indications
Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II, other than chronic hepatitis C and chronic hepatitis B, when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

IV. REFERENCES

1. Intron A [package insert]. Whitehouse Station, NJ: Merck Sharp & Dohme Corp.; November 2021.

2. The NCCN Drugs & Biologics Compendium® © 2022 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed April 5, 2022.
3. Micromedex Solutions [database online]. Truven Health Analytics, Greenwood Village, Colorado, USA. Available at: http://www.micromedexsolutions.com/. Accessed April 5, 2022.
4. Lexicomp Online®, AHFS® Drug Information, Hudson, Ohio: Wolters Kluwer Clinical Drug Information, Inc.; http://online.lexi.com [available with subscription]. Accessed April 5, 2022.
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6. Avastin [package insert]. South San Francisco, CA: Genentech, Inc.; January 2021.
7. American Academy of Ophthalmology (AAO). Ocular surface squamous neoplasia. EyeWiki. San Francisco, CA: AAO; last modified on November 8, 2017
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9. Shields CL, Kaliki S, Kim HJ, Al-Dahmash S, Shah SU, Lally SE, et al. Interferon for ocular surface squamous neoplasia in 81 cases: outcomes based on the American Joint Committee on Cancer classification. Cornea. 2013;32(3):248–56.

STEP THERAPY CRITERIA

BRAND NAME*
(generic)

INTUNIV
(guanfacine extended-release)

KAPVAY
(clonidine extended-release)

Status: CVS Caremark Criteria
Type: Initial Step Therapy; Post Step Therapy Prior Authorization ***Ref # 781-D***

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Intuniv
Intuniv is indicated for the treatment of Attention Deficit Hyperactivity Disorder (ADHD) as monotherapy and as adjunctive therapy to stimulant medications.
Kapvay
Kapvay (clonidine hydrochloride) extended-release is indicated for the treatment of attention deficit hyperactivity disorder (ADHD) as monotherapy and as adjunctive therapy to stimulant medications.

INITIAL STEP THERAPY

**Include Rx and OTC products unless otherwise stated.*

If the patient has filled a prescription for at least a 30 day supply of an amphetamine product (e.g., amphetamine, amphetamine-dextroamphetamine, dextroamphetamine, methamphetamine, lisdexamfetamine) OR a methylphenidate product (e.g., methylphenidate, dexmethylphenidate) within the past 180 days under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit. If the patient does not meet the initial step therapy criteria, then the claim will reject with a message indicating that a prior authorization (PA) is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has the diagnosis of Attention-Deficit Hyperactivity Disorder (ADHD) or Attention Deficit Disorder (ADD)

AND

- The patient has experienced an inadequate treatment response to an amphetamine product (e.g., amphetamine, amphetamine-dextroamphetamine, dextroamphetamine, methamphetamine, lisdexamfetamine) or a methylphenidate product (e.g., methylphenidate, dexmethylphenidate)

  OR
- The patient has experienced an intolerance to an amphetamine product (e.g., amphetamine, amphetamine-dextroamphetamine, dextroamphetamine, methamphetamine, lisdexamfetamine) or a methylphenidate product (e.g., methylphenidate, dexmethylphenidate)

  OR
- The patient has a contraindication that would prohibit a trial of an amphetamine product (e.g., amphetamine, amphetamine-dextroamphetamine, dextroamphetamine, methamphetamine, lisdexamfetamine) and a methylphenidate product (e.g., methylphenidate, dexmethylphenidate)

RATIONALE

If the patient has filled a prescription for at least a 30 day supply of an amphetamine product (e.g., amphetamine, amphetamine-dextroamphetamine, dextroamphetamine, methamphetamine, lisdexamfetamine) OR a methylphenidate product (e.g., methylphenidate, dexmethylphenidate) within the past 180 days under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit.

If the patient does not meet the initial step therapy criteria, then prior authorization is required.

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Intuniv and Kapvay are indicated for the treatment of Attention Deficit Hyperactivity Disorder (ADHD) as monotherapy and as adjunctive therapy to stimulant medications.

Stimulants (e.g., methylphenidates, amphetamines) remain the drugs of choice for the management of ADHD.[3] The American Academy of Pediatrics Clinical Practice Guideline states that stimulant medications are highly effective for most children in reducing core symptoms of ADHD. The evidence base that supports the use of extended-release guanfacine (Intuniv) and extended-release clonidine (Kapvay), although adequate for FDA approval, is considerably smaller than that for stimulants; neither agent has been approved for use in preschool-aged children. Additionally, compared with stimulant medications that have an effect size [effect size = (treatment mean – control mean)/control SD] of approximately 1.0, the effects of non-stimulants are slightly weaker. Extended-release guanfacine (Intuniv) and extended release clonidine (Kapvay) have an effect size of approximately 0.7.[5]

Therefore, Intuniv and Kapvay will be covered if the patient has experienced an inadequate treatment response or intolerance to an amphetamine product (e.g., amphetamine, amphetamine-dextroamphetamine, dextroamphetamine, methamphetamine, lisdexamfetamine) or a methylphenidate product (e.g., methylphenidate, dexmethylphenidate); or the patient has a contraindication that would prohibit a trial of an amphetamine product (e.g., amphetamine, amphetamine-dextroamphetamine, dextroamphetamine, methamphetamine, lisdexamfetamine) and a methylphenidate product (e.g., methylphenidate, dexmethylphenidate).

REFERENCES

1. Intuniv [package insert]. Lexington, MA: Takeda Pharmaceuticals America, Inc.; August 2020.
2. Kapvay [package insert]. Dublin 9, Ireland: Concordia Pharmaceuticals, Inc.; February 2020.
3. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2021; Accessed November 8, 2021.
4. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed November 8, 2021.
5. Wolraich ML, Hagan JF, Allan C, et al. AAP Subcommittee on Children and Adolescents with Attention-Deficit/Hyperactive Disorder. Clinical Practice Guideline for the Diagnosis, Evaluation, and Treatment of Attention-Deficit/Hyperactivity Disorder in Children and Adolescents. *Pediatrics*. 2019;144(4).

Written by:	UM Development (PL)
Date Written:	05/2012
Revised:	(RP) 11/2012 (added Kapvay), 11/2013, 11/2014; (MS) 11/2015; (RP) 11/2016 (no clinical changes), 11/2017 (no clinical changes), 11/2018, 11/2019; (PM) 11/2020 (no clinical changes), 11/2021 (no clinical changes)
Reviewed:	Medical Affairs (KP) 05/2012; (LS) 11/2012; (LS) 11/2013; (DNC) 11/2014; (LS) 11/2015; (GAD) 11/2018; (CHART) 11/27/2019; (CHART) 12/3/2020, 12/2/2021 External Review: 06/2012, 02/2013, 02/2014, 02/2015, 02/2016, 02/2017, 02/2018, 02/2019, 02/2020; 02/2021, 02/2022

CRITERIA FOR APPROVAL

1	Does the patient have the diagnosis of Attention-Deficit Hyperactivity Disorder (ADHD) or Attention Deficit Disorder (ADD)? [If no, then no further questions.]	Yes	No

CVS caremark®

2	Has the patient experienced an inadequate treatment response to an amphetamine product (e.g., amphetamine, amphetamine-dextroamphetamine, dextroamphetamine, methamphetamine, lisdexamfetamine) or a methylphenidate product (e.g., methylphenidate, dexmethylphenidate)? [If yes, then no further questions.]	Yes	No
3	Has the patient experienced an intolerance to an amphetamine product (e.g., amphetamine, amphetamine-dextroamphetamine, dextroamphetamine, methamphetamine, lisdexamfetamine) or a methylphenidate product (e.g., methylphenidate, dexmethylphenidate)? [If yes, then no further questions.]	Yes	No
4	Does the patient have a contraindication that would prohibit a trial of an amphetamine product (e.g., amphetamine, amphetamine-dextroamphetamine, dextroamphetamine, methamphetamine, lisdexamfetamine) and a methylphenidate product (e.g., methylphenidate, dexmethylphenidate)?	Yes	No

Mapping Instructions			
	Yes	**No**	**DENIAL REASONS – DO NOT USE FOR MEDICARE PART D**
1.	Go to 2	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you meet these conditions: - You have Attention-Deficit Hyperactivity Disorder (ADHD) or Attention Deficit Disorder (ADD) Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]
2.	Approve, 36 months	Go to 3	
3.	Approve, 36 months	Go to 4	
4.	Approve, 36 months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you tried an amphetamine product or a methylphenidate product and it did not work for you, or you cannot use it. Your request has been denied based on the information we have. [Short Description: No trial of amphetamines/methylphenidates]

Reference number(s)
1660-A

SPECIALTY GUIDELINE MANAGEMENT

IRESSA (gefitinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication
Iressa is indicated for the first-line treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 (L858R) substitution mutations as detected by an FDA-approved test.

Limitation of Use: Safety and efficacy of Iressa have not been established in patients who have EGFR mutations other than exon 19 deletions or exon 21 (L858R) substitution mutations.

B. Compendial Use
EGFR mutation-positive recurrent, advanced, or metastatic NSCLC

All other indications are considered experimental/investigational and not medically necessary.

II. REQUIRED DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: EGFR mutation testing results.

III. CRITERIA FOR INITIAL APPROVAL

Non-small cell lung cancer (NSCLC)
Authorization of 12 months may be granted for treatment of recurrent, advanced, or metastatic NSCLC in members with sensitizing EGFR mutation-positive disease as a single agent.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for EGFR positive NSCLC when either of the following criteria are met:
1. There is no evidence of unacceptable toxicity or disease progression while on the current regimen.
2. Disease is T790M negative and there is no evidence of unacceptable toxicity.

V. REFERENCES

1. Iressa [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; May 2021.

2. The NCCN Drugs & Biologics Compendium® © 2022 National Comprehensive Cancer Network, Inc. Available at: https://www.nccn.org. Accessed March 4, 2022.

PRIOR AUTHORIZATION CRITERIA

DRUG CLASS	**ISOTRETINOINS (ALL ORAL)**
BRAND NAME* **(generic)**	**ABSORICA, ABSORICA LD (isotretinoin)** **ACCUTANE (isotretinoin)** **AMNESTEEM (isotretinoin)** **CLARAVIS (isotretinoin)** **MYORISAN (isotretinoin)** **ZENATANE (isotretinoin)**
Status: CVS Caremark Criteria	
Type: Initial Prior Authorization	***Ref # 118-A***

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Absorica, Absorica LD

Absorica and Absorica LD are indicated for the treatment of severe recalcitrant nodular acne in non-pregnant patients 12 years of age and older with multiple inflammatory nodules with a diameter of 5 mm or greater. Because of significant adverse reactions associated with its use, Absorica and Absorica LD are reserved for patients with severe nodular acne who are unresponsive to conventional therapy, including systemic antibiotics.

Limitations of Use:

If a second course of Absorica/Absorica LD therapy is needed, it is not recommended before a two-month waiting period because the patient's acne may continue to improve following a 15 to 20-week course of therapy.

Accutane, Amnesteem, Claravis, Myorisan, Zenatane

Isotretinoin is indicated for the treatment of severe recalcitrant nodular acne. Nodules are inflammatory lesions with a diameter of 5 mm or greater. The nodules may become suppurative or hemorrhagic. "Severe," by definition, means "many" as opposed to "few or several" nodules. Because of significant adverse effects associated with its use, isotretinoin should be reserved for patients with severe nodular acne who are unresponsive to conventional therapy, including systemic antibiotics. In addition, isotretinoin is indicated only for those female patients who are not pregnant, because isotretinoin can cause severe birth defects.

A single course of therapy for 15 to 20 weeks has been shown to result in complete and prolonged remission of disease in many patients. If a second course of therapy is needed, it should not be initiated until at least 8 weeks after completion of the first course, because experience has shown that patients may continue to improve while off isotretinoin. The optimal interval before retreatment has not been defined for patients who have not completed skeletal growth.

Compendial Uses
Acne – refractory[8]
Cutaneous T-Cell Lymphoma (CTCL) (e.g., mycosis fungoides, Sézary syndrome)[7]
Keratosis follicularis (Darier Disease) – severe[8]
Lamellar ichthyosis – severe skin involvement[7]
Neuroblastoma[8]
Pityriasis rubra pilaris[7]
Rosacea – severe refractory[8]
Squamous Cell Cancers – to reduce the development of precancers and skin cancers in high risk patients[8]
Transient acantholytic dermatosis (Grover's Disease) – severe[8]

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has any of the following diagnoses: A) severe recalcitrant nodular acne vulgaris, B) refractory acne vulgaris, C) severe refractory rosacea
  AND
  - The patient has tried and had an inadequate treatment response to any topical acne product AND an oral antibiotic
    [Note: Topical products include salicylic acid, benzoyl peroxide, azelaic acid, adapalene, tretinoin, tazarotene, clindamycin, erythromycin, or metronidazole for rosacea. Oral antibiotics include minocycline, doxycycline, tetracycline, erythromycin, trimethoprim-sulfamethoxazole, trimethoprim, azithromycin.]
    AND
  - Treatment will be limited to 40 weeks (2 courses) or less AND with at least 8 weeks between each course

OR

- The patient has any of the following diagnoses: A) neuroblastoma, B) cutaneous T-cell lymphoma (CTCL) (e.g., mycosis fungoides, Sézary syndrome), C) is at high risk for developing skin cancer (squamous cell cancers), D) transient acantholytic dermatosis (Grover's Disease), E) keratosis follicularis (Darier Disease), F) lamellar ichthyosis, G) pityriasis rubra pilaris

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Isotretinoin is indicated for the treatment of severe recalcitrant nodular acne. Nodules are inflammatory lesions with a diameter of 5 mm or greater. The nodules may become suppurative or hemorrhagic. "Severe," by definition, means "many" as opposed to "few or several" nodules. Because of significant adverse effects associated with its use, isotretinoin should be reserved for patients with severe nodular acne who are unresponsive to conventional therapy, including systemic antibiotics. In addition, isotretinoin is indicated only for those female patients who are not pregnant, because isotretinoin can cause severe birth defects.[1-6]

A single course of therapy for 15 to 20 weeks has been shown to result in complete and prolonged remission of disease in many patients. If a second course of therapy is needed, it should not be initiated until at least 8 weeks after completion of the first course, because experience has shown that patients may continue to improve while off isotretinoin. The optimal interval before retreatment has not been defined for patients who have not completed skeletal growth. Long-term use of isotretinoin even in low doses, has not been studied, and is not recommended. It is important that isotretinoin be given at the recommended doses for no longer than the recommended duration. The effect of long-term use of isotretinoin on bone loss is unknown.[1-6]

Patients with acne vulgaris may be treated with antibacterial, comedolytic, retinoid, or antibiotic topical products (e.g., salicylic acid, benzoyl peroxide, azelaic acid, adapalene, tretinoin, tazarotene, clindamycin, erythromycin).[9] Combinations of products, if compatible, may be used when monotherapy is inadequate. Systemic antibiotics are a standard of care in

the management of moderate and severe acne and treatment-resistant forms of inflammatory acne. There is evidence to support the use of tetracycline, doxycycline, minocycline, erythromycin, trimethoprim-sulfamethoxazole, trimethoprim, and azithromycin.[9] For patients with severe inflammatory acne that does not improve with other medications, isotretinoin may be prescribed.[1-9] The compendia state that isotretinoin is effective in treating acne, however, should be reserved for patients who are unresponsive to conventional acne therapies, including oral and/or topical anti-infectives.[7,8]

The National Cancer Institute states that patients with neuroblastoma categorized as high risk are generally treated with dose-intensive multiagent chemotherapy, resection of the primary tumor, followed by myeloablative chemotherapy and autologous stem cell transplantation. Radiation of residual tumor and original sites of metastases is often performed. After recovery, patients are treated with oral isotretinoin for 6 months. Both myeloablative chemotherapy and isotretinoin improve outcomes in patients categorized as high risk.[7,8,13]

The National Comprehensive Cancer Network (NCCN) guidelines state that certain patient groups are at high risk for developing multiple squamous cell skin cancers and tumors that can behave aggressively. These include organ transplant recipients, other settings of immunosuppression (e.g., lymphoma, drug-induced, HIV), and patients with xeroderma pigmentosum. Use of oral retinoids (acitretin, isotretinoin) has been effective in reducing the development of actinic keratoses and cutaneous squamous cell cancer (CSCC) in some high-risk patients. Side effects may be significant. Therapeutic effects disappear shortly after cessation of the drug.[7,8,14]

Isotretinoin has also produced partial and complete responses in some patients with advanced cutaneous T-cell lymphomas, including mycosis fungoides and Sézary syndrome.[7] The NCCN guidelines also state that retinoic-acid receptor (RAT) agonists such as all-trans retinoic acid (ATRA), acitretin, and isotretinoin (13-cis retinoic acid) have been shown to be effect for the treatment of early-stage mycosis fungoides.[15]

According to Micromedex, based on the results of several studies, isotretinoin is highly effective in the treatment of severe, refractory rosacea at doses of 0.05 to 2 mg/kg/day. Good-to-excellent results were reported in 83% to 100% of patients receiving isotretinoin, after approximately 2 to 6 months of treatment. The papulopustular lesions in particular cleared promptly. A dose of 0.5 mg/kg/day is the preferred dosage in rosacea patients, since the incidence of adverse effects increases with increasing dose.[8] Oral and topical products are FDA-approved for rosacea, while isotretinoins are not. In addition, the Consensus Recommendations From the American Acne & Rosacea Society on the Management of Rosacea, Part 3: A Status Report on Systemic Therapies state that isotretinoin is an option to consider in selected cases of refractory papulopustular rosacea and early rhinophyma, though prolonged remissions are not likely after the drug is stopped. The recommendations also favor oral antibiotics over isotretinoin as the initial systemic therapy.[12]

For transient acantholytic dermatosis (Grover's Disease), treatment is usually based on a person's symptoms. Initial treatment options include topical steroids, topical antihistamines, or topical selenium sulfide. For more severe cases, tetracycline has been reported to be effective and the use of oral retinoids (acitretin or isotretinoin) has been reported. More troubling eruptions usually clear up after taking isotretinoin or tetracycline for one to three months.[8,16-18]

For keratosis follicularis (Darier Disease), moisturizers with urea or lactic acid can help reduce scaling and thickening of the lesions. Low to medium potency topical steroids are sometimes useful for reducing inflammation and when bacterial growth is suspected, application of antiseptics can be helpful. Topical retinoids have been shown to be effective in reducing the localized symptoms of this disease in 3 months. The most effective medical treatment for severe cases has been the use oral retinoids such as acitretin and isotretinoin.[7,8,19,20]

For lamellar ichthyosis, petrolatum-based creams and ointments are used to keep the skin soft. As affected children become older, keratolytic agents such as alpha-hydroxy acid or urea preparations may be used to promote peeling and thinning of the stratum corneum. For individuals with ectropion, lubrication of the cornea with artificial tears or prescription ointments is helpful in preventing drying out of the cornea. Oral retinoid therapy such as acitretin or isotretinoin may be recommended for those with severe skin involvement.[7,8,21]

Management of pityriasis rubra pilaris (PRP) often involves systemic and topical therapies combined. Topical therapies can help with the symptoms and may be enough for people with mild PRP. Topical treatments used for PRP may include topical corticosteroids, keratolytics, tar, calcipotriol, topical tretinoin, and tazarotene. Topical treatments are usually combined with systemic therapy for PRP that affects a large part of the body. Oral retinoids (synthetic vitamin A derivatives) are usually preferred as a first-line systemic treatment. Methotrexate may be an alternative option for people

who should not use systemic retinoids, or who don't respond to systemic retinoid therapy. For people who don't respond well to retinoid or methotrexate therapy, options may include biologic TNF-alpha inhibitors, azathioprine, cyclosporine, and/or phototherapy.[7,8,22,23]

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Written by:	UM Development (LS)
Date Written:	02/1995
Revised:	(LS) 12/1998, 08/1999, 05/1999, 01/2001, 08/2001, 3/2002; (JG) 09/2002 (labeling change); (MG) 02/2003, 03/2004; (MC) 10/2005; (MG) 09/2006; (CT) 08/2007; (MS) 08/2008, 9/2009, 08/2010 (new non-Medicare version), 02/2011; (CY) 07/2011 (changes for compendia uses), 07/2012 (added Myorisan), 08/2012 (added Absorica), 04/2013 (added Zenatane); (TM) 06/2013; (MS) 06/2014, 03/2015 (non-clinical update to Q3),(LN) 04/2015 (added denial reasons); (RP) 06/2015; (CT) 05/2016 (revised per CMS response); (MS) 06/2016 (no clinical changes), (SE) 06/2016 (created separate Med D); RP 06/2017 (Non-clinical changes to questions); (KC) 06/2018, 06/2019 (removed MDC-1 from title, no clinical changes), 12/2019 (added Absorica LD), 07/2020 (no clinical changes); (DS) 06/2021 (added Accutane), 07/2021 (no clinical changes); (RZ) 07/2022 (no clinical changes)

Reviewed: CRC 12/1998, 8/1999, 02/2001, 09/10/2001, 04/2002, 02/2003, 03/2004; (MM) 10/2005, 09/2006; (WF) 08/2007, 08/2008; (DL) 09/2009; (KP) 08/2010, 03/2011, 08/2011; (LB) 07/2012; (LS) 08/2012; (KP) 04/2013, (SS) 06/2013; (LB) 06/2014; (MCM) 06/2015; (DHR) 05/2016; (ME) 06/2017; (DNC) 06/2018; (CHART) 01/02/20, 07/30/20, 08/05/2021, 07/28/2022
External Review: 05/2002, 04/2003, 04/2004, 12/2005, 12/2006, 02/2008, 04/2009, 12/2009, 02/2011, 02/2012, 12/2012, 10/2013, 10/2014, 10/2015, 10/2016, 10/2017, 10/2018, 10/2019, 02/2020 (FYI), 10/2020, 10/2021, 10/2022

CRITERIA FOR APPROVAL

1	Does the patient have any of the following diagnoses: A) severe recalcitrant nodular acne vulgaris, B) refractory acne vulgaris, C) severe refractory rosacea? [If yes, go to 2. If no, go to 4.]	Yes	No
2	Has the patient tried and had an inadequate treatment response to any topical acne product AND an oral antibiotic? [If yes, go to 3. If no, then no further questions.] Note: Topical products include salicylic acid, benzoyl peroxide, azelaic acid, adapalene, tretinoin, tazarotene, clindamycin, erythromycin, or metronidazole for rosacea. Oral antibiotics include minocycline, doxycycline, tetracycline, erythromycin, trimethoprim-sulfamethoxazole, trimethoprim, azithromycin.	Yes	No
3	Will treatment be limited to 40 weeks (2 courses) or less AND with at least 8 weeks between each course? [No further questions]	Yes	No
4	Does the patient have any of the following diagnoses: A) neuroblastoma, B) cutaneous T-cell lymphoma (CTCL) (e.g., mycosis fungoides, Sezary syndrome), C) is at high risk for developing skin cancer (squamous cell cancers), D) transient acantholytic dermatosis (Grover's Disease), E) keratosis follicularis (Darier Disease), F) lamellar ichthyosis, G) pityriasis rubra pilaris? [No further questions]	Yes	No

Mapping Instructions			
	Yes	**No**	**DENIAL REASONS**
1.	Go to 2	Go to 4	
2.	Go to 3	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you meet all of these conditions: - You tried another topical acne product first, which did not work for you - You tried an oral antibiotic first, which did not work for you Your request has been denied based on the information we have. [Short Description: No trial of topical acne products and oral antibiotics]
3.	Approve, 12 Months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you meet all of the following conditions: - You will not use it for more than 40 weeks (2 treatment courses) - You will take an 8-week break between treatment courses Your request has been denied based on the information we have. [Short Description: Over max duration of use]

4.	Approve, 12 Months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you meet any of these conditions: - You have severe recalcitrant nodular acne vulgaris - You have refractory acne vulgaris - You have severe refractory rosacea - You have neuroblastoma - You have cutaneous T-cell lymphoma - You are at high risk for developing skin cancer - You have transient acantholytic dermatosis (Grover's Disease) - You have keratosis follicularis (Darier Disease) - You have lamellar ichthyosis - You have pityriasis rubra pilaris Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]

Reference number(s)
3667-A

SPECIALTY GUIDELINE MANAGEMENT

ISTURISA (osilodrostat)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Isturisa is indicated for the treatment of adult patients with Cushing's disease for whom pituitary surgery is not an option or has not been curative.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Cushing's disease
Submission of the following information is necessary to initiate the prior authorization review:

A. For initial requests, pretreatment cortisol level as measured by one of the following tests:
   1. Urinary free cortisol (UFC)
   2. Late-night salivary cortisol (LNSC)
   3. 1 mg overnight dexamethasone suppression test (DST)
   4. Longer, low dose DST (2 mg per day for 48 hours)

B. For continuation of therapy requests (if applicable), laboratory report indicating current cortisol level has decreased from baseline as measured by one of the following tests:
   1. Urinary free cortisol (UFC)
   2. Late-night salivary cortisol (LNSC)
   3. 1 mg overnight dexamethasone suppression test (DST)
   4. Longer, low dose DST (2 mg per day for 48 hours)

III. CRITERIA FOR INITIAL APPROVAL

Cushing's disease
Authorization of 6 months may be granted for treatment of Cushing's disease in members who either have had surgery that was not curative OR for members who are not candidates for surgery.

IV. CONTINUATION OF THERAPY

Cushing's disease

Authorization of 12 months may be granted for members that meet one of the following criteria:

A. Lower cortisol levels since the start of therapy per one of the following tests:
   1. Urinary free cortisol (UFC)
   2. Late-night salivary cortisol (LNSC)
   3. 1 mg overnight dexamethasone suppression test (DST)
   4. Longer, low dose DST (2 mg per day for 48 hours)

B. Improvement in signs and symptoms of the disease

V. REFERENCES

1. Isturisa [package insert]. Lebanon, NJ: Recordati Rare Disease, Inc.; March 2020.
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PRIOR AUTHORIZATION CRITERIA

BRAND NAME
(generic)

SPORANOX ORAL CAPSULES
(itraconazole)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

POLICY

FDA-APPROVED INDICATIONS
Sporanox (itraconazole) Capsules are indicated for the treatment of the following fungal infections in immunocompromised and non-immunocompromised patients:
1. Blastomycosis, pulmonary and extrapulmonary
2. Histoplasmosis, including chronic cavitary pulmonary disease and disseminated, non-meningeal histoplasmosis, and
3. Aspergillosis, pulmonary and extrapulmonary, in patients who are intolerant of or who are refractory to amphotericin B therapy.

Specimens for fungal cultures and other relevant laboratory studies (wet mount, histopathology, serology) should be obtained before therapy to isolate and identify causative organisms. Therapy may be instituted before the results of the cultures and other laboratory studies are known; however, once these results become available, antiinfective therapy should be adjusted accordingly.

Sporanox Capsules are also indicated for the treatment of the following fungal infections in non-immunocompromised patients:
1. Onychomycosis of the toenail, with or without fingernail involvement, due to dermatophytes (tinea unguium), and
2. Onychomycosis of the fingernail due to dermatophytes (tinea unguium).

Prior to initiating treatment, appropriate nail specimens for laboratory testing (KOH preparation, fungal culture, or nail biopsy) should be obtained to confirm the diagnosis of onychomycosis.

Compendial Uses
Coccidioidomycosis[2,3]
Coccidioidomycosis prophylaxis in HIV infection[2,3]
Cryptococcosis[2,3]
Histoplasmosis prophylaxis in HIV infection[2,3]
Invasive fungal infection prophylaxis in liver transplant patients[3]
Invasive fungal infection prophylaxis in patients with hematologic malignancies[3]
Invasive fungal infection prophylaxis in patients with chronic granulomatous disease[3]
Microsporidiosis[2]
Talaromycosis (formerly Penicilliosis)[2]
Pityriasis versicolor/Tinea versicolor[3]
Sporotrichosis[2,3]
Tinea corporis, Tinea cruris, Tinea capitis, Tinea manuum, Tinea pedis[3]
Primary Therapy for Allergic Bronchopulmonary Aspergillosis, in combination with systemic corticosteroids[2,3,4]
Primary Therapy for Chronic Cavitary Pulmonary Aspergillosis[2,3,4]

COVERAGE CRITERIA
The requested drug will be covered with prior authorization when the following criteria are met:
- The requested drug is not being used in a footbath
  AND

- The requested drug is being prescribed for any of the following: A) Pityriasis versicolor, B) Tinea versicolor, C) Onychomycosis due to dermatophytes (Tinea unguium) confirmed by a fungal diagnostic test (e.g., potassium hydroxide [KOH] preparation, fungal culture, or nail biopsy)

OR

- The requested drug is being prescribed for any of the following: A) Disseminated histoplasmosis, B) Central nervous system (CNS) histoplasmosis, C) Histoplasmosis prophylaxis in HIV infection, D) Coccidioidomycosis prophylaxis in HIV infection, E) Invasive fungal infection prophylaxis in a patient with chronic granulomatous disease, F) Primary therapy for chronic cavitary pulmonary aspergillosis

OR

- The requested drug is being prescribed for any of the following: A) Blastomycosis, B) Histoplasmosis, C) Primary therapy for allergic bronchopulmonary aspergillosis, in combination with systemic corticosteroids, D) Aspergillosis in a patient intolerant of or refractory to amphotericin B therapy, E) Coccidioidomycosis, F) Cryptococcosis, G) Sporotrichosis, H) Talaromycosis (formerly Penicilliosis), I) Microsporidiosis, J) Invasive fungal infection prophylaxis in a liver transplant patient, K) Invasive fungal infection prophylaxis in a patient with a hematologic malignancy

OR

- The requested drug is being prescribed for any of the following: A) Tinea corporis, B) Tinea cruris, C) Tinea capitis, D) Tinea manuum, E) Tinea pedis

  AND

  - The patient experienced an inadequate treatment response, intolerance, or has a contraindication to any of the following: A) fluconazole, B) griseofulvin, C) terbinafine

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PRIOR AUTHORIZATION CRITERIA

BRAND NAME
(generic)

SPORANOX ORAL SOLUTION
(itraconazole)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

POLICY

FDA-APPROVED INDICATIONS
Sporanox (itraconazole) Oral Solution is indicated for the treatment of oropharyngeal and esophageal candidiasis.

COVERAGE CRITERIA
The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for the treatment of oropharyngeal candidiasis or esophageal candidiasis
  AND
  - The patient has experienced an inadequate treatment response to fluconazole
  OR
  - The patient has experienced an intolerance to fluconazole
  OR
  - The patient has a contraindication that would prohibit a trial of fluconazole

REFERENCES

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PRIOR AUTHORIZATION CRITERIA

BRAND NAME
(generic)

STROMECTOL
(ivermectin)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization with Quantity Limit

POLICY

FDA-APPROVED INDICATIONS

Stromectol is indicated for the treatment of the following infections:

- Strongyloidiasis of the intestinal tract. Stromectol is indicated for the treatment of intestinal (i.e., non-disseminated) strongyloidiasis due to the nematode parasite *Strongyloides stercoralis*.
- Onchocerciasis. Stromectol is indicated for the treatment of onchocerciasis due to the nematode parasite *Onchocerca volvulus*.

Stromectol has no activity against adult *Onchocerca volvulus* parasites. The adult parasites reside in subcutaneous nodules which are infrequently palpable. Surgical excision of these nodules (nodulectomy) may be considered in the management of patients with onchocerciasis, since this procedure will eliminate the microfilariae-producing adult parasites.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is NOT being prescribed for the prevention or treatment of coronavirus disease 2019 (COVID-19)

Quantity Limits apply.
9 tablets/75 days*
**The duration of 75 days is used for a 90-day fill period.*

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Reference number
1999-A

SPECIALTY GUIDELINE MANAGEMENT

JAKAFI (ruxolitinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
1. Jakafi is indicated for treatment of intermediate or high-risk myelofibrosis (MF), including primary MF, post-polycythemia vera MF and post-essential thrombocythemia MF in adults.
2. Jakafi is indicated for treatment of polycythemia vera (PV) in adults who have had an inadequate response to or are intolerant of hydroxyurea.
3. Jakafi is indicated for treatment of steroid-refractory acute graft-versus-host disease (aGVHD) in adult and pediatric patients 12 years and older.
4. Jakafi is indicated for treatment of chronic graft-versus-host disease (cGVHD) after failure of one or two lines of systemic therapy in adult and pediatric patients 12 years and older.

B. Compendial Uses
1. Symptomatic lower risk myelofibrosis
2. Accelerated phase or blast phase myelofibrosis/acute myeloid leukemia
3. Polycythemia vera in patients with inadequate response or loss of response to interferon therapy
4. Philadelphia chromosome (Ph-like) B-cell Acute Lymphoblastic Leukemia (ALL)/Lymphoblastic lymphoma (LL)
5. Acute and Chronic GVHD
6. Chronic myelomonocytic leukemia (CMML)-2
7. BCR-ABL negative atypical chronic myeloid leukemia (aCML)
8. Essential Thrombocythemia
9. Myeloid/lymphoid neoplasms with eosinophilia and JAK2 rearrangement in chronic phase
10. Myeloid, lymphoid, or mixed lineage neoplasms with eosinophilia and JAK2 rearrangement in blast phase
11. CAR T-cell-related toxicities - Cytokine release syndrome (CRS)

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
A. For Ph-like B-cell acute lymphoblastic leukemia/lymphoblastic lymphoma (LL), medical record documentation confirming either a cytokine receptor-like factor 2 (CRLF2) mutation or a mutation associated with activation of the Janus kinase/signal transducers and activators of transcription (JAK/STAT) pathway.
B. For myeloid and/or lymphoid neoplasms with eosinophilia: Testing or analysis confirming JAK2 rearrangement

III. CRITERIA FOR INITIAL APPROVAL

A. Myelofibrosis/Acute Myeloid Leukemia
Authorization of 12 months may be granted for the treatment of myelofibrosis/acute myeloid leukemia.

B. Polycythemia Vera
Authorization of 12 months may be granted for the treatment of polycythemia vera in members who have had an inadequate response or intolerance to hydroxyurea or peginterferon alfa-2a.

C. Acute Graft-versus-Host Disease (aGVHD) or Chronic Graft-versus-Host Disease (cGVHD)
Authorization of 12 months may be granted for the treatment of graft-vs-host disease when any of the following criteria are met:
1. Member has steroid-refractory acute GVHD
2. Member has chronic GVHD and has failed at least one prior line of systemic therapy

D. Acute Lymphoblastic Leukemia (ALL)/Lymphoblastic Lymphoma (LL)
Authorization of 12 months may be granted for the treatment of Ph-like B-cell acute lymphoblastic leukemia/lymphoblastic lymphoma for members with either a cytokine receptor-like factor 2 (CRLF2) mutation or a mutation associated with activation of the Janus kinase/signal transducers and activators of transcription (JAK/STAT) pathway.

E. Chronic Myelomonocytic Leukemia (CMML)-2
Authorization of 12 months may be granted for the treatment of chronic myelomonocytic leukemia (CMML)-2 in combination with a hypomethylating agent.

F. Atypical Chronic Myeloid Leukemia (aCML)
Authorization of 12 months may be granted for the treatment of BCR-ABL negative atypical chronic myeloid leukemia (aCML) as a single agent or in combination with a hypomethylating agent.

G. Essential Thrombocythemia
Authorization of 12 months may be granted for the treatment of essential thrombocythemia in members who have had an inadequate response or intolerance to hydroxyurea, peginterferon alfa-2a, or anagrelide.

H. Myeloid/Lymphoid Neoplasms with Eosinophilia
Authorization of 12 months may be granted for the treatment of myeloid and/or lymphoid neoplasms with eosinophilia and JAK2 rearrangement in the chronic phase or blast phase.

I. Cytokine Release Syndrome
Authorization of 1 month may be granted for treatment of chimeric antigen receptor (CAR) T-cell-induced cytokine release syndrome that is refractory to high-dose corticosteroids and anti-IL-6 therapy.

IV. CONTINUATION OF THERAPY

A. Myelofibrosis/Acute Myeloid Leukemia, Polycythemia Vera, Acute GVHD, Chronic GVHD, and Essential Thrombocythemia
Authorization of 12 months may be granted for continued treatment in members requesting reauthorization who have improvement in symptoms and no unacceptable toxicity.

B. Acute Lymphoblastic Leukemia (ALL)/Lymphoblastic Lymphoma (LL), Atypical Chronic Myeloid Leukemia (aCML), Chronic Myelomonocytic Leukemia (CMML)-2, and Myeloid/Lymphoid Neoplasms with Eosinophilia
Authorization of 12 months may be granted for continued treatment in members requesting reauthorization when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

C. Cytokine Release Syndrome
All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

V. REFERENCES

1. Jakafi [package insert]. Wilmington, DE: Incyte Corporation; September 2021.
2. The NCCN Drugs & Biologics Compendium® © 2022 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed January 7, 2022.
3. Zeiser R, Burchert A, Lengerke C, et al: Ruxolitinib in corticosteroid-refractory graft-versus-host disease after allogeneic stem cell transplantation: a multicenter survey. Leukemia 2015; 29(10):2062-2068.
4. Zeiser R, Burchert A, Lengerke C, et al: Long-term follow-up of patients with corticosteroid-refractory graft-versus-host disease treated with ruxolitinib. Blood 2016; 128(22):4561
5. Raetz Elizabeth, Loh Mignon. A Phase 2 Study of the JAK1/JAK2 Inhibitor Ruxolitinib with Chemotherapy in Children with De Novo High-Risk CRLF2-Rearranged and/or JAK Pathway-Mutant Acute Lymphoblastic Leukemia. *American Society of Hematology.* 2016: 13(3).
6. Ding YY, Stern JW, Jubelirer TF, et al. Clinical efficacy of Ruxolitinib and chemotherapy in a child with Philadelphia chromosome-like acute lymphoblastic leukemia with GOLGAS-JAK2 fusion and induction failure. *Haematologica.* 2018 Sep;103(9):e427-e431. doi: 10.3324/haematol.2018.192088. Epub 2018 May 17.
7. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Pediatric Acute Lymphoblastic Leukemia. Available at: http://www.nccn.org. Version 1.2022. https://www.nccn.org/professionals/physician_gls/pdf/ped_all.pdf. Accessed July 8, 2020.

Reference number(s)
5767-A

SPECIALTY GUIDELINE MANAGEMENT

JAYPIRCA (pirtobrutinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication
Relapsed or Refractory Mantle Cell Lymphoma (MCL)
Jaypirca is indicated for the treatment of adult patients with relapsed or refractory mantle cell lymphoma (MCL) after at least two lines of systemic therapy, including a Bruton tyrosine kinase (BTK) inhibitor.

B. Compendial Use
Chronic Lymphocytic Leukemia (CLL)/Small Lymphocytic Lymphoma (SLL)

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Mantle Cell Lymphoma (MCL)
Authorization of 12 months may be granted for treatment of relapsed or refractory MCL when the member has tried at least two lines of prior systemic therapy, including a BTK inhibitor.

B. Chronic Lymphocytic Leukemia (CLL)/Small Lymphocytic Lymphoma (SLL)
Authorization of 12 months may be granted as a single agent for treatment of relapsed or refractory CLL/SLL when the member has previously tried BTK inhibitor and venetoclax based regimens, or when member has had resistance or intolerance to prior covalent BTK inhibitor therapy (e.g., acalabrutinib, zanubrutinib).

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

IV. REFERENCES

1. Jaypirca [package insert]. Indianapolis, IN: Eli Lilly and Company; January 2023.
2. The NCCN Drugs & Biologics Compendium® © 2023 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed June 13, 2023.

QUANTITY LIMIT PRIOR AUTHORIZATION CRITERIA

BRAND NAME*
(generic)

JUBLIA
(efinaconazole topical solution)

Status: CVS Caremark Criteria
Type: Quantity Limit; Post Limit Prior Authorization ***Ref # 2906-HJ***

**Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS
Jublia (efinaconazole) topical solution, 10% is an azole antifungal indicated for the topical treatment of onychomycosis of the toenail(s) due to Trichophyton rubrum and Trichophyton mentagrophytes.

INITIAL QUANTITY LIMIT**

LIMIT CRITERIA

Drug	1 Month Limit*	3 Month Limit*
Jublia	4 mL / 21 days	12 mL / 63 days

**The duration of 21 days is used for a 28-day fill period and 63 days is used for an 84-day fill period to allow time for refill processing.*

**If the patient is requesting more than the initial quantity limit, the claim will reject with a message indicating that a prior authorization is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

COVERAGE CRITERIA
The requested drug will be covered with prior authorization when the following criteria is met:

- The requested drug is being prescribed for onychomycosis of the toenail(s) due to Trichophyton rubrum or Trichophyton mentagrophytes

AND

- The patient's diagnosis has been confirmed with a fungal diagnostic test (e.g., potassium hydroxide [KOH] preparation, fungal culture, or nail biopsy)

AND

- Multiple toenails are being treated

AND

- The requested drug is not being used in a footbath

Quantity Limits apply.

RATIONALE
The initial quantity limit is set at 4 mL per month.

If the patient is requesting more than the initial quantity limit, the claim will reject with a message indicating that a prior authorization is required.

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Jublia (efinaconazole) topical solution, 10% is an azole antifungal indicated for the topical treatment of onychomycosis of the toenail(s) due to Trichophyton rubrum and Trichophyton mentagrophytes.[1-3]

The prior authorization criteria do not approve Jublia for use in a footbath, as this is not an FDA-approved use. Jublia is for topical use only and not for oral, ophthalmic, or intravaginal use.[1]

Jublia is available as a solution supplied in 4 mL and 8 mL bottles.[1] Jublia is to be applied to affected toenails once daily for 48 weeks, using the integrated flow-through brush applicator. When applying Jublia, the toenail, the toenail folds, toenail bed, hyponychium, and the undersurface of the toenail plate are to be completely covered. Apply one drop of Jublia onto the toenail. For the big toenail, also apply a second drop to the end of the toenail using the tip of the brush.[1]

While not published by manufacturer, judging from patient use, there are approximately 80 drops in a 4 mL bottle.[4] Therefore, if the patient has an infection that requires less than or equal to 3 drops per day, then the initial limit of 4 mL is approximately sufficient for a 28 day period. For example: A patient with an infection of one big toenail and one other toenail requires:

- 2 drops to the big toenail daily = 2 drops X 28 days = 56 drops per 28 days
- 1 drop to any other toenail daily = 1 drop X 28 days = 28 drops per 28 days

For a total of approximately 84 drops per 28 days.

If the patient has an affected area that requires more than 3 drops per day, then the post-limit PA criteria will apply.

Onychomycosis may be diagnosed by the presence of fungi by culture, microscopy (Potassium hydroxide [KOH] stain), or histological examination of the nail plate.[5] Microscopy is a commonly used method because it is inexpensive and easy to perform; nail clippings or scrapings are placed in a drop of KOH and examined under a microscope for the presence of fungal elements.[6]

The post-limit PA allows for additional quantities if the patient requires treatment of onychomycosis affecting multiple toenails. The post-limit PA allows for a quantity approximately sufficient to treat an infection of all toenails. The quantity allowed upon approval of post-limit PA is approximately sufficient to allow treatment of two big toenails daily (112 drops, or 5.6 mL, per 28 days) and eight other toenails daily (224 drops, or 11.2 mL, per 28 days). Therefore, the post-limit quantity will be set at 16 mL per 28 days.

REFERENCES

1. Jublia [package insert]. Bridgewater, NJ: Bausch Health US LLC; July 2020.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2021; Accessed July 29, 2021.
3. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed July 29, 2021.
4. Lipner SR, Scher RK. Efinaconazole in the treatment of onychomycosis. *Infect Drug Resist*. 2015;8:163–172.
5. Kreijkamp-Kaspers S, Hawke K, Guo L, et al. Oral antifungal medication for toenail onychomycosis. Cochrane Database of Systematic Reviews 2017, Issue 7. Art. No.: CD010031.
6. Centers for Disease Control (CDC) and Prevention. Fungal Nail infections. https://www.cdc.gov/fungal/nail-infections.html. Accessed August 5, 2021.

Written by:	UM Development (ME)
Date Written:	03/2019
Revised:	(PM) 02/2020; (KC) 12/2020 (added footbath question); (PM) 09/2021 (no clinical changes)
Reviewed:	Medical Affairs: (GAD) 04/2019; (CHART) 02/27/20, 12/31/20, 09/30/21 External Review: 06/2019, 06/2020, 04/2021, 12/2021

CRITERIA FOR APPROVAL

1	Is the requested drug being prescribed for onychomycosis of the toenail(s) due to Trichophyton rubrum or Trichophyton mentagrophytes? [If no, then no further questions.]	Yes	No
2	Has the patient's diagnosis been confirmed with a fungal diagnostic test (e.g., potassium hydroxide [KOH] preparation, fungal culture, or nail biopsy)? [If no, then no further questions.]	Yes	No

3	Are multiple toenails being treated? [If no, then no further questions.]	Yes	No
4	Is the requested drug being used in a footbath? [If yes, then no further questions.]	Yes	No
5	Does the patient require MORE than the plan allowance of 16 mL per month? [RPh Note: If yes, then deny and enter a partial approval for 16 mL / 21 days or 48 mL / 63 days]	Yes	No

Mapping Instructions			
	Yes	**No**	**DENIAL REASONS – DO NOT USE FOR MEDICARE PART D**
1.	Go to 2	Deny	You do not meet the requirements of your plan. Your plan covers additional quantities of this drug when you have a specific fungal infection of the toenail(s). Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]
2.	Go to 3	Deny	You do not meet the requirements of your plan. Your plan covers additional quantities of this drug when you meet all of these conditions: - You have a specific fungal infection of the toenail(s) - You had a test to confirm your toenail fungal infection Your request has been denied based on the information we have. [Short Description: No confirmation of diagnosis]
3.	Go to 4	Deny	You do not meet the requirements of your plan. Your plan covers additional quantities of this drug when multiple toenails are being treated. Your request has been denied based on the information we have. [Short Description: Not enough area affected]
4.	Deny	Go to 5	You do not meet the requirements of your plan. Your plan covers additional quantities of this drug when it is not being used in a footbath. Your request has been denied based on the information we have. [Short Description: Used in footbath]
5.	Deny	Approve, 12 months, 16 mL/21 days* or 48 mL/63 days*	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 16 mL per month of the requested drug and strength. Your request has been partially approved. You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity]

**The duration of 21 days is used for a 28-day fill period and 63 days is used for an 84-day fill period to allow time for refill processing.*

PRIOR AUTHORIZATION CRITERIA

BRAND NAME*
(generic)

JUBLIA
(efinaconazole topical solution)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization with Quantity Limit ***Ref # 1160-C***

**Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Jublia (efinaconazole) topical solution, 10% is an azole antifungal indicated for the topical treatment of onychomycosis of the toenail(s) due to Trichophyton rubrum and Trichophyton mentagrophytes.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for onychomycosis of the toenail(s) due to Trichophyton rubrum or Trichophyton mentagrophytes

AND

- The patient's diagnosis has been confirmed with a fungal diagnostic test (e.g., potassium hydroxide [KOH] preparation, fungal culture, or nail biopsy)

AND

- The patient has experienced an inadequate treatment response to an oral antifungal therapy (e.g., terbinafine, itraconazole)

OR

- The patient has experienced an intolerance to an oral antifungal therapy (e.g., terbinafine, itraconazole)

OR

- The patient has a contraindication that would prohibit a trial of an oral antifungal therapy (e.g., terbinafine, itraconazole)

AND

- The requested drug is not being used in a footbath

AND

- If additional quantities are required, multiple toenails are being treated

Quantity Limits Apply.

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Jublia (efinaconazole) topical solution, 10% is an azole antifungal indicated for the topical treatment of onychomycosis of the toenail(s) due to Trichophyton rubrum and Trichophyton mentagrophytes.[1-3]

Onychomycosis may be diagnosed by the presence of fungi by culture, microscopy (Potassium hydroxide [KOH] stain), or histological examination of the nail plate.[5] Microscopy is a commonly used method because it is inexpensive and easy to perform; nail clippings or scrapings are placed in a drop of KOH and examined under a microscope for the presence of fungal elements.[6]

Per the CDC, oral antifungal therapy (terbinafine) is considered first line treatment for confirmed onychomycosis.[6] According to the Cochrane review, medication taken orally appears to cure the condition more quickly and effectively than topical treatment. There was high-quality evidence that oral azole (itraconazole) and terbinafine treatments were more effective for achieving mycological cure and clinical cure for onychomycosis compared to placebo, and when compared directly, terbinafine was probably more effective than azoles and likely not associated with excess adverse events (griseofulvin was associated with more adverse reactions than azoles and terbinafine).[5] Oral treatment of onychomycosis is the standard of care, however, drug interactions and risk of acute liver injury can limit their use.[4] Difficulties in formulating topical treatment to penetrate the nail and reach the site of infection in the nail bed has hampered the development and the use of topical agents.[4] Jublia is the first triazole antifungal developed for the treatment of onychomycosis. In 2 randomized trials, complete cure rate, defined as no evidence of fungal infection at week 52, was demonstrated in 15.2% to 17.8% of patients receiving efinaconazole (N=1236) compared with 3.3% to 5.5% receiving placebo (N=415) for the treatment of onychomycosis of the toenail. Jublia provided an effective and well-tolerated treatment and may be the first topical treatment that can be considered a viable alternative to oral treatments.[4]

The prior authorization criteria do not approve Jublia for use in a footbath, as this is not an FDA-approved use. Jublia is for topical use only and not for oral, ophthalmic, or intravaginal use.[1]

Jublia is available as a solution supplied in 4 mL and 8 mL bottles.[1] Jublia is to be applied to affected toenails once daily for 48 weeks, using the integrated flow-through brush applicator. When applying Jublia, the toenail, the toenail folds, toenail bed, hyponychium, and the undersurface of the toenail plate are to be completely covered. Apply one drop of Jublia onto the toenail. For the big toenail, also apply a second drop to the end of the toenail using the tip of the brush.[1]

While not published by manufacturer, judging from patient use, there are approximately 80 drops in a 4 mL bottle.[7] Therefore, if the patient has an infection that requires less than or equal to 3 drops per day, then the initial limit of 4 mL is approximately sufficient for a 28 day period. For example: A patient with an infection of one big toenail and one other toenail requires:

- 2 drops to the big toenail daily = 2 drops X 28 days = 56 drops per 28 days
- 1 drop to any other toenail daily = 1 drop X 28 days = 28 drops per 28 days

For a total of approximately 84 drops per 28 days.

If the patient has an affected area that requires more than 4 mL per month, additional criteria will apply.

The PA allows for additional quantities if the patient requires treatment of onychomycosis affecting multiple toenails. The PA allows for a quantity approximately sufficient to treat an infection of all toenails. The quantity allowed upon approval of PA is approximately sufficient to allow treatment of two big toenails daily (112 drops, or 5.6 mL, per 28 days) and eight other toenails daily (224 drops, or 11.2 mL, per 28 days). Therefore, the quantity for patients requiring treatment of multiple toenails will be set at 16 mL per 28 days.

REFERENCES

1. Jublia [package insert]. Bridgewater, NJ: Bausch Health US LLC; July 2020.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2021; Accessed July 29, 2021.
3. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed July 29, 2021.
4. Elewski BE, Rich P, Pollak R, et al. Efinaconazole 10% solution in the treatment of toenail onychomycosis: Two phase III multicenter randomized, double-blind studies. *J Am Acad Dermatol* 2013;68:600-8.
5. Kreijkamp-Kaspers S, Hawke K, Guo L, et al. Oral antifungal medication for toenail onychomycosis. Cochrane Database of Systematic Reviews 2017, Issue 7. Art. No.: CD010031.
6. Centers for Disease Control (CDC) and Prevention. Fungal Nail infections. https://www.cdc.gov/fungal/nail-infections.html. Accessed August 5, 2021.
7. Lipner SR, Scher RK. Efinaconazole in the treatment of onychomycosis. *Infect Drug Resist*. 2015;8:163–172.

Written by: UM Development (CT)
Date Written: 06/2014

CRITERIA FOR APPROVAL

1	Is the requested drug being prescribed for onychomycosis of the toenail(s) due to Trichophyton rubrum or Trichophyton mentagrophytes? [If no, then no further questions.]	Yes	No
2	Has the patient's diagnosis been confirmed with a fungal diagnostic test (e.g., potassium hydroxide [KOH] preparation, fungal culture, or nail biopsy)? [If no, then no further questions.]	Yes	No
3	Has the patient experienced an inadequate treatment response to an oral antifungal therapy (e.g., terbinafine, itraconazole)? [If yes, then skip to question 6.]	Yes	No
4	Has the patient experienced an intolerance to an oral antifungal therapy (e.g., terbinafine, itraconazole)? [If yes, then skip to question 6.]	Yes	No
5	Does the patient have a contraindication that would prohibit a trial of an oral antifungal therapy (e.g., terbinafine, itraconazole)? [If no, then no further questions.]	Yes	No
6	Is the requested drug being used in a footbath? [If yes, then no further questions.]	Yes	No
7	Does the patient require MORE than the plan allowance of 4 mL per month? [Note: If higher quantities are needed, additional questions are required.] [If no, then no further questions.]	Yes	No
8	Are multiple toenails being treated? [If no, then no further questions.] [RPh Note: If no, then deny and enter a partial approval for 4 mL / 21 days or 12 mL / 63 days.]	Yes	No
9	Does the patient require MORE than the plan allowance of 16 mL per month? [RPh Note: If yes, then deny and enter a partial approval for 16 mL / 21 days or 48 mL / 63 days.]	Yes	No

Mapping Instructions			
	Yes	**No**	**DENIAL REASONS – DO NOT USE FOR MEDICARE PART D**
1.	Go to 2	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have a specific fungal infection of the toenail(s).

CVS caremark

			Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]
2.	Go to 3	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you meet all of these conditions: - You have a specific fungal infection of the toenail(s) - You had a test to confirm your toenail fungal infection Your request has been denied based on the information we have. [Short Description: No confirmation of diagnosis]
3.	Go to 6	Go to 4	
4.	Go to 6	Go to 5	
5.	Go to 6	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have tried an oral antifungal medicine first and it did not work for you or you cannot use it. Your request has been denied based on the information we have. [Short Description: No inadequate response, intolerance, or contraindication to oral antifungals]
6.	Deny	Go to 7	You do not meet the requirements of your plan. Your plan covers this drug when it is not being used in a footbath. Your request has been denied based on the information we have. [Short Description: Used in footbath]
7.	Go to 8	Approve, 12 months, 4 mL/21 days* or 12 mL/63 days*	
8.	Go to 9	Deny	You do not meet the requirements of your plan. Your plan covers additional quantities of this drug when multiple toenails are being treated. Current plan approved criteria cover up to 4 mL per month of the requested drug and strength. Your request has been partially approved. You have been approved for the quantity that your plan covers for a duration of 12 months. Your request for additional quantities has been denied based on the information we have. [Short Description: Not enough area affected]
9.	Deny	Approve, 12 months, 16 mL/21 days* or 48 mL/63 days*	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 16 mL per month of the requested drug and strength. Your request has been partially approved. You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity]

**The duration of 21 days is used for a 28-day fill period and 63 days is used for an 84-day fill period to allow time for refill processing.*

Reference number(s)
2071-A

SPECIALTY GUIDELINE MANAGEMENT

JUXTAPID (lomitapide)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Juxtapid is indicated as an adjunct to a low-fat diet and other lipid-lowering treatments, including LDL apheresis where available, to reduce low-density lipoprotein cholesterol (LDL-C), total cholesterol (TC), apolipoprotein B (APOB), and non-high-density lipoprotein cholesterol (non-HDL-C) in patients with homozygous familial hypercholesterolemia (HoFH).

Limitations of Use:
- The safety and effectiveness of Juxtapid have not been established in patients with hypercholesterolemia who do not have HoFH, including those with heterozygous familial hypercholesterolemia (HeFH).
- The effect of Juxtapid on cardiovascular morbidity and mortality has not been determined.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
A. Current LDL-C level for both initial requests and continuation requests. The level must be dated within the six months preceding the authorization request.
B. Genetic testing or medical records confirming the diagnosis of HoFH.
C. Medical records confirming the member is currently on lipid lowering therapy for both initial requests and continuation requests.

III. CRITERIA FOR INITIAL APPROVAL

Homozygous familial hypercholesterolemia (HoFH)
Authorization of 6 months may be granted for treatment of homozygous familial hypercholesterolemia when all of the following criteria are met:
A. Member has a documented diagnosis of homozygous familial hypercholesterolemia confirmed by any of the following criteria:
   1. Variant in two low-density lipoprotein receptor (LDLR) alleles
   2. Presence of homozygous or compound heterozygous variants in apolipoprotein B (APOB) or proprotein convertase subtilisin-kexin type 9 (PCSK9)
   3. Member has compound heterozygosity or homozygosity for variants in the gene encoding low-density lipoprotein receptor adaptor protein 1 (LDLRAP1)
   4. An untreated LDL-C of greater than 500 mg/dL or treated LDL-C greater than or equal to 300 mg/dL and either of the following:

a. Presence of cutaneous or tendinous xanthomas before the age of 10 years
b. An untreated LDL-C level of greater than or equal to 190 mg/dL in both parents

B. Prior to initiation of treatment with the requested medication, both of the following criteria are/were met:
1. Member is/was receiving a combination lipid-lowering regimen consisting of a high-intensity statin, ezetimibe, and PCSK9 directed therapy unless the member has known LDL-receptor negative mutations in both alleles.
2. Member is/was experiencing an inadequate response to such a combination regimen, as demonstrated by a treated LDL-C of greater than or equal to 100 mg/dL (or greater than or equal to 70 mg/dL with clinical atherosclerotic cardiovascular disease [ASCVD]), unless the member has known LDL-receptor negative mutations in both alleles.

C. Member will continue to receive concomitant lipid-lowering therapy.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members (including new members) who meet all of the following criteria:

A. Member meets all initial authorization criteria
B. Member has had at least 20% reduction of LDL-C from baseline
C. Member is currently receiving concomitant lipid-lowering therapy

V. REFERENCES

1. Juxtapid [package insert]. Cambridge, MA: Aegerion Pharmaceuticals, Inc.; September 2020
2. Nordestgaard BG, Chapman MJ, Humphries SE, et al. Familial hypercholesterolaemia is underdiagnosed and undertreated in the general population: guidance for clinicians to prevent coronary heart disease Consensus Statement of the European Atherosclerosis Society. [published correction appears in Eur Heart J. 2020 Dec 14;41(47):4517] *Eur Heart J* 2013;34(45):3478–90a. doi:10.1093/eurheartj/eht273
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Reference number
2572-A

SPECIALTY GUIDELINE MANAGEMENT

JYNARQUE (tolvaptan)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Jynarque is indicated to slow kidney function decline in adults at risk of rapidly progressing autosomal dominant polycystic kidney disease (ADPKD).

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
A. Imaging used for diagnosis and confirmation of rapidly progressing disease (ultrasonography, magnetic resonance imaging [MRI], computed tomography [CT])
B. Genetic testing results if applicable

III. CRITERIA FOR INITIAL APPROVAL

Authorization of 12 months may be granted for treatment of autosomal dominant polycystic kidney disease (ADPKD) when all of the following criteria are met:
A. The member is 18 years of age or older and with a diagnosis of ADPKD as confirmed by any of the following:
    1. In members aged 18 to less than 40 years with a first degree relative with ADPKD: greater than or equal to 3 cysts (unilateral or bilateral) using any radiologic method[7]
    2. In members aged 40 to less than 60 years with a first degree relative with ADPKD: greater than or equal to 2 cysts per kidney using any radiologic method[7]
    3. In members aged 60 or older with a first degree relative with ADPKD: greater than or equal to 4 cysts per kidney using any radiologic method[7]
    4. In members with no family history (no first degree relative with disease): positive genetic test for ADPKD (mutation in PKD1 or PKD2 gene)[3]
B. The member has or is at risk for rapidly progressing disease as confirmed by height-adjusted total kidney volume compatible with Mayo class 1C, 1D, or 1E disease[5]
C. The member's estimated glomerular filtration rate (eGFR) is greater than or equal to 25 mL/min/1.73m^2.[1,6]

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III when the member has demonstrated a beneficial response to Jynarque

therapy (e.g., slowed kidney function decline, decreased kidney pain) and the member's estimated glomerular filtration rate (eGFR) is greater than or equal to 25 mL/min/1.73m^2.

V. REFERENCES

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Reference number(s)
3878-A

SPECIALTY GUIDELINE MANAGEMENT

TABRECTA (capmatinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Tabrecta is indicated for the treatment of adult patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have a mutation that leads to mesenchymal-epithelial transition (MET) exon 14 skipping as detected by an FDA-approved test.

Compendial Use
Non-small cell lung cancer

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: Documentation of a mutation that leads to mesenchymal-epithelial transition (MET) exon 14 skipping or MET amplification in tumor or plasma specimens.

III. CRITERIA FOR INITIAL APPROVAL

Non-Small Cell Lung Cancer
Authorization of 12 months may be granted for treatment of NSCLC when either of the following criteria are met:
A. The requested medication will be used as a single agent for advanced or metastatic NSCLC (including brain metastases from NSCLC) with MET exon 14 skipping positive tumors.
B. The requested medication will be used for NSCLC with high-level MET amplification.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

V. REFERENCES

1. Tabrecta [package insert]. East Hanover, NJ: Novartis Pharmaceutical Corporation; January 2022.
2. The NCCN Drugs & Biologics Compendium® © 2022 National Comprehensive Cancer Network, Inc. Available at: https://www.nccn.org. Accessed July 19, 2022.

Reference number(s)
1609-A

SPECIALTY GUIDELINE MANAGEMENT

KALBITOR (ecallantide)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Kalbitor is indicated for the treatment of acute attacks of hereditary angioedema (HAE) in patients 12 years of age and older.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
A. For initial authorization, the following should be documented:
   1. C1 inhibitor functional and antigenic protein levels
   2. F12, angiopoietin-1, plasminogen, kininogen-1 (KNG1), heparan sulfate-glucosamine 3-O-sulfotransferase 6 (HS3ST6), or myoferlin (MYOF) gene mutation testing, if applicable
   3. Chart notes confirming family history of angioedema and the angioedema was refractory to a trial of high-dose antihistamine therapy, if applicable
B. For continuation of therapy, chart notes demonstrating a reduction in severity and/or duration of attacks

III. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with a prescriber who specializes in the management of HAE.

IV. CRITERIA FOR INITIAL APPROVAL

Hereditary angioedema (HAE)
Authorization of 6 months may be granted for treatment of acute HAE attacks when the requested medication will not be used in combination with any other medication used for the treatment of acute HAE attacks and either of the following criteria is met at the time of diagnosis:
A. Member has C1 inhibitor deficiency or dysfunction as confirmed by laboratory testing and meets one of the following criteria:
   1. C1 inhibitor (C1-INH) antigenic level below the lower limit of normal as defined by the laboratory performing the test, or
   2. Normal C1-INH antigenic level and a low C1-INH functional level (functional C1-INH less than 50% or C1-INH functional level below the lower limit of normal as defined by the laboratory performing the test)

B. Member has normal C1 inhibitor as confirmed by laboratory testing and meets one of the following criteria:
   1. Member has an F12, angiopoietin-1, plasminogen, kininogen-1 (KNG1), heparan sulfate-glucosamine 3-O-sulfotransferase 6 (HS3ST6), or myoferlin (MYOF) gene mutation as confirmed by genetic testing, or
   2. Member has a documented family history of angioedema and the angioedema was refractory to a trial of high-dose antihistamine therapy (i.e., cetirizine at 40 mg per day or the equivalent) for at least one month.

V. CONTINUATION OF THERAPY

Authorization of 6 months may be granted for continuation of therapy when all of the following criteria are met:
A. Member meets the criteria for initial approval.
B. Member has experienced a reduction in severity and/or duration of acute attacks.
C. Prophylaxis should be considered based on the attack frequency, attack severity, comorbid conditions, and member's quality of life.

VI. REFERENCES

1. Kalbitor [package insert]. Lexington, MA: Dyax Corp., a Takeda company; December 2020.
2. Bowen T, Cicardi M, Farkas H, et al. 2010 International consensus algorithm for the diagnosis, therapy, and management of hereditary angioedema. *Allergy Asthma Clin Immunol*. 2010;6(1):24.
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Reference number(s)
1884-A

SPECIALTY GUIDELINE MANAGEMENT

KALYDECO (ivacaftor)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Kalydeco is indicated for the treatment of cystic fibrosis (CF) in patients age 4 months and older who have one mutation in the cystic fibrosis transmembrane conductance regulator *(CFTR)* gene that is responsive to ivacaftor potentiation based on clinical and/or *in vitro* assay data.

If the patient's genotype is unknown, an FDA-cleared CF mutation test should be used to detect the presence of *CFTR* mutation followed by verification with bi-directional sequencing when recommended by the mutation test instructions for use.

All other indications are considered experimental/investigational and are not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: genetic testing report confirming the presence of the appropriate *CFTR* gene mutation.

III. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with a pulmonologist.

IV. CRITERIA FOR INITIAL APPROVAL

Cystic Fibrosis
Authorization of 12 months may be granted for treatment of cystic fibrosis when all of the following criteria are met:
A. Genetic testing was conducted to detect a mutation in the *CFTR* gene.
B. The member has one of the following mutations in the *CFTR* gene: A120T, A234D, A349V, A455E, A1067T, D110E, D110H, D192G, D579G, D924N, D1152H, D1270N, E56K, E193K, E822K, E831X, F311del, F311L, F508C, F508C;S1251N, F1052V, F1074L, G178E, G178R, G194R, G314E, G551D, G551S, G576A, G970D, G1069R, G1244E, G1249R, G1349D, H939R, H1375P, I148T, I175V, I807M, I1027T, I1139V, K1060T, L206W, L320V, L967S, L997F, L1480P, M152V, M952I, M952T, P67L, Q237E, Q237H, Q359R, Q1291R, R74W, R75Q, R117C, R117G, R117H, R117L, R117P, R170H, R347H, R347L, R352Q, R553Q, R668C, R792G, R933G, R1070Q, R1070W, R1162L, R1283M, S549N, S549R, S589N,

S737F, S945L, S977F, S1159F, S1159P, S1251N, S1255P, T338I, T1053I, V232D, V562I, V754M, V1293G, W1282R, Y1014C, Y1032C, 711+3A→G, 2789+5G→A, 3272-26A→G, 3849+10kbC→T.

C. The member is at least 4 months of age.
D. Kalydeco will not be used in combination with other medications containing ivacaftor.

V. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section IV who are experiencing benefit from therapy as evidenced by disease stability or disease improvement (e.g., improvement in FEV1 from baseline).

VI. REFERENCES

1. Kalydeco [package insert]. Boston, MA: Vertex Pharmaceuticals Inc.; December 2020.
2. Mogayzel PJ, Naureckas ET, Robinson KA, et al. Cystic fibrosis pulmonary guidelines. Chronic medications for maintenance of lung health. *Am J Respir Crit Care Med.* 2013;187:680-689.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME*
(generic)

KERENDIA
(finerenone)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization ***Ref # 4871-A***

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Kerendia is indicated to reduce the risk of sustained eGFR decline, end-stage kidney disease, cardiovascular death, non-fatal myocardial infarction, and hospitalization for heart failure in adult patients with chronic kidney disease (CKD) associated with type 2 diabetes (T2D).

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has a diagnosis of chronic kidney disease (CKD) associated with type 2 diabetes (T2D)

AND

- The patient is currently receiving a maximally tolerated dose of an angiotensin-converting enzyme inhibitor (ACEi) or angiotensin receptor blocker (ARB)
  OR
- The patient has experienced an intolerance to an angiotensin-converting enzyme inhibitor (ACEi) or angiotensin receptor blocker (ARB)
  OR
- The patient has a contraindication that would prohibit a trial of an angiotensin-converting enzyme inhibitor (ACEi) or angiotensin receptor blocker (ARB)

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Kerendia is indicated to reduce the risk of sustained eGFR decline, end-stage kidney disease, cardiovascular death, non-fatal myocardial infarction, and hospitalization for heart failure in adult patients with chronic kidney disease (CKD) associated with type 2 diabetes (T2D).[1]

Both the American Diabetes Association (ADA) Standards of Medical Care in Diabetes and the Kidney Disease Improving Global Outcomes (KDIGO) guidelines recommend treatment with an angiotensin-converting enzyme inhibitor (ACEi) or an angiotensin II receptor blocker (ARB) in patients with diabetes, hypertension and albuminuria.[4,5] KDIGO guidelines recommend that these medications be titrated to the highest approved dose that is tolerated. This recommendation places a high value on the potential benefits of RAS blockade with ACEi or ARB for slowing the progression of CKD in patients with diabetes. The benefits of RAS blockade have been less studied in patients with diabetes and CKD without hypertension; however, the KDIGO guidelines state that treatment with an ACEi or ARB may be considered for patients with diabetes, albuminuria and normal blood pressure.[5]

The Finerenone in Reducing Kidney Failure and Disease Progression in Diabetic Kidney Disease (FIDELIO-DKD) study was a randomized, double-blind placebo-controlled multicenter study in adult patients with chronic kidney disease (CKD) associated with type 2 diabetes (T2D). At baseline, 99.8% of patients in the FIDELIO-DKD study were treated with an ACE inhibitor or ARB. A total of 14 patients were not receiving an ACE inhibitor or ARB at baseline, and 7 patients received treatment with both an ACE inhibitor and an angiotensin-receptor blocker.[1,6] Therefore, coverage for Kerendia

CVS caremark®

will be considered in patients who are receiving concomitant therapy with, have experienced an intolerance to or have a contraindication to an ACEi or ARB.

REFERENCES

1. Kerendia [package insert]. Whippany, NJ: Bayer HealthCare Pharmaceuticals Inc.; July 2021.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2021; Accessed September 28,2021.
3. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed September 28, 2021
4. ADA's Standards of Medical Care in Diabetes - 2022. *Dia Care.* 2021;45(S1):S1-S264.
5. de Boer IH, Caramori ML, Chan JCN, et al. KDIGO 2020 Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease. *Kidney International*. 2020;98(4):S1-S115.
6. Bakris GL, Agarwal R, Anker SD, et. al. Effect of Finerenone on Chronic Kidney Disease Outcomes in Type 2 Diabetes. *New Engl J Med*, 2020;383(23):2219-2229.

Written by: UM Development (EC)
Date Written: 07/2021
Revised: (DFW) 10/2021 (removed SGLT2 step)
Reviewed: Medical Affairs: (CHART) 08/05/2021, 10/28/2021, 01/20/2022
External Review: 08/2021, 02/2022

CRITERIA FOR APPROVAL

1	Does the patient have a diagnosis of chronic kidney disease (CKD) associated with type 2 diabetes (T2D)? [If no, then no further questions.]	Yes	No
2	Is the patient currently receiving a maximally tolerated dose of an angiotensin-converting enzyme inhibitor (ACEi) or angiotensin receptor blocker (ARB)? [If yes, then no further questions.]	Yes	No
3	Has the patient experienced an intolerance to an angiotensin-converting enzyme inhibitor (ACEi) or angiotensin receptor blocker (ARB)? [If yes, then no further questions.]	Yes	No
4	Does the patient have a contraindication that would prohibit a trial of an angiotensin-converting enzyme inhibitor (ACEi) or angiotensin receptor blocker (ARB)?	Yes	No

Mapping Instructions			
	Yes	**No**	**DENIAL REASONS – DO NOT USE FOR MEDICARE PART D**
1.	Go to 2	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have chronic kidney disease associated with type 2 diabetes. Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]
2.	Approve, 12 months	Go to 3	
3.	Approve, 12 months	Go to 4	

4.	Approve, 12 months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you are taking a maximally tolerated ACE inhibitor or ARB or you cannot use an ACE inhibitor or ARB. Your request has been denied based on the information we have. [Short Description: No concurrent use, intolerance, or contraindication to an ACE inhibitor or ARB]

PRIOR AUTHORIZATION CRITERIA

BRAND NAME*
(generic)

KERYDIN
(tavaborole topical solution)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization with Quantity Limit ***Ref # 1169-C***

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Kerydin (tavaborole) topical solution, 5% is an oxaborole antifungal indicated for the treatment of onychomycosis of the toenails due to Trichophyton rubrum or Trichophyton mentagrophytes.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for onychomycosis of the toenail(s) due to Trichophyton rubrum or Trichophyton mentagrophytes

AND

- The patient's diagnosis has been confirmed with a fungal diagnostic test (e.g., potassium hydroxide [KOH] preparation, fungal culture, or nail biopsy)

AND

- The patient has experienced an inadequate treatment response to an oral antifungal therapy (e.g., terbinafine, itraconazole)

OR

- The patient has experienced an intolerance to an oral antifungal therapy (e.g., terbinafine, itraconazole)

OR

- The patient has a contraindication that would prohibit a trial of an oral antifungal therapy (e.g., terbinafine, itraconazole)

AND

- The requested drug is not being used in a footbath

AND

- If additional quantities are required, multiple toenails are being treated

Quantity Limits Apply.

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Kerydin (tavaborole) topical solution, 5% is an oxaborole antifungal indicated for the treatment of onychomycosis of the toenails due to Trichophyton rubrum or Trichophyton mentagrophytes.[1-3]

Onychomycosis may be diagnosed by the presence of fungi by culture, microscopy (Potassium hydroxide [KOH] stain), or histological examination of the nail plate.[5] Microscopy is a commonly used method because it is inexpensive and easy to perform; nail clippings or scrapings are placed in a drop of KOH and examined under a microscope for the presence of fungal elements.[6]

Per the CDC, oral antifungal therapy (terbinafine) is considered first line treatment for confirmed onychomycosis.[6] According to the Cochrane review, medication taken orally appears to cure the condition more quickly and effectively than

topical treatment; there was high-quality evidence that oral azole (itraconazole) and terbinafine treatments were more effective for achieving mycological cure and clinical cure for onychomycosis compared to placebo, and when compared directly, terbinafine was probably more effective than azoles and likely not associated with excess adverse events (griseofulvin was associated with more adverse reactions than azoles and terbinafine).[5] Even though oral treatment is limited by drug interactions and risk of acute liver injury, topical lacquer treatments have negligible efficacy and low success rates due to the nail's physical properties.[4,5] In 2 randomized trials, complete cure rate, defined as no evidence of fungal infection at week 52, was demonstrated in 6.5% and 9.1% of patients receiving tavaborole compared with 0.5% and 1.5% receiving placebo for the treatment of onychomycosis of the toenail.[1]

The prior authorization criteria do not approve Kerydin for use in a footbath, as this is not an FDA-approved use. Kerydin is for topical use only and not for oral, ophthalmic, or intravaginal use.[1]

Kerydin is available as a solution supplied in 4 mL and 10 mL bottles. Kerydin is to be applied to affected toenails once daily for 48 weeks. Kerydin should be applied to the entire toenail surface and under the tip of each toenail being treated. Using the dropper provided, patients should squeeze the bulb to draw Kerydin into the dropper. Squeeze the bulb to apply Kerydin to the toenail, using enough to completely cover the toenail. More than one drop may be needed. Using the dropper, spread Kerydin to the entire toenail and under the tip of the toenail.[1] While not published by manufacturer, judging from patient use, there are approximately 80 drops in a 4 mL bottle of Jublia (efinaconazole).[7] Based on the dosing recommendations for Kerydin, 4 mL would be sufficient to treat one big toenail and one smaller toenail (allowing for a second drop to completely cover the big toenail):

- 2 drops to the big toenail daily = 2 drops X 28 days = 56 drops per 28 days
- 1 drop to any other toenail daily = 1 drop X 28 days = 28 drops per 28 days

For a total of approximately 84 drops per 28 days.

The PA allows for additional quantities if the patient requires treatment of onychomycosis affecting multiple toenails. The PA allows for a quantity approximately sufficient to treat an infection of all toenails. The quantity allowed upon approval of PA is approximately sufficient to allow treatment of two big toenails daily (at two drops per day per big toenail, a quantity of 112 drops, or 5.6 mL per 28 days) and eight other toenails daily (assuming one drop per day per toenail, 224 drops, or 11.2 mL per 28 days). As the applications instructions for Kerydin state that more than one drop may be required to cover the entire nail surface, the quantity for patients requiring treatment of multiple toenails will be set at 20 mL per 28 days.

REFERENCES

1. Kerydin [package insert]. Palo Alto, CA. Anacor Pharmaceuticals; August 2018.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2021; Accessed July 29, 2021.
3. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed July 29, 2021.
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6. Centers for Disease Control (CDC) and Prevention. Fungal Nail infections. https://www.cdc.gov/fungal/nail-infections.html. Accessed August 5, 2021.
7. Lipner SR, Scher RK. Efinaconazole in the treatment of onychomycosis. *Infect Drug Resist*. 2015;8:163–172.

Written by:	UM Development (PL/WW)
Date Written:	07/2014
Revised:	(MS) 05/2015; (KM) 05/2016; (JH) 04/2017 (no clinical changes); (KC) (04/2018); (ME) 02/2019 (no clinical changes); (NZ) 02/2020 (no clinical changes; removed MDC designation); (KC) 12/2020 (added footbath question, quantity limits); (PM) 09/2021 (no clinical changes)
Reviewed:	Medical Affairs (LMS) 07/2014; (KU) 05/2015; (ME) 05/2016; (CHART) 02/27/20, 12/31/20, 09/30/21 External Review: 07/2014, 10/2015, 08/2016, 08/2017, 06/2018, 06/2019, 06/2020, 04/2021, 12/2021

CRITERIA FOR APPROVAL

1	Is the requested drug being prescribed for onychomycosis of the toenail(s) due to Trichophyton rubrum or Trichophyton mentagrophytes? [If no, then no further questions.]	Yes	No
2	Has the patient's diagnosis been confirmed with a fungal diagnostic test (e.g., potassium hydroxide [KOH] preparation, fungal culture, or nail biopsy)? [If no, then no further questions.]	Yes	No
3	Has the patient experienced an inadequate treatment response to an oral antifungal therapy (e.g., terbinafine, itraconazole)? [If yes, then skip to question 6.]	Yes	No
4	Has the patient experienced an intolerance to an oral antifungal therapy (e.g., terbinafine, itraconazole)? [If yes, then skip to question 6.]	Yes	No
5	Does the patient have a contraindication that would prohibit a trial of an oral antifungal therapy (e.g., terbinafine, itraconazole)? [If no, then no further questions.]	Yes	No
6	Is the requested drug being used in a footbath? [If yes, then no further questions.]	Yes	No
7	Does the patient require MORE than the plan allowance of 4 mL per month? [Note: If higher quantities are needed, additional questions are required.] [If no, then no further questions.]	Yes	No
8	Are multiple toenails being treated? [If no, then no further questions.] [RPh Note: If no, then deny and enter a partial approval for 4 mL / 21 days or 12 mL / 63 days.]	Yes	No
9	Does the patient require MORE than the plan allowance of 20 mL per month? [RPh Note: If yes, then deny and enter a partial approval for 20 mL / 21 days or 60 mL / 63 days.]	Yes	No

Mapping Instructions			
	Yes	**No**	**DENIAL REASONS – DO NOT USE FOR MEDICARE PART D**
1.	Go to 2	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have a specific fungal infection of the toenail(s). Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]
2.	Go to 3	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you meet all of these conditions: - You have a specific fungal infection of the toenail(s) - You had a test to confirm your toenail fungus Your request has been denied based on the information we have.

			[Short Description: No confirmation of diagnosis]
3.	Go to 6	Go to 4	
4.	Go to 6	Go to 5	
5.	Go to 6	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have tried an oral antifungal medicine and it did not work for you, or you cannot use it. Your request has been denied based on the information we have. [Short Description: No inadequate response, intolerance, or contraindication to an oral antifungal]
6.	Deny	Go to 7	You do not meet the requirements of your plan. Your plan covers this drug when it is not being used in a footbath. Your request has been denied based on the information we have. [Short Description: Used in footbath]
7.	Go to 8	Approve, 12 months, 4 mL/21 days* or 12 mL/63 days*	
8.	Go to 9	Deny	You do not meet the requirements of your plan. Your plan covers additional quantities of this drug when multiple toenails are being treated. Current plan approved criteria cover up to 4 mL per month of the requested drug and strength. Your request has been partially approved. You have been approved for the quantity that your plan covers for a duration of 12 months. Your request for additional quantities has been denied based on the information we have. [Short Description: Not enough area affected]
9.	Deny	Approve, 12 months, 20 mL/21 days* or 60 mL/63 days*	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 20 mL per month of the requested drug and strength. Your request has been partially approved. You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity]

**The duration of 21 days is used for a 28-day fill period and 63 days is used for a 84-day fill period to allow time for refill processing.*

Reference number(s)
4129-A

SPECIALTY GUIDELINE MANAGEMENT

KESIMPTA (ofatumumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Kesimpta is indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease and active secondary progressive disease, in adults.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Relapsing forms of multiple sclerosis
Authorization of 12 months may be granted to members who have been diagnosed with a relapsing form of multiple sclerosis (including relapsing-remitting and secondary progressive disease for those who continue to experience relapse).

B. Clinically isolated syndrome
Authorization of 12 months may be granted to members for the treatment of clinically isolated syndrome.

III. CONTINUATION OF THERAPY

For all indications: Authorization of 12 months may be granted for members who are experiencing disease stability or improvement while receiving Kesimpta.

IV. OTHER CRITERIA

Members will not use Kesimpta concomitantly with other disease modifying multiple sclerosis agents (Note: Ampyra and Nuedexta are not disease modifying).

V. REFERENCES

1. Kesimpta [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; August 2020.

QUANTITY LIMIT CRITERIA

BRAND NAME*
(generic)

(ketorolac tablets)

SPRIX
(ketorolac nasal spray)

Status: CVS Caremark Criteria
Type: Quantity Limit ***Ref # 233-H***

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Ketorolac Tablets
Carefully consider the potential benefits and risks of ketorolac tromethamine tablets and other treatment options before deciding to use ketorolac tromethamine tablets. Use the lowest effective dose for the shortest duration consistent with individual patient treatment goals.

Acute Pain in Adult Patients
Ketorolac tromethamine tablets are indicated for the short-term (≤ 5 days) management of moderately severe acute pain that requires analgesia at the opioid level, usually in a postoperative setting. Therapy should always be initiated with ketorolac tromethamine-IV or IM and ketorolac tromethamine tablets are to be used only as continuation treatment, if necessary.

The total combined duration of use of ketorolac tromethamine-IV/IM and ketorolac tromethamine tablets is not to exceed five days of use because of the potential of increasing the frequency and severity of adverse reactions associated with the recommended doses. Patients should be switched to alternative analgesics as soon as possible, but ketorolac tromethamine tablet therapy is not to exceed 5 days.

Sprix
Sprix is indicated in adult patients for the short term (up to 5 days) management of moderate to moderately severe pain that requires analgesia at the opioid level.

Limitations of Use
Sprix is not for use in pediatric patients less than 2 years of age.

RATIONALE

Ketorolac tablets are only indicated as continuation treatment after initial therapy with ketorolac injection. Combined use beyond five days increases the risk of serious adverse events such as peptic ulcers and gastrointestinal bleeding and/or perforation of the stomach or intestines, which can be fatal. The maximum dose of ketorolac tablets per day is 40 mg, or 4 tablets. The maximum number of tablets per prescription should be 20 tablets or less due to the fact that combined usage of injection and oral should not exceed five days. Ketorolac oral is not to exceed five days of use because of the potential of increasing the frequency and severity of adverse reactions associated with the recommended doses.[1,3,4] Because ketorolac tablets are indicated for short-term (up to 5 days) use, the limit is 20 tablets per month, and 3 month limits will not apply.

Sprix is indicated in adult patients for the short-term (up to 5 days) management of moderate to moderately severe pain that requires analgesia at the opioid level. The total duration of use of Sprix alone or sequentially with other formulations of ketorolac (IM/IV or oral) must not exceed 5 days because of the potential for increasing the frequency and severity of

adverse reactions associated with the recommended doses. The maximum daily dose of Sprix is 126 mg (four doses). For adult patients < 65 years of age, the recommended dose of Sprix is 31.5 mg (one 15.75 mg spray in each nostril) every 6 to 8 hours. Each single-day nasal spray bottle contains a sufficient quantity of solution to deliver 8 sprays for a total of 126 mg of ketorolac tromethamine. Each Sprix nasal spray bottle contains one day's supply of pain medication and should be discarded within 24 hours after taking the first dose.[2-4] Because Sprix is indicated for short-term (up to 5 days) use, the limit is 5 bottles per month and 3 month limits will not apply.

If the patient is requesting more than the initial quantity limit, the claim will reject with a message indicating that quantity limits are exceeded.

Because no safety data is available for any combination of injectable, oral and intranasal use beyond five days, post limit authorization will not be available for ketorolac.

REFERENCES

1. Ketorolac [package insert]. Morgantown, WV: Mylan Pharmaceuticals Inc.; May 2021.
2. Sprix [package insert]. Wayne, PA: Zyla Life Sciences US Inc.; April 2021.
3. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2021; Accessed August 5, 2021.
4. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed August 5, 2021.

Written by:	UM Development (DP)
Date Written:	03/1998
Revised:	(LS) 03/2001; (PJ) 11/2002; (MG) 10/2003, 10/2004; (NB) 08/2005, 08/2006; (CT) 07/2007, 08/2008, 08/2009, 12/2009, 06/2010 (addition of Sprix), 06/2011, 03/2012, 01/2013, 01/2014, (SF) 01/2015; (CT) 01/2016 (no clinical changes); (SF) 01/2017 (no clinical changes); (CF) 09/2017 (no clinical changes); (DS) 09/2018 (no clinical changes); (KC) 09/2019 (no clinical changes); (CJM) 09/2020 (no clinical changes); (PM) 09/2021 (no clinical changes)
Reviewed:	CRC 03/1998, 03/2001; 12/2002; 10/2003; CDPR/Medical Affairs (MM) 10/2004, 08/2005, 08/2006; (WF) 07/2007, 08/2008, 08/2009, 12/2009, 06/2010; (KP) 06/2011, 03/2012; (LMS) 01/2013; (KP) 01/2014 (SES) 01/2015; (CHART) 09/26/19; 09/24/20, 09/30/21 External Review: 05/2001; 02/2003; 12/2003; 12/2004; 12/2005; 12/2006, 02/2008, 12/2008, 10/2009, 10/2010, 10/2011, 08/2012, 06/2013, 06/2014, 04/2015, 04/2016, 04/2017, 02/2018, 02/2019, 02/2020, 12/2020, 12/2021

LIMIT CRITERIA

Limits should accumulate across all drugs and strengths up to highest quantity listed depending on the order the claims are processed. Accumulation does not apply if limit is coded for daily dose.

Drug	1 Month Limit*	3 Month Limit*
Ketorolac tablets	20 tablets / 25 days	Does Not Apply*
Sprix nasal spray	5 bottles / 25 days	Does Not Apply*

** The duration of 25 days is used for a 30-day fill period to allow time for refill processing.*

**** These drugs are for short-term acute use; therefore, the mail limit will be the same as the retail limit. The intent is for prescriptions of the requested drug to be filled one month at a time, even if filled at mail order; there should be no 3 month supplies filled.***

Reference number
2491-A

SPECIALTY GUIDELINE MANAGEMENT

KEVEYIS (dichlorphenamide)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Treatment of primary hyperkalemic periodic paralysis, primary hypokalemic periodic paralysis, and related variants.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Primary Hypokalemic Periodic Paralysis
Authorization of 60 days may be granted to members who are initiating Keveyis therapy when the following criteria is met:
1. The diagnosis was supported by at least one of the following:
    a. Genetic test results, or
    b. Patient has a family history of primary hypokalemic periodic paralysis, or
    c. Patient's attacks are associated with hypokalemia AND both Andersen-Tawil syndrome and thyrotoxic periodic paralysis have been ruled out.
2. Trial with suboptimal response to treatment with acetazolamide

B. Primary Hyperkalemic Periodic Paralysis
Authorization of 60 days may be granted to members who are initiating Keveyis therapy when the following criteria is met:
1. The diagnosis was supported by at least one of the following:
    a. Genetic test results, or
    b. Patient has a family history of primary hyperkalemic periodic paralysis, or
    c. Patient's attacks are associated with hyperkalemia AND Andersen-Tawil syndrome has been ruled out.
2. Trial with suboptimal response to treatment with acetazolamide

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted to members who have demonstrated a response to Keveyis therapy as demonstrated by an improvement in their condition (e.g. decrease in the number or severity of attacks).

IV. REFERENCES

1. Keveyis [package insert]. Trevose, PA: Strongbridge Biopharma; November 2019.
2. Levitt JO. Practical aspects in the management of hypokalemic periodic paralysis. *Journal of Translational Medicine* 2008; 6:18.
3. Charles G, Zheng C, Lehmann-Horn F, et al. Characterization of hyperkalemic periodic paralysis: a survey of genetically diagnosed individuals. *JNeurol* 2013; 260:2606-2613.
4. Statland JM, Fontaine, B, Hanna MG, et al. A review of the diagnosis and treatment of periodic paralysis. *Muscle & Nerve* 2018; 57:522-530.

Reference number
1957-A

SPECIALTY GUIDELINE MANAGEMENT

KEVZARA (sarilumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Kevzara is indicated for treatment of adult patients with moderately to severely active rheumatoid arthritis who have had an inadequate response or intolerance to one or more disease-modifying antirheumatic drugs (DMARDs).

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

A. For initial requests:
   1. Chart notes, medical record documentation, or claims history supporting previous medications tried (if applicable), including response to therapy. If therapy is not advisable, documentation of clinical reason to avoid therapy.
   2. Laboratory results, chart notes, or medical record documentation of biomarker testing (i.e., rheumatoid factor [RF], anti-cyclic citrullinated peptide [anti-CCP], and C-reactive protein [CRP] and/or erythrocyte sedimentation rate [ESR]) (if applicable).

B. For continuation requests: Chart notes or medical record documentation supporting positive clinical response.

III. CRITERIA FOR INITIAL APPROVAL

Moderately to severely active rheumatoid arthritis (RA)

A. Authorization of 12 months may be granted for members who have previously received a biologic or targeted synthetic DMARD (e.g., Rinvoq, Xeljanz) indicated for moderately to severely active rheumatoid arthritis.

B. Authorization of 12 months may be granted for treatment of moderately to severely active RA when all of the following criteria are met:
   1. Member meets either of the following criteria:
      i. Member has been tested for either of the following biomarkers and the test was positive:
         a. Rheumatoid factor (RF)
         b. Anti-cyclic citrullinated peptide (anti-CCP)
      ii. Member has been tested for ALL of the following biomarkers:
         a. RF
         b. Anti-CCP
         c. C-reactive protein (CRP) and/or erythrocyte sedimentation rate (ESR)

2. Member meets either of the following criteria:
   i. Member has experienced an inadequate response to at least a 3-month trial of methotrexate despite adequate dosing (i.e., titrated to at least 15 mg/week).
   ii. Member has an intolerance or contraindication to methotrexate (see Appendix).

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for all members (including new members) who are using the requested medication for an indication outlined in Section III and who achieve or maintain a positive clinical response as evidenced by disease activity improvement of at least 20% from baseline in tender joint count, swollen joint count, pain, or disability.

V. OTHER

For all indications: Member has had a documented negative TB test (which can include a tuberculosis skin test [PPD], an interferon-release assay [IGRA], or a chest x-ray)* within 6 months of initiating therapy for persons who are naïve to biologic DMARDs or targeted synthetic DMARDs associated with an increased risk of TB.

* If the screening testing for TB is positive, there must be further testing to confirm there is no active disease. Do not administer the requested medication to members with active TB infection. If there is latent disease, TB treatment must be started before initiation of the requested medication.

For all indications: Members cannot use the requested medication concomitantly with any other biologic DMARD or targeted synthetic DMARD.

VI. DOSAGE AND ADMINISTRATION

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

VII. APPENDIX: Examples of Contraindications to Methotrexate

1. Clinical diagnosis of alcohol use disorder, alcoholic liver disease or other chronic liver disease
2. Breastfeeding
3. Blood dyscrasias (e.g., thrombocytopenia, leukopenia, significant anemia)
4. Elevated liver transaminases
5. History of intolerance or adverse event
6. Hypersensitivity
7. Interstitial pneumonitis or clinically significant pulmonary fibrosis
8. Myelodysplasia
9. Pregnancy or currently planning pregnancy
10. Renal impairment
11. Significant drug interaction

VIII. REFERENCES

1. Kevzara [package insert]. Bridgewater, NJ: Sanofi-aventis, U.S. LLC /Regeneron Pharmaceuticals, Inc.; April 2018.

2. Genovese MC, Fleischmann R, Kivitz AJ, et al. Sarilumab plus methotrexate in patients with active rheumatoid arthritis and inadequate response to methotrexate: results of a phase III study. *Arthritis Rheumatol.* June 2015;67(6):1424-37.
3. Strand V, Reaney M, Chen C, et al. Sarilumab improves patient-reported outcomes in rheumatoid arthritis patients with inadequate response/intolerance to tumour necrosis factor inhibitors. *RMD Open.* 2017; 3**:**e000416. doi: 10.1136/rmdopen-2016-000416.
4. Tuberculosis (TB). TB risk factors. Centers for Disease Control and Prevention. Retrieved on November 15, 2021 from: https://www.cdc.gov/tb/topic/basics/risk.htm.
5. Smolen JS, Landewé R, Bijlsma J, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2019 update. *Ann Rheum Dis.* 2020;79:685-699.
6. Aletaha D, Neogi T, Silman, et al. 2010 Rheumatoid arthritis classification criteria: an American College of Rheumatology/European League Against Rheumatism collaborative initiative. *Arthritis Rheum*. 2010;62(9):2569-81.
7. Smolen JS, Aletaha D. Assessment of rheumatoid arthritis activity in clinical trials and clinical practice. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. Available with subscription. URL: www.uptodate.com. Accessed March 19, 2021.
8. Fraenkel L, Bathon JM, England BR, et al. 2021 American College of Rheumatology guideline for the treatment of rheumatoid arthritis. *Arthrit Care Res*. 2021;0:1-16.

Reference number(s)
2104-A

SPECIALTY GUIDELINE MANAGEMENT

KISQALI FEMARA CO-PACK (ribociclib tablets; letrozole tablets)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication
The Kisqali Femara Co-Pack is indicated as initial endocrine-based therapy for the treatment of adult patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer.

B. Compendial Uses
Breast cancer: Therapy for recurrent HR-positive, HER2-negative disease

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of hormone receptor (HR) and human epidermal growth factor receptor 2 (HER2) status is necessary to initiate the prior authorization review.

III. CRITERIA FOR INITIAL APPROVAL

Breast cancer
Authorization of 12 months may be granted to members for the treatment of HR-positive, HER2-negative recurrent, advanced or metastatic breast cancer.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication outlined in section III when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

V. REFERENCES

1. Kisqali Femara Co-Pack [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; December 2021.
2. Ribociclib. The NCCN Drugs & Biologics Compendium® © 2021 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed December 1, 2021.

Reference number
1802-A

SPECIALTY GUIDELINE MANAGEMENT

KINERET (anakinra)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
1. Moderately to severely active rheumatoid arthritis (RA), in patients 18 years of age or older who have failed 1 or more disease modifying antirheumatic drugs (DMARDs)
2. Cryopyrin-Associated Periodic Syndromes (CAPS), including Neonatal-Onset Multisystem Inflammatory Disease (NOMID)
3. Deficiency of Interleukin-1 Receptor Antagonist (DIRA)

B. Compendial Uses
1. Systemic juvenile idiopathic arthritis (sJIA)
2. Adult-onset Still's disease (AOSD)
3. Multicentric Castleman disease
4. Recurrent pericarditis (RP)
5. Hyperimmunoglobulin D syndrome (HIDS)/Mevalonate Kinase Deficiency (MKD)
6. Schnitzler syndrome
7. Gout and pseudogout (calcium pyrophosphate deposition)
8. Chimeric antigen receptor (CAR) T-Cell-Related Toxicities – Cytokine release syndrome (CRS)
9. Erdheim-Chester Disease

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

A. Rheumatoid arthritis (RA)
1. For initial requests
   a. Chart notes, medical record documentation, or claims history supporting previous medications tried (if applicable), including response to therapy. If therapy is not advisable, documentation of clinical reason to avoid therapy.
   b. Laboratory results, chart notes, or medical record documentation of biomarker testing (i.e., rheumatoid factor [RF], anti-cyclic citrullinated peptide [anti-CCP], and C-reactive protein [CRP] and/or erythrocyte sedimentation rate [ESR]) (if applicable).
2. For continuation requests: Chart notes or medical record documentation supporting positive clinical response.

B. Adult-onset Still's disease (AOSD) and systemic juvenile idiopathic arthritis (sJIA)
   1. Initial requests: Chart notes, medical record documentation, or claims history supporting previous medications tried, including response to therapy (if applicable).
   2. Continuation requests: Chart notes or medical record documentation supporting positive clinical response.

C. Neonatal-onset multisystem inflammatory disease (NOMID): For continuation requests: Chart notes, medical record documentation, or laboratory results supporting positive clinical response.

D. Deficiency of interleukin-1 receptor antagonist (DIRA): For initial requests: *IL1RN* mutation status.

E. Recurrent pericarditis (RP)
   1. Initial requests: Chart notes, medical record documentation, or claims history supporting previous medications tried, including response to therapy.
   2. Continuation requests: Chart notes or medical record documentation supporting positive clinical response.

F. Hyperimmunoglobulin D syndrome (HIDS)/Mevalonate Kinase Deficiency (MKD): For initial requests: Chart notes, medical record documentation, or laboratory result (if applicable) indicating number of active flares within the last 6 months and Physician's Global Assessment (PGA) score or C-reactive protein (CRP) level.

G. Gout and pseudogout flares and CAR T-Cell-related toxicities: For initial requests: Chart notes, medical record documentation, or claims history supporting previous medications tried (if applicable), including response to therapy. If therapy is not advisable, documentation of clinical reason to avoid therapy.

III. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with one of the following:
A. Rheumatoid arthritis (RA), adult-onset Still's disease (AOSD), systemic juvenile idiopathic arthritis (sJIA), gout, and pseudogout: rheumatologist
B. Cryopyrin-associated periodic syndromes (CAPS), including neonatal-onset multisystem inflammatory disease (NOMID), deficiency of interleukin-1 receptor antagonist (DIRA), and hyperimmunoglobulin D syndrome (HIDS)/mevalonate kinase deficiency (MKD): rheumatologist or immunologist
C. Recurrent pericarditis (RP): cardiologist, rheumatologist, or immunologist
D. Schnitzler syndrome: rheumatologist, dermatologist, or immunologist
E. Multicentric Castleman disease, CAR T-cell-related toxicities, and Erdheim-Chester disease: oncologist or hematologist

IV. CRITERIA FOR INITIAL APPROVAL

A. Rheumatoid arthritis (RA)

1. Authorization of 12 months may be granted for adult members who have previously received a biologic or targeted synthetic drug (e.g., Rinvoq, Xeljanz) indicated for moderately to severely active rheumatoid arthritis.

2. Authorization of 12 months may be granted for adult members for treatment of moderately to severely active RA when all of the following criteria are met:
   i. Member meets either of the following criteria:

a. Member has been tested for either of the following biomarkers and the test was positive:
   1. Rheumatoid factor (RF)
   2. Anti-cyclic citrullinated peptide (anti-CCP)
b. Member has been tested for ALL of the following biomarkers:
   1. RF
   2. Anti-CCP
   3. C-reactive protein (CRP) and/or erythrocyte sedimentation rate (ESR)

ii. Member has experienced an inadequate response to at least a 3-month trial of methotrexate despite adequate dosing (i.e., titrated to at least 15 mg/week), or the member has an intolerance or contraindication to methotrexate (see Appendix).

iii. Member has experienced an inadequate response to at least a 3-month trial of a biologic or a targeted synthetic drug (e.g., Rinvoq, Xeljanz) or has an intolerance to a biologic or targeted synthetic drug.

B. Adult-onset Still's disease (AOSD)

1. Authorization of 12 months may be granted for members who have received a biologic indicated for active adult-onset Still's disease.

2. Authorization of 12 months may be granted for treatment of active adult-onset Still's disease when both of the following criteria are met:
   i. Member has active systemic features (e.g., fever, arthralgia/arthritis, evanescent rash, lymphadenopathy, hepatomegaly, splenomegaly, sore throat).
   ii. Member meets any of the following:
      a. Member has had an inadequate response to a trial of nonsteroidal anti-inflammatory drugs (NSAIDs).
      b. Member has had an inadequate response to a trial of corticosteroids.
      c. Member has had an inadequate response to a trial of a conventional synthetic drug (e.g., methotrexate).

C. Systemic juvenile idiopathic arthritis (sJIA)

1. Authorization of 12 months may be granted for members who have previously received a biologic indicated for active systemic juvenile idiopathic arthritis.

2. Authorization of 12 months may be granted for treatment of active systemic juvenile idiopathic arthritis when both of the following criteria are met:
   i. Member has active systemic features (e.g., fever, evanescent rash, lymphadenopathy, hepatomegaly, splenomegaly, or serositis).
   ii. Member has had an inadequate response to non-steroidal anti-inflammatory drugs (NSAIDs) or systemic glucocorticoids.

D. Neonatal-onset multisystem inflammatory disease (NOMID)

Authorization of 12 months may be granted for treatment of cryopyrin-associated periodic syndromes (CAPS), including NOMID (also known as chronic infantile neurologic cutaneous and articular [CINCA] syndrome).

E. Deficiency of interleukin-1 receptor antagonist (DIRA)

Authorization of 12 months may be granted for treatment of genetically confirmed deficiency of interleukin-1 receptor antagonist (DIRA) due to *IL1RN* mutations.

F. Recurrent pericarditis (RP)

Authorization of 12 months may be granted for treatment of recurrent pericarditis when both of the following criteria are met:
1. Member has had at least two episodes of pericarditis.
2. Member has failed at least 2 agents of standard therapy (e.g., colchicine, non-steroidal anti-inflammatory drugs [NSAIDs], corticosteroids).

G. Multicentric Castleman disease
Authorization of 12 months may be granted for treatment of multicentric Castleman disease when both of the following criteria are met:
1. The requested medication will be used as a single agent.
2. The disease has progressed following treatment of relapsed/refractory or progressive disease.

H. Hyperimmunoglobulin D syndrome (HIDS)/Mevalonate Kinase Deficiency (MKD)
Authorization of 12 months may be granted for treatment of HIDS/MKD when both of the following criteria are met:
1. Member has had active flares within the last 6 months.
2. Physician's Global Assessment (PGA) score greater than or equal to 2 or C-reactive protein (CRP) greater than 10 mg/L.

I. Schnitzler syndrome
Authorization of 12 months may be granted for treatment of Schnitzler syndrome when both of the following criteria are met:
1. Member has an urticarial rash, monoclonal IgM (or IgG) gammopathy, and at least two of the following signs and symptoms: fever, joint pain or inflammation, bone pain, lymphadenopathy, hepatomegaly, splenomegaly, leukocytosis, elevated erythrocyte sedimentation rate (ESR), or abnormalities on bone morphological study (e.g., increased bone density).
2. Other possible causes of the signs and symptoms have been ruled out, including but not limited to: hyperimmunoglobulin D syndrome, adult-onset Still's disease, urticarial hypocomplementemic vasculitis, acquired C1 inhibitor deficiency, and cryoglobulinemia.

J. Management of gout and pseudogout flares
Authorization of 6 months may be granted for management of flares for gout or pseudogout (also known as calcium pyrophosphate deposition disease) when either of the following criteria is met:
1. Member has had an inadequate response or intolerance to maximum tolerated doses of non-steroidal anti-inflammatory drugs (NSAIDs), colchicine, and oral and injectable corticosteroids.
2. Member has a contraindication to NSAIDs and colchicine and has a clinical reason to avoid repeated courses of corticosteroids.

K. Cytokine release syndrome (CRS)
Authorization of 1 month may be granted for the management of chimeric antigen receptor (CAR) T-cell-induced cytokine release syndrome when either of the following criteria is met:
1. Cytokine release syndrome is refractory to high-dose corticosteroids and anti-IL-6 therapy.
2. Kineret will be used as a replacement for the second dose of tocilizumab when supplies are limited or unavailable.

L. Erdheim-Chester Disease
Authorization of 12 months may be granted for the treatment of Erdheim-Chester disease.

V. CONTINUATION OF THERAPY

A. Rheumatoid arthritis (RA)
Authorization of 12 months may be granted for all adult members (including new members) who are using the requested medication for moderately to severely active rheumatoid arthritis and who achieve or maintain a positive clinical response as evidenced by disease activity improvement of at least 20% from baseline in tender joint count, swollen joint count, pain, or disability.

B. Adult-onset Still's disease (AOSD) and systemic juvenile idiopathic arthritis (sJIA)
Authorization of 12 months may be granted for all members (including new members) who are using the requested medication for adult-onset Still's disease or systemic juvenile idiopathic arthritis and who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition when there is improvement in any of the following from baseline:
1. Number of joints with active arthritis (e.g., swelling, pain, limitation of motion)
2. Number of joints with limitation of movement
3. Functional ability
4. Systemic features (e.g., fever, evanescent rash, lymphadenopathy, hepatomegaly, splenomegaly, or serositis)

C. Neonatal-onset multisystem inflammatory disease (NOMID)
Authorization of 12 months may be granted for all members (including new members) who are using the requested medication for CAPS, including NOMID (also known as CINCA), and who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition when there is improvement in any of the following from baseline:
1. Fever
2. Skin rash
3. Joint pain and/or inflammation
4. Central nervous system (CNS) symptoms (e.g., meningitis, headache, cerebral atrophy, uveitis, hearing loss)
5. Inflammatory markers (e.g., serum amyloid A [SAA], C-reactive protein [CRP], erythrocyte sedimentation rate [ESR])

D. Recurrent pericarditis (RP)
Authorization of 12 months may be granted for all members (including new members) who are using the requested medication for recurrent pericarditis and who achieve or maintain a positive clinical response as evidenced by decreased recurrence of pericarditis or improvement in signs and symptoms of the condition when there is improvement in any of the following:
1. Pericarditic chest pain
2. Pericardial rubs
3. Findings on electrocardiogram (ECG)
4. Pericardial effusion
5. C-reactive protein (CRP)

E. Multicentric Castleman disease
Authorization of 12 months may be granted for continued treatment of multicentric Castleman disease in members requesting reauthorization who have not experienced disease progression or an unacceptable toxicity.

F. Cytokine release syndrome
All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

G. All other indications

Authorization of 12 months may be granted for all members (including new members) who are using the requested medication for an indication outlined in Section IV and who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition.

VI. OTHER

For all indications: Member has had a documented negative tuberculosis (TB) test (which can include a tuberculosis skin test [PPD], an interferon-release assay [IGRA], or a chest x-ray)* within 6 months of initiating therapy for persons who are naïve to biologic drugs or targeted synthetic drugs associated with an increased risk of TB.

* If the screening testing for TB is positive, there must be further testing to confirm there is no active disease. Do not administer the requested medication to members with active TB infection. If there is latent disease, TB treatment must be started before initiation of the requested medication.

For all indications: Member cannot use the requested medication concomitantly with any other biologic drug or targeted synthetic drug.

VII. DOSAGE AND ADMINISTRATION

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

VIII. APPENDIX: Examples of clinical reasons to avoid pharmacologic treatment with methotrexate

1. Clinical diagnosis of alcohol use disorder, alcoholic liver disease, or other chronic liver disease
2. Drug interaction
3. Risk of treatment-related toxicity
4. Pregnancy or currently planning pregnancy
5. Breastfeeding
6. Significant comorbidity prohibits use of systemic agents (e.g., liver or kidney disease, blood dyscrasias, uncontrolled hypertension)
7. Hypersensitivity
8. History of intolerance or adverse event

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PRIOR AUTHORIZATION CRITERIA

BRAND NAME*
(generic)

KLISYRI
(tirbanibulin)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization with Quantity Limit ***Ref # 4404-C***

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Klisyri is indicated for the topical treatment of actinic keratosis on the face or scalp.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for the topical treatment of actinic keratosis on the face or scalp

AND

- The patient experienced an inadequate treatment response, intolerance, or has a contraindication to ONE of the following: A) imiquimod 5 percent cream, B) fluorouracil cream or solution

Quantity Limits apply.

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Klisyri is indicated for the topical treatment of actinic keratosis (AK) on the face or scalp.[1]

Per National Comprehensive Cancer Care Network (NCCN) guidelines, actinic keratoses (AKs) are a premalignant skin condition that should be treated at first development, particularly in patients with diffuse AKs and/or field cancerization, as these patients are at high risk of developing multiple primary cutaneous squamous cell carcinomas (CSCCs). In more recent years, large prospective randomized trials in patients with AKs have shown that each of the following therapies provides better complete clearance rates compared with placebo: topical fluorouracil (5-FU) with or without calcipotriol, topical Imiquimod, topical tirbanibulin, and photodynamic therapy (PDT). The NCCN panel currently assigns a preference for 5-FU based on data from a randomized trial which reported the cumulative probability of remaining free from treatment failure was significantly higher for 5-FU (74.7%) than imiquimod (53.9%), methyl aminolevulinate plus photodynamic therapy (MAL-PDT) (37.7%), or ingenol mebutate (28.9%). Topical tirbanibulin was added to the list of recommended treatment for AK based on results from two identically designed double-blind phase III trials in which patients received either tirbanibulin or vehicle ointment for the treatment of AKs on the face or scalp. In both trials, complete clearance by day 57 occurred in significantly more patients in the tirbanibulin group compared to the vehicle group. The utility of topical diclofenac is less clear, as efficacy results vary across large, randomized trials, with some studies reporting no significant difference between diclofenac/hyaluronan and hyaluronan alone. Diclofenac/hyaluronan has also been shown to be inferior to MAL-PDT and to 5-FU for the treatment of AKs. The panel therefore assigns category 2b for diclofenac in this setting.[4]

Per the American Academy of Dermatology Guidelines of care for the management of actinic keratosis, the literature on AK treatment supports a strong recommendation for field treatment with either 5-fluorouracil (5-FU) or imiquimod. Due to the various commercial preparations of these drugs, the treatment regimens studied often vary in terms of the concentration, dosing interval, and duration. The Work Group conditionally recommends the use of diclofenac, based on lower quality of evidence than that of the evidence supporting strong recommendations for the use of 5-FU or imiquimod.[5]

Two double-blind, vehicle-controlled clinical trials (NCT03285477 and NCT03285490) were conducted with 702 adult subjects with actinic keratosis on the face or scalp. Subjects enrolled had 4 to 8 clinically typical, visible, and discrete AK lesions in a contiguous area of 25 cm^2 on the face or scalp. Treatment groups were comparable across all demographics and baseline characteristics, including AK lesion count and distribution on the face or scalp. Subjects received 5 consecutive days of once daily treatment with either Klisyri (353) or vehicle control (349) to the treatment field. In the first study, complete clearance was observed in 44% of the patients treated with tirbanibulin versus 5% for the vehicle treated groups. In the second study, complete clearance was observed in 54% of the patients treated with tirbanibulin and 13% for vehicle treated groups. Subjects with complete (100%) clearance of AK lesions in the treatment area at Day 57 returned to the clinic for recurrence assessment every 3 months for a total of 12 months post-Day 57. Subjects who achieved 100% clearance of AK lesions in the treatment area at Day 57 continued to be followed for up to 12 months following Day 57 to determine the recurrence rate. Recurrence was defined as the proportion of subjects with any identified AK lesion (new or previous lesion) in the previously treated area who achieved 100% clearance at Day 57. Of the 174 subjects treated with Klisyri who were followed, the recurrence rate at 12 months post-Day 57 was 73%.[1]

Klisyri is supplied in a package of 5 single-dose packets, each packet containing 250 mg of tirbanibulin ointment 1%. A sufficient amount of Klisyri should be applied to evenly cover up to a 25 cm^2 treatment field on the face or scalp. The patient should use 1 single-dose packet per application, once daily, for 5 consecutive days.[1] The quantity limit is set at one package (5 packets) per month since new actinic keratoses may develop.

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Written by:	UM Development (RP)
Date Written:	12/2020
Revised:	05/2021 (no clinical changes), (VLS) 05/2022 (no clinical changes)
Reviewed:	Medical Affairs (CHART) 02/11/2021, 07/01/2021, (CHART) 06/30/2022 External Review: 02/2021, 08/2021, 08/2022

CRITERIA FOR APPROVAL

1	Is the requested drug being prescribed for the topical treatment of actinic keratosis on the face or scalp? [If yes, go to 2. If no, then no further questions.]	Yes	No
2	Has the patient experienced an inadequate treatment response, intolerance, or does the patient have a contraindication to ONE of the following: A) imiquimod 5 percent cream, B) fluorouracil cream or solution? [If yes, go to 3. If no, then no further questions.]	Yes	No
3	Does the patient require more than the plan allowance of 5 packets per month? [No further questions] [RPh Note: If yes, then deny and enter a partial approval for 5 packets / 25 days of Klisyri.]	Yes	No

Mapping Instructions			
	Yes	**No**	**DENIAL REASONS**
1.	Go to 2	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have actinic keratosis on the face or scalp. Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]
2.	Go to 3	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have tried imiquimod 5 percent cream or fluorouracil cream/solution and it did not work for you, or you cannot use it. Your request has been denied based on the information we have. [Short Description: No inadequate response, intolerance or contraindication to imiquimod 5 percent cream, topical fluorouracil cream/solution]
3.	Deny	Approve, 12 Months, PA approved for 12 month(s), 5 packets per 25 days.	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 5 packets per month with the requested drug and strength. Your request has been partially approved. You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity]

PRIOR AUTHORIZATION CRITERIA

BRAND NAME*
(generic)

KONVOMEP
(omeprazole/sodium bicarbonate)

ZEGERID
(omeprazole/sodium bicarbonate)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization with Quantity Limit ***Ref # 1518-C***

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Konvomep is indicated in adults for:

- Short term treatment (4-8 weeks) of active benign gastric ulcer.
- Reduction of risk of upper gastrointestinal (GI) bleeding in critically ill adult patients.

Zegerid for oral suspension and Zegerid capsules are indicated in adults for the:

- Short-term treatment of active duodenal ulcer. Most patients heal within four weeks. Some patients may require an additional four weeks of therapy.
- Short-term treatment (4 to 8 weeks) of active benign gastric ulcer.
- Treatment of heartburn and other symptoms associated with GERD for up to 4 weeks.
- Short-term treatment (4 to 8 weeks) of EE due to acid-mediated GERD which has been diagnosed by endoscopy in adults.
    - The efficacy of Zegerid used for longer than 8 weeks in patients with EE has not been established. If a patient does not respond to 8 weeks of treatment, an additional 4 weeks of treatment may be given. If there is recurrence of EE or GERD symptoms (e.g., heartburn), additional 4 to 8 week courses of Zegerid may be considered.
- Maintenance of healing of EE due to acid-mediated GERD. Controlled studies do not extend beyond 12 months

Zegerid for oral suspension is indicated in adults for the:

- Reduction of risk of upper GI bleeding in critically ill adult patients.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has experienced an inadequate treatment response, intolerance, or a contraindication to THREE generic proton pump inhibitors. Documentation is required for approval.

AND

- The request is for Zegerid **AND**
    - The requested drug is being prescribed for any of the following: A) Gastroesophageal reflux disease (GERD), B) Duodenal ulcer, C) Gastric ulcer, D) Short-term treatment of erosive esophagitis
      OR
    - The requested drug is being prescribed for the maintenance of healing of erosive esophagitis

OR

- The request is for Konvomep **AND**
    - The requested drug is being prescribed for treatment of gastric ulcer

Quantity Limits apply.

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Konvomep is indicated in adults for the short-term treatment of active benign gastric ulcer and reduction of risk of upper gastrointestinal (GI) bleeding in critically ill patients. Zegerid is indicated in adults for the short-term treatment of active duodenal ulcer, short-term treatment of active benign gastric ulcer, treatment of heartburn and other symptoms associated with GERD, short-term treatment of erosive esophagitis (EE) due to acid-mediated GERD which has been diagnosed by endoscopy in adults, and the maintenance of healing of EE due to acid-mediated GERD. Zegerid for oral suspension is indicated in adults for the reduction of risk of upper GI bleeding in critically ill patients.[1-4] The use of Konvomep and Zegerid for the risk reduction of upper gastrointestinal bleeding in critically ill patients will not be addressed in the criteria because this indication is not applicable to an outpatient benefit.

Proton pump inhibitors (PPIs) are the therapy of choice for symptom relief and healing of erosive esophagitis.[5] PPIs are also used in the treatment of peptic ulcer disease.[6] There are currently seven available PPIs (omeprazole, lansoprazole, omeprazole-sodium bicarbonate, rabeprazole, pantoprazole, esomeprazole, dexlansoprazole). There are no major differences in efficacy between the different PPIs.[5] The patient must experience an inadequate treatment response, intolerance or contraindication to three generic proton pump inhibitors.

The recommended dosage regimen for Zegerid for a duodenal ulcer is 20 mg once daily for four weeks and 40 mg once daily for four to eight weeks for a benign gastric ulcer. The recommended dosage regimen for Zegerid for symptomatic gastroesophageal reflux disease (GERD) with no esophageal erosions is 20 mg once daily for 4 weeks, and 20 mg once daily for erosive esophagitis four to eight weeks. Some patients may require an additional 4 weeks of therapy if they do not respond within the usual treatment duration.[2-4] The recommended dosage regimen for Konvomep for benign gastric ulcer is 40 mg once daily for four to eight weeks.[1] Therefore, the duration of approval will be 3 months for GERD, duodenal ulcer, gastric ulcer, and short-term treatment of erosive esophagitis. The duration of approval for the maintenance of healing of erosive esophagitis will be 12 months because controlled studies do not extend beyond 12 months of therapy.[2-4]

Zegerid is available as a capsule and as a powder for oral suspension in 20 mg and 40 mg strengths of omeprazole for adult use. Each 20 mg and 40 mg capsule of Zegerid contains 1,100 mg (13 mEq) of sodium bicarbonate and each 20 mg and 40 mg packet for oral suspension of Zegerid contains 1,680 mg (20 mEq) of sodium bicarbonate. Due to the sodium bicarbonate content, two packets of 20 mg Zegerid for oral suspension are not interchangeable with one packet of 40 mg Zegerid for oral suspension and two 20 mg Zegerid capsules are not interchangeable with one 40 mg Zegerid capsule. Konvomep is available for oral suspension: 2 mg omeprazole and 84 mg sodium bicarbonate per mL of a pink to red hazy,strawberry-flavored liquid after reconstitution in 90 mL, 150 mL, or 300 mL bottles. Each Konvomep kit contains a bottle of omeprazole as a white to off-white powder and a strawberry-flavored diluent containing sodium bicarbonate as a slightly hazy red liquid. All recommended doses throughout the labeling are based upon omeprazole. The sodium content of Konvomep and Zegerid should be taken into consideration when prescribing this product[1-4] Therefore, the quantity of 20 mL of Konvomep, one packet of Zegerid for oral suspension and one capsule of Zegerid per day will apply.

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Date Written:	09/2016
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Reviewed:	Medical Affairs: (AN) 09/2016, 09/2017; (CHART) 9/26/2019, 09/24/2020, 01/28/2021, 02/03/2022, 08/15/2022 External Review: 12/2016, 12/2017, 12/2018, 12/2019, 12/2020, 06/2021, 06/2022, (FYI) 10/2022

CRITERIA FOR APPROVAL

1	Has the patient experienced an inadequate treatment response, intolerance, or does the patient have a contraindication to THREE generic proton pump inhibitors? [If yes, then documentation is required for approval.] Document the drug names: _____ [If no, then no further questions.]	Yes	No
2	Is this request for Zegerid? [If no, the skip to question 7.]	Yes	No
3	Is the requested drug being prescribed for any of the following: A) Gastroesophageal reflux disease (GERD), B) Duodenal ulcer, C) Gastric ulcer, D) Short-term treatment of erosive esophagitis? [If no, then skip to question 5.]	Yes	No
4	Does the patient require more than the plan allowance of 30 capsules or 30 packets for oral suspension per month? [No further questions.] [RPh Note: If yes, then deny and enter partial approval of 30 capsules or packets / 25 days or 90 capsules or packets / 75 days of Zegerid.]	Yes	No
5	Is the requested drug being prescribed for the maintenance of healing of erosive esophagitis? [If no, then no further questions.]	Yes	No
6	Does the patient require more than the plan allowance of 30 capsules or 30 packets for oral suspension per month? [No further questions.] [RPh Note: If yes, then deny and enter partial approval of 30 capsules or packets / 25 days or 90 capsules or packets / 75 days of Zegerid.]	Yes	No
7	Is the requested drug being prescribed for the short-term treatment of gastric ulcer? [If no, then no further questions.]	Yes	No
8	Does the patient require more than the plan allowance of 600 mL of Konvomep per month? [RPh Note: If yes, then deny and enter partial approval of 600 mL / 25 days or 1800 mL / 75 days of Konvomep.]	Yes	No

Mapping Instructions

	Yes	No	DENIAL REASONS – DO NOT USE FOR MEDICARE PART D
1.	Go to 2	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have tried THREE generic proton pump inhibitors and they did not work for you, or you cannot use them. Supporting documentation must be submitted. Your request has been denied based on the information we have. [Short Description: No documentation of trial of 3 generic PPIs.]
2.	Go to 3	Go to 7	
3.	Go to 4	Go to 5	
4.	Deny	Approve 3 months, 30 capsules or packets / 25 days or 90 capsules or packets / 75 days	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 30 capsules or packets per month of the requested drug. You have been approved for the maximum quantity that your plan covers for a duration of 3 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity of Zegerid, 3 month]
5.	Go to 6	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have any of these conditions: - Gastroesophageal reflux disease (GERD) - Duodenal ulcer - Gastric ulcer - Erosive esophagitis that needs short-term treatment - Erosive esophagitis that needs maintenance of healing Your request has been denied based on the information we have. [Short Description: No approvable diagnosis for Zegerid]
6.	Deny	Approve 12 months, 30 capsules or packets / 25 days or 90 capsules or packets / 75 days	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 30 capsules or packets per month of the requested drug. You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity of Zegerid, 12 month]
7.	Go to 8	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have a gastric ulcer Your request has been denied based on the information we have. [Short Description: No approvable diagnosis for Konvomep]
8.	Deny	Approve, 3 months, 600 mL / 25 days or 1800 mL/ 75 days	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 600 mL per month of the requested drug. You have been approved for the maximum quantity that your plan covers for a duration of 3 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity of Konvomep, 3 month]

Reference number(s)
2160-A

SPECIALTY GUIDELINE MANAGEMENT

KORLYM (mifepristone)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Korlym is a cortisol receptor blocker indicated to control hyperglycemia secondary to hypercortisolism in adult patients with endogenous Cushing's syndrome who have type 2 diabetes mellitus or glucose intolerance and have failed surgery or are not candidates for surgery.

Limitations of Use: Korlym should not be used in the treatment of patients with type 2 diabetes unless it is secondary to Cushing's syndrome.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: pretreatment hemoglobin A1C level (for initial requests)

III. CRITERIA FOR INITIAL APPROVAL

Cushing's syndrome/disease
Authorization of 6 months may be granted for treatment of Cushing's syndrome/disease when all of the following criteria are met:
A. Member has type 2 diabetes mellitus or glucose intolerance
B. Korlym is being prescribed to control hyperglycemia secondary to hypercortisolism
C. Member has had surgery that was not curative OR member is not a candidate for surgery
D. If the member is able to become pregnant, a negative pregnancy test is required before initiating therapy

IV. CONTINUATION OF THERAPY

Cushing's syndrome/disease
Authorization of 12 months may be granted if the member has achieved or maintained adequate positive response, or there is improvement in signs and symptoms of the condition.

V. REFERENCES

1. Korlym [package insert]. Menlo Park, CA: Corcept Therapeutics Incorporated; November 2019.
2. Nieman LK, Biller BM, Findling JW, et al. Treatment of Cushing's Syndrome: An Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab*. 2015;100(8):2807-2831. doi:10.1210/jc.2015-1818
3. Fleseriu M, Auchus R, Bancos I, et al. Consensus on Diagnosis and Management of Cushing's Disease: A Guideline Update. *Lancet Diabetes Endocrinol*. 2021;9(12):847-875. doi:10.1016/S2213-8587(21)00235-7

Reference number(s)
3770-A

SPECIALTY GUIDELINE MANAGEMENT

KOSELUGO (selumetinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
Koselugo is indicated for the treatment of pediatric patients 2 years of age and older with neurofibromatosis type 1 (NF1) who have symptomatic, inoperable plexiform neurofibromas (PN).

B. Compendial Uses
1. Pilocytic astrocytoma
2. Langerhans cell histiocytosis

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: Documentation of BRAF mutation status, where applicable.

III. CRITERIA FOR INITIAL APPROVAL

A. Neurofibromatosis type 1
Authorization of 12 months may be granted for treatment of pediatric members 2 years of age and older with neurofibromatosis type 1 (NF1) who have symptomatic, inoperable plexiform neurofibromas (PN).

B. Pilocytic Astrocytoma
Authorization of 12 months may be granted for treatment of recurrent or progressive pilocytic astrocytoma with a BRAF fusion or BRAF V600E activating mutation, as a single agent.

C. Langerhans Cell Histiocytosis
Authorization of 12 months may be granted as a single agent for treatment of Langerhans cell histiocytosis.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

V. REFERENCES

1. Koselugo [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; December 2021.
2. The NCCN Drugs & Biologics Compendium® © 2022 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed June 6, 2022.

Reference number(s)
5699-A

SPECIALTY GUIDELINE MANAGEMENT

KRAZATI (adagrasib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication
Krazati is indicated for the treatment of adult patients with Kirsten rat sarcoma (KRAS) G12C-mutated locally advanced or metastatic non-small cell lung cancer (NSCLC), as determined by an FDA approved test, who have received at least one prior systemic therapy.

B. Compendial Uses
1. Recurrent KRAS mutation positive NSCLC
2. Pancreatic adenocarcinoma

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
Documentation of the presence of KRAS G12C mutation

III. CRITERIA FOR INITIAL APPROVAL

A. NSCLC
Authorization of 12 months may be granted for treatment of recurrent, advanced, or metastatic NSCLC when both of the following criteria are met:
1. The tumor or plasma specimen is positive for the KRAS G12C mutation
2. The member has received at least one prior systemic therapy

B. Pancreatic Adenocarcinoma
Authorization of 12 months may be granted for treatment of recurrent, locally advanced or metastatic pancreatic adenocarcinoma when all of the following criteria are met:
1. The tumor or plasma specimen is positive for the KRAS G12C mutation
2. Member has an Eastern Cooperative Oncology Group (ECOG) performance status of 0-2
3. The requested medication will be used as a single agent.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

V. REFERENCES

1. Krazati [package insert]. San Diego, CA: Mirati Therapeutics, Inc.; December 2022.
2. The NCCN Drugs & Biologics Compendium® © 2023 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed May 5, 2023

Reference number(s)
1902-A

SPECIALTY GUIDELINE MANAGEMENT

TYKERB (lapatinib)
lapatinib

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
Tykerb is indicated in combination with:
1. Capecitabine for the treatment of patients with advanced or metastatic breast cancer whose tumors overexpress human epidermal growth factor receptor 2 (HER2) and who have received prior therapy including an anthracycline, a taxane, and trastuzumab
Limitations of Use: Patients should have disease progression on trastuzumab prior to initiation of treatment with Tykerb in combination with capecitabine.
2. Letrozole for the treatment of postmenopausal women with hormone receptor (HR)-positive metastatic breast cancer that overexpresses the HER2 receptor for whom hormonal therapy is indicated

B. Compendial Uses
1. Breast cancer
2. Central Nervous System (CNS) metastases from breast cancer
3. Recurrent epidermal growth factor receptor (EGFR)-positive chordoma
4. HER2-amplified and RAS and BRAF wild-type colorectal cancer in combination with trastuzumab

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: Hormone receptor status, HER2 status, RAS and BRAF mutation status, EGFR mutation testing results (where applicable).

III. CRITERIA FOR INITIAL APPROVAL

A. Breast cancer
Authorization of 12 months may be granted for treatment of breast cancer with no response to preoperative systemic therapy or recurrent, advanced, or metastatic HER2-positive breast cancer when any of the following criteria are met:
1. The requested medication is used in combination with an aromatase inhibitor (e.g., letrozole, anastrozole, or exemestane) either with or without trastuzumab for the treatment of hormone receptor-positive disease; or
2. The requested medication will be used in combination with capecitabine or trastuzumab.

B. Central nervous system metastases (CNS) from breast cancer
Authorization of 12 months may be granted for treatment of brain metastases from HER2-positive breast cancer in combination with capecitabine.

C. Chordoma
Authorization of 12 months may be granted for treatment of EGFR-positive recurrent chordoma, as a single agent.

D. Colorectal Cancer
Authorization of 12 months may be granted for treatment of colorectal cancer (including appendiceal adenocarcinoma) with HER2-amplified and RAS and BRAF wild-type disease in combination with trastuzumab if no previous treatment with a HER2 inhibitor when either of the following are met:
1. Member is not appropriate for intensive therapy
2. The requested medication will be used as subsequent therapy for progression of advanced or metastatic disease.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

V. REFERENCES

1. Tykerb [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; March 2022.
2. Lapatinib [package insert]. Baltimore, MD: Lupin Pharmaceuticals, Inc.; July 2022.
3. The NCCN Drugs & Biologics Compendium 2022 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed November 6, 2022.

Reference number(s)
2232-A

SPECIALTY GUIDELINE MANAGEMENT

REVLIMID (lenalidomide)
lenalidomide

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
Revlimid is indicated for the treatment of adult patients with:
1. Multiple myeloma (MM) in combination with dexamethasone.
2. Multiple myeloma (MM), as maintenance following autologous hematopoietic stem cell transplantation (auto-HSCT).
3. Transfusion-dependent anemia due to low- or intermediate-1-risk myelodysplastic syndromes (MDS) associated with a deletion 5q cytogenetic abnormality with or without additional cytogenetic abnormalities.
4. Mantle cell lymphoma (MCL) whose disease has relapsed or progressed after two prior therapies, one of which included bortezomib.
5. Previously treated follicular lymphoma (FL), in combination with a rituximab product.
6. Previously treated marginal zone lymphoma (MZL), in combination with a rituximab product.

B. Compendial Uses
1. Multiple myeloma
2. Systemic light chain amyloidosis
3. Classic Hodgkin lymphoma
4. Myelodysplastic syndrome without the 5q deletion cytogenetic abnormality
5. Myelofibrosis-associated anemia
6. POEMS (polyneuropathy, organomegaly, endocrinopathy, monoclonal protein, skin changes) syndrome
7. Myelodysplastic syndrome/myeloproliferative neoplasms
8. T-cell Lymphomas
    a. Peripheral T-Cell Lymphomas not otherwise specified
    b. Angioimmunoblastic T-cell lymphoma
    c. Enteropathy-associated T-cell lymphoma
    d. Monomorphic epitheliotropic intestinal T-cell lymphoma
    e. Nodal peripheral T-cell lymphoma with TFH phenotype
    f. Follicular T-cell lymphoma
    g. Adult T-cell leukemia/lymphoma
    h. Hepatosplenic T-cell lymphoma
9. Primary central nervous system (CNS) lymphoma
10. Chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL)
11. B-Cell Lymphomas

a. AIDS-related B-Cell lymphomas, including non-germinal center diffuse large B-cell lymphoma, AIDS-related diffuse large B-cell lymphoma, primary effusion lymphoma, HHV8+ diffuse large B-cell lymphoma, and AIDS-related plasmablastic lymphoma
b. Monomorphic post-transplant lymphoproliferative disorder
c. Diffuse large B-cell lymphoma
d. Follicular lymphoma
e. Marginal zone lymphoma with any of the following subtypes: Nongastric/Gastric mucosa associated lymphoid tissue (MALT) lymphoma, splenic/nodal marginal zone lymphoma
f. Multicentric Castleman disease
g. High-grade B-cell lymphomas
h. Histologic transformation of indolent lymphomas to diffuse large B-cell lymphoma
i. Mantle cell lymphoma

12. Kaposi Sarcoma
13. Smoldering myeloma
14. Langerhans cell histiocytosis

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Multiple myeloma

Authorization of 12 months may be granted for treatment of multiple myeloma.

B. T-cell Lymphomas

Authorization of 12 months may be granted for treatment of T-cell lymphoma, as a single agent, with any of the following subtypes:

1. Peripheral T-Cell Lymphomas not otherwise specified as initial palliative therapy or subsequent therapy.
2. Angioimmunoblastic T-cell lymphoma as initial palliative therapy or subsequent therapy.
3. Enteropathy-associated T-cell lymphoma as initial palliative therapy or subsequent therapy.
4. Monomorphic epitheliotropic intestinal T-cell lymphoma as initial palliative therapy or subsequent therapy.
5. Nodal peripheral T-cell lymphoma with TFH phenotype as initial palliative therapy or subsequent therapy.
6. Follicular T-cell lymphoma as initial palliative therapy or subsequent therapy.
7. Adult T-cell leukemia/lymphoma as subsequent therapy.
8. Hepatosplenic T-cell lymphoma as subsequent therapy.

C. Primary central nervous system (CNS) lymphoma

Authorization of 12 months may be granted for treatment of primary central nervous system (CNS) lymphoma as a single agent or in combination with rituximab.

D. Chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL)

Authorization of 12 months may be granted for treatment of CLL/SLL as a single agent or in combination with rituximab.

E. B-Cell Lymphomas

Authorization of 12 months may be granted for treatment of B-cell lymphoma with any of the following subtypes:

1. AIDS-related B-Cell lymphomas, including non-germinal center diffuse large B-cell lymphoma, AIDS-related diffuse large B-cell lymphoma, primary effusion lymphoma, HHV8+ diffuse large B-cell lymphoma, and AIDS-related plasmablastic lymphoma, as subsequent therapy.
2. Monomorphic post-transplant lymphoproliferative disorder as subsequent therapy.
3. Diffuse large B-cell lymphoma as subsequent therapy.
4. Follicular lymphoma.
5. Marginal zone lymphoma with any of the following subtypes: Nongastric/Gastric mucosa-associated lymphoid tissue (MALT) lymphoma, splenic/nodal marginal zone lymphoma, as subsequent therapy.
6. Multicentric Castleman disease as subsequent therapy.
7. High-grade B-cell lymphomas as subsequent therapy.
8. Histologic transformation of indolent lymphomas to diffuse large B-cell lymphoma as subsequent therapy.
9. Mantle cell lymphoma.

F. Myelodysplastic syndrome
Authorization of 12 months may be granted for treatment of lower risk myelodysplastic syndrome (defined as Revised International Prognostic Scoring System (IPSS-R) (Very Low, Low, Intermediate), International Prognostic Scoring System (IPSS) (Low/Intermediate-1), WHO classification-based Prognostic Scoring System (WPSS) (Very Low, Low, Intermediate)) for those with symptomatic anemia.

G. Myelofibrosis-associated anemia
Authorization of 12 months may be granted for treatment of myelofibrosis-associated anemia when all of the following criteria are met:
1. The requested medication will be given in combination with prednisone.
2. The member has serum erythropoietin (EPO) levels of either of the following:
   a. 500 mU/mL or greater
   b. Less than 500 mU/mL and no response or loss of response to erythropoiesis-stimulating agents

H. Systemic light chain amyloidosis
Authorization of 12 months may be granted for treatment of systemic light chain amyloidosis.

I. Classic Hodgkin lymphoma
Authorization of 12 months may be granted for treatment of classic Hodgkin lymphoma that is refractory to at least 3 prior lines of therapy, as a single agent.

J. POEMS Syndrome
Authorization of 12 months may be granted for treatment of POEMS syndrome in combination with dexamethasone.

K. Myelodysplastic/myeloproliferative neoplasms
Authorization of 12 months may be granted for treatment of myelodysplastic/myeloproliferative neoplasms, as a single agent or in combination with a hypomethylating agent.

L. Kaposi Sarcoma
Authorization of 12 months may be granted for treatment of Kaposi sarcoma as subsequent therapy.

M. Smoldering Myeloma
Authorization of 12 months may be granted for treatment of asymptomatic high-risk smoldering myeloma.

N. Langerhans Cell Histiocytosis
Authorization of 12 months may be granted for treatment of Langerhans cell histiocytosis as a single agent.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

IV. REFERENCES

1. Revlimid [package insert]. Summit, NJ: Celgene Corporation; May 2022.
2. Lenalidomide [package insert]. Parsippany, NJ: Teva Pharmaceuticals; May 2022.
3. The NCCN Drugs & Biologics Compendium® © 2022 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed October 6, 2022.
4. Lexicomp Online®, Lexi-Drugs. Waltham, MA: UpToDate, Inc.; Updated October 4, 2022. http://online.lexi.com [available with subscription]. Accessed October 6, 2022.
5. DRUGDEX® System (electronic version). Micromedex Truven Health Analytics, Greenwood Village, Colorado, USA. Available at: http://www.micromedexsolutions.com. Accessed October 6, 2022.

Reference number
1865-A

SPECIALTY GUIDELINE MANAGEMENT

LENVIMA (lenvatinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Lenvima is indicated for the treatment of patients with locally recurrent or metastatic, progressive, radioactive iodine-refractory differentiated thyroid cancer (DTC).
2. Lenvima is indicated in combination with pembrolizumab for the first line treatment of adult patients with advanced renal cell carcinoma.
3. Lenvima is indicated in combination with everolimus, for the treatment of adult patients with advanced renal cell carcinoma (RCC) following one prior anti-angiogenic therapy.
4. Lenvima is indicated for the first-line treatment of patients with unresectable hepatocellular carcinoma (HCC).
5. Lenvima is indicated in combination with pembrolizumab, for the treatment of patients with advanced endometrial carcinoma (EC) that is mismatch repair proficient (pMMR), as determined by an FDA-approved test, or not microsatellite instability-high (MSI-H), who have disease progression following prior systemic therapy in any setting and are not candidates for curative surgery or radiation.

B. Compendial Uses

1. Medullary, follicular, oncocytic/Hurthle cell, or papillary thyroid carcinoma
2. HCC
3. Relapsed RCC
4. Recurrent endometrial carcinoma
5. Thymic carcinoma
6. Cutaneous melanoma

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: Documentation of laboratory report confirming mismatch repair (MMR) tumor status, where applicable.

III. CRITERIA FOR INITIAL APPROVAL

A. Thyroid carcinoma

Authorization of 12 months may be granted for treatment of thyroid carcinoma when any of the following criteria are met:

1. Member has follicular, oncocytic/Hürthle cell, or papillary thyroid carcinoma not amenable to radioactive iodine therapy (RAI).

2. Member has medullary thyroid carcinoma and has progressed on vandetanib (Caprelsa) or cabozantinib (Cometriq) OR these therapies are inappropriate

B. Renal Cell Carcinoma

Authorization of 12 months may be granted for treatment of advanced, relapsed or stage IV renal cell carcinoma when used in any of the following settings.

1. The requested drug will be used in combination with everolimus (Afinitor) and either of the following is met:
   i. The disease histology is predominantly clear cell and the member has used prior therapy OR
   ii. The disease histology is non-clear cell
2. The requested drug will be used in combination with pembrolizumab (Keytruda).

C. Hepatocellular Carcinoma

Authorization of 12 months may be granted for treatment of hepatocellular carcinoma as a single agent when any of the following criteria are met:

1. Member has unresectable disease and is not a transplant candidate
2. Member has local disease, inoperable by performance status, comorbidity, or with minimal or uncertain extrahepatic disease
3. Member has metastatic disease or extensive liver tumor burden

D. Endometrial Carcinoma

Authorization of 12 months may be granted for treatment of advanced, metastatic or recurrent endometrial carcinoma when used in combination with pembrolizumab (Keytruda) when either of the following are met:

1. The disease is mismatch repair proficient (pMMR)
2. The disease is mismatch repair deficient (dMMR) and has progressed following prior platinum-based chemotherapy

E. Thymic Carcinoma

Authorization of 12 months may be granted for treatment of thymic carcinoma when used as a single agent.

F. Cutaneous Melanoma

Authorization of 12 months may be granted for treatment of metastatic or unresectable cutaneous melanoma that has progressed following treatment with an anti-PD-1/PD-L1-based therapy, in combination with pembrolizumab.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

V. REFERENCES

1. Lenvima [package insert]. Nutley, NJ: Eisai Inc.; November 2022.
2. The NCCN Drugs & Biologics Compendium 2023 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed August 21, 2023.

3. National Comprehensive Cancer Network (NCCN) Guidelines: Thyroid Carcinoma V4.2023. National Comprehensive Cancer Network, Inc. https://www.nccn.org/professionals/physician_gls/pdf/thyroid.pdf. Accessed August 21, 2023.
4. Micromedex (electronic version). Truven Health Analytics. Greenwood Village, Colorado, USA https://www.micromedexsolutions.com/. Accessed August 21, 2023.

Reference number(s)
1929-A

SPECIALTY GUIDELINE MANAGEMENT

LEUKINE (sargramostim)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
1. Acute Myeloid Leukemia Following Induction Chemotherapy
   Leukine is indicated to shorten time to neutrophil recovery and to reduce the incidence of severe, life-threatening, or fatal infections following induction chemotherapy in adult patients 55 years and older with acute myeloid leukemia (AML).
2. Autologous Peripheral Blood Progenitor Cells Mobilization and Collection
   Leukine is indicated in adult patients with cancer undergoing autologous hematopoietic stem cell transplantation for the mobilization of hematopoietic progenitor cells into peripheral blood for collection by leukapheresis.
3. Autologous Peripheral Blood Progenitor Cell and Bone Marrow Transplantation
   Leukine is indicated for acceleration of myeloid reconstitution following autologous peripheral blood progenitor cell (PBPC) or bone marrow transplantation in adult and pediatric patients 2 years of age and older with non-Hodgkin's lymphoma (NHL), acute lymphoblastic leukemia (ALL) and Hodgkin's lymphoma (HL).
4. Allogeneic Bone Marrow Transplantation (BMT)
   Leukine is indicated for the acceleration of myeloid reconstitution in adult and pediatric patients 2 years of age and older undergoing allogeneic BMT from human leukocyte antigens (HLA)-matched related donors.
5. Allogenic or Autologous Bone Marrow Transplantation: Treatment of Delayed Neutrophil Recovery or Graft Failure
   Leukine is indicated for the treatment of adult and pediatric patients 2 years and older who have undergone allogeneic or autologous BMT in whom neutrophil recovery is delayed or failed.
6. Acute Exposure to Myelosuppressive Doses of Radiation (H-ARS)
   Leukine is indicated to increase survival in adult and pediatric patients from birth to 17 years of age acutely exposed to myelosuppressive doses of radiation (Hematopoietic Syndrome of Acute Radiation Syndrome [H-ARS]).

B. Compendial Uses
1. Prophylaxis and treatment of chemotherapy-induced febrile neutropenia in non-myeloid malignancies
2. Treatment of neutropenia and anemia in patients with myelodysplastic syndromes (MDS)
3. Acute myeloid leukemia
4. Agranulocytosis (non-chemotherapy drug induced)
5. Aplastic anemia
6. Neutropenia related to HIV/AIDS
7. Stem cell transplantation-related indications
8. Neuroblastoma

9. Severe chronic neutropenia (congenital, cyclic, or idiopathic)

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Primary Prophylaxis of Febrile Neutropenia

1. Documentation must be provided of the member's diagnosis and chemotherapeutic regimen.
2. If chemotherapeutic regimen has an intermediate risk of febrile neutropenia (10-19% [See Appendix B]), documentation must be provided outlining the member's risk factors that confirm the member is at high risk for febrile neutropenia.

III. CRITERIA FOR INITIAL APPROVAL

A. Neutropenia in cancer patients receiving myelosuppressive chemotherapy

Authorization of 6 months may be granted for prevention or treatment of febrile neutropenia when all of the following criteria are met (1, 2, and 3):

1. The requested medication will not be used in combination with other colony stimulating factors within any chemotherapy cycle.
2. The member will not be receiving chemotherapy and radiation therapy at the same time.
3. One of the following criteria is met (i, ii, or iii):
   - i. The requested medication will be used for primary prophylaxis in members with solid tumors or non-myeloid malignancies who have received, are currently receiving, or will be receiving myelosuppressive anti-cancer therapy that is expected to result in 20% or higher incidence of febrile neutropenia (FN) *(See Appendix A)* OR 10 – 19% risk of FN *(See Appendix B)* and who are considered to be at high risk of FN because of bone marrow compromise or co-morbidity, including any of the following (not an all-inclusive list):
     a. Active infections, open wounds, or recent surgery
     b. Age greater than or equal to 65 years
     c. Bone marrow involvement by tumor producing cytopenias
     d. Previous chemotherapy or radiation therapy
     e. Poor nutritional status
     f. Poor performance status
     g. Previous episodes of FN
     h. Other serious co-morbidities, including renal dysfunction, liver dysfunction, HIV infection, cardiovascular disease
     i. Persistent neutropenia
   - ii. The requested medication will be used for secondary prophylaxis in members with solid tumors or non-myeloid malignancies who experienced a febrile neutropenic complication or a dose-limiting neutropenic event (a nadir or day of treatment count impacting the planned dose of chemotherapy) from a prior cycle of similar chemotherapy, with the same dose and schedule planned for the current cycle (for which primary prophylaxis was not received).
   - iii. The requested medication will be used for treatment of high risk febrile neutropenia (FN) in members who have any of the following prognostic factors that are predictive of clinical deterioration:
     a. Age greater than 65 years
     b. Being hospitalized at the time of the development of fever
     c. Sepsis syndrome
     d. Invasive fungal infection
     e. Pneumonia or other clinically documented infection

f. Prolonged (neutropenia expected to last greater than 10 days) or profound (absolute neutrophil count less than 0.1 x 10^9/L) neutropenia
g. Prior episodes of febrile neutropenia

B. Neuroblastoma

Authorization of 6 months may be granted for treatment of high-risk neuroblastoma when used with either of the following:

1. Dinutuximab (Unituxin), interleukin-2 (aldesleukin [Proleukin]), and isotretinoin (13-cis-retinoic acid [RA])
2. Naxitamab-gqgk (Danyelza)

C. Other indications

Authorization of 6 months may be granted for members with any of the following indications:

1. Myelodysplastic syndrome (anemia or neutropenia)
2. Acute myeloid leukemia
3. Agranulocytosis (non-chemotherapy drug induced)
4. Aplastic anemia
5. Neutropenia related to HIV/AIDS
6. Stem cell transplantation-related indications
7. Severe chronic neutropenia (congenital, cyclic, or idiopathic)
8. Hematopoietic Syndrome of Acute Radiation Syndrome
   Treatment for radiation-induced myelosuppression following a radiological/nuclear incident

IV. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

V. APPENDIX

A. APPENDIX A: Selected Chemotherapy Regimens with an Incidence of Febrile Neutropenia of 20% or Higher*†

1. Acute Lymphoblastic Leukemia:
   Select ALL regimens as directed by treatment protocol (see NCCN guidelines ALL)
2. Bladder Cancer:
   i. Dose dense MVAC (methotrexate, vinblastine, doxorubicin, cisplatin)
   ii. CBDCa/Pac (carboplatin, paclitaxel)
3. Bone Cancer:
   i. VAI (vincristine, doxorubicin or dactinomycin, ifosfamide)
   ii. VDC-IE (vincristine, doxorubicin or dactinomycin, and cyclophosphamide alternating with ifosfamide and etoposide)
   iii. Cisplatin/doxorubicin
   iv. VDC (cyclophosphamide, vincristine, doxorubicin or dactinomycin)
   v. VIDE (vincristine, ifosfamide, doxorubicin or dactinomycin, etoposide)
4. Breast Cancer:
   i. Docetaxel + trastuzumab
   ii. Dose-dense AC (doxorubicin, cyclophosphamide) + paclitaxel (or dose dense paclitaxel)
   iii. TAC (docetaxel, doxorubicin, cyclophosphamide)
   iv. AT (doxorubicin, docetaxel)

v. Doc (docetaxel)
vi. TC (docetaxel, cyclophosphamide)
vii. TCH (docetaxel, carboplatin, trastuzumab)

5. Colorectal Cancer:
   FOLFOXIRI (fluorouracil, leucovorin, oxaliplatin, irinotecan)
6. Esophageal and Gastric Cancers:
   Docetaxel/cisplatin/fluorouracil
7. Head and Neck Squamous Cell Carcinoma
   TPF (docetaxel, cisplatin, 5-fluorouracil)
8. Hodgkin Lymphoma:
   i. Brentuximab vedotin + AVD (doxorubicin, vinblastine, dacarbazine)
   ii. Escalated BEACOPP (bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, prednisone)
9. Kidney Cancer:
   Doxorubicin/gemcitabine
10. Non-Hodgkin's Lymphoma:
    i. CHP (cyclophosphamide, doxorubicin, prednisone) + brentuximab vedotin
    ii. Dose-adjusted EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin)
    iii. ICE (ifosfamide, carboplatin, etoposide)
    iv. Dose-dense CHOP-14 (cyclophosphamide, doxorubicin, vincristine, prednisone) ± rituximab
    v. MINE (mesna, ifosfamide, mitoxantrone, etoposide)
    vi. DHAP (dexamethasone, cisplatin, cytarabine)
    vii. ESHAP (etoposide, methylprednisolone, cisplatin, cytarabine (Ara-C))
    viii. HyperCVAD ± rituximab (cyclophosphamide, vincristine, doxorubicin, dexamethasone ± rituximab)
    ix. VAPEC-B (vincristine, doxorubicin, prednisolone, etoposide, cyclophosphamide, bleomycin)
11. Melanoma:
    Dacarbazine-based combination with IL-2, interferon alpha (dacarbazine, cisplatin, vinblastine, IL-2, interferon alfa)
12. Multiple Myeloma:
    i. VTD-PACE (dexamethasone/thalidomide/cisplatin/doxorubicin/cyclophosphamide/etoposide + bortezomib)
    ii. DT-PACE (dexamethasone/thalidomide/cisplatin/doxorubicin/cyclophosphamide/etoposide)
13. Ovarian Cancer:
    i. Topotecan
    ii. Docetaxel
14. Pancreatic Cancer:
    FOLFIRINOX (fluorouracil, leucovorin, irinotecan, oxaliplatin)
15. Soft Tissue Sarcoma:
    i. MAID (mesna, doxorubicin, ifosfamide, dacarbazine)
    ii. Doxorubicin
    iii. Ifosfamide/doxorubicin
16. Small Cell Lung Cancer:
    i. Top (topotecan)
    ii. CAV (cyclophosphamide, doxorubicin, vincristine)
17. Testicular Cancer:
    i. VeIP (vinblastine, ifosfamide, cisplatin)
    ii. VIP (etoposide, ifosfamide, cisplatin)
    iii. TIP (paclitaxel, ifosfamide, cisplatin)

*Applies to chemotherapy regimens with or without monoclonal antibodies (e.g., trastuzumab, rituximab)

† This list is not comprehensive; there are other agents/regimens that have an intermediate/high risk for development of febrile neutropenia.

B. APPENDIX B: Selected Chemotherapy Regimens with an Incidence of Febrile Neutropenia of 10% to 19%*†

1. Occult Primary – Adenocarcinoma:
   Gemcitabine/docetaxel
2. Breast Cancer:
   i. Docetaxel
   ii. CMF classic (cyclophosphamide, methotrexate, fluorouracil)
   iii. CA (doxorubicin, cyclophosphamide) (60 mg/m2) (hospitalized)
   iv. AC (doxorubicin, cyclophosphamide) + sequential docetaxel (taxane portion only)
   v. AC + sequential docetaxel + trastuzumab
   vi. A (doxorubicin) (75 mg/m2)
   vii. AC (doxorubicin, cyclophosphamide)
   viii. CapDoc (capecitabine, docetaxel)
   ix. Paclitaxel every 21 days
3. Cervical Cancer:
   i. Irinotecan
   ii. Cisplatin/topotecan
   iii. Paclitaxel/cisplatin
   iv. Topotecan
4. Colorectal Cancer:
   i. FL (fluorouracil, leucovorin)
   ii. CPT-11 (irinotecan) (350 mg/m2 q 3 wk)
   iii. FOLFOX (fluorouracil, leucovorin, oxaliplatin)
5. Esophageal and Gastric Cancers:
   i. Irinotecan/cisplatin
   ii. Epirubicin/cisplatin/5-fluorouracil
   iii. Epirubicin/cisplatin/capecitabine
6. Non-Hodgkin's Lymphomas:
   i. EPOCH-IT chemotherapy
   ii. GDP (gemcitabine, dexamethasone, cisplatin/carboplatin)
   iii. GDP (gemcitabine, dexamethasone, cisplatin/carboplatin) + rituximab
   iv. FMR (fludarabine, mitoxantrone, rituximab)
   v. CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) including regimens with pegylated liposomal doxorubicin
   vi. CHOP + rituximab (cyclophosphamide, doxorubicin, vincristine, prednisone, rituximab) including regimens with pegylated liposomal doxorubicin
   vii. Bendamustine
7. Non-Small Cell Lung Cancer:
   i. Cisplatin/paclitaxel
   ii. Cisplatin/vinorelbine
   iii. Cisplatin/docetaxel
   iv. Cisplatin/etoposide
   v. Carboplatin/paclitaxel
   vi. Docetaxel
8. Ovarian Cancer:
   Carboplatin/docetaxel
9. Prostate Cancer:

Cabazitaxel
10. Small Cell Lung Cancer:
    Etoposide/carboplatin
11. Testicular Cancer:
    i. BEP (bleomycin, etoposide, cisplatin)
    ii. Etoposide/cisplatin
12. Uterine Sarcoma:
    Docetaxel

*Applies to chemotherapy regimens with or without monoclonal antibodies (e.g., trastuzumab, rituximab)
† This list is not comprehensive; there are other agents/regimens that have an intermediate/high risk for development of febrile neutropenia.

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Reference number(s)
1989-A, 1990-A, 2117-A

SPECIALTY GUIDELINE MANAGEMENT

leuprolide acetate injection

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication
Leuprolide acetate is indicated in the palliative treatment of advanced prostate cancer.

B. Compendial Uses
1. Central precocious puberty (CPP)
2. Use as a stimulation test to confirm the diagnosis of CPP
3. Use in combination with growth hormone for children with growth failure and advancing puberty
4. Prostate cancer
5. Inhibition of premature luteinizing hormone (LH) surges in members undergoing ovulation induction or assisted reproductive technology
6. Androgen receptor positive salivary gland tumors
7. Triggering of oocyte maturation and ovulation in assisted reproductive technology cycle

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: For central precocious puberty, laboratory report or medical record of a pubertal response to a gonadotropin releasing hormone (GnRH) agonist test or a pubertal level of a third-generation luteinizing hormone (LH) assay.

III. CRITERIA FOR INITIAL APPROVAL

A. Central precocious puberty (CPP)
1. Authorization of 12 months may be granted for treatment of CPP in a female member when all of the following criteria are met:
   i. Intracranial tumor has been evaluated by appropriate lab tests and diagnostic imaging (e.g., computed tomography [CT] scan, magnetic resonance imaging [MRI]).
   ii. The diagnosis of CPP has been confirmed by a pubertal response to a gonadotropin releasing hormone (GnRH) agonist test or a pubertal level of a third-generation luteinizing hormone (LH) assay.
   iii. The assessment of bone age versus chronological age supports the diagnosis of CPP.
   iv. The member was less than 8 years of age at the onset of secondary sexual characteristics.
2. Authorization of 12 months may be granted for treatment of CPP in a male member when all of the following criteria are met:
   i. Intracranial tumor has been evaluated by appropriate lab tests and diagnostic imaging (e.g., CT scan, MRI).

ii. The diagnosis of CPP has been confirmed by a pubertal response to a GnRH agonist test or a pubertal level of a third-generation LH assay.
iii. The assessment of bone age versus chronological age supports the diagnosis of CPP.
iv. The member was less than 9 years of age at the onset of secondary sexual characteristics.

B. Stimulation test for CPP diagnosis
Authorization of one dose may be granted for use as a stimulation test to confirm the diagnosis of CPP.

C. Advancing puberty and growth failure
Authorization of 12 months may be granted for treatment of advancing puberty and growth failure in a pediatric member when leuprolide acetate is used in combination with growth hormone.

D. Prostate cancer
Authorization of 12 months may be granted for treatment of prostate cancer.

E. Salivary gland tumors
Authorization of 12 months may be granted for treatment of recurrent salivary gland tumors as a single agent when the tumor is androgen receptor positive.

F. Inhibition of premature luteinizing hormone (LH) surge‡
Authorization of 12 months may be granted for the inhibition of premature LH surge in a member undergoing ovulation induction or assisted reproductive technology (ART).

G. Oocyte maturation and ovulation trigger‡
Authorization of 12 months may be granted for the triggering of oocyte maturation and ovulation in members undergoing ovulation induction or assisted reproductive technology (ART).

‡ Specialty Guideline Management coverage review will be bypassed for leuprolide if it is being requested for a procedure that has been approved under a member's medical benefit plan. Such members will be exempt from the requirements in Section III. A medical authorization number and confirmation of the approved procedure(s) will be required. *NOTE: Some plans may opt-out of medical benefit alignment. Members receiving coverage under such plans must meet the requirements in Section III.*

IV. CONTINUATION OF THERAPY

A. Central precocious puberty
1. Authorization of up to 12 months may be granted for continuation of therapy for CPP in a female member if the member is currently less than 12 years of age and the member meets both of the following:
   i. The member is currently receiving the requested medication through a paid pharmacy or medical benefit.
   ii. The member is not experiencing treatment failure (e.g., clinical pubertal progression, lack of growth deceleration, continued excessive bone age advancement).
2. Authorization of up to 12 months may be granted for continuation of therapy for CPP in a male member if the member is currently less than 13 years of age and the member meets both of the following:
   i. The member is currently receiving the requested medication through a paid pharmacy or medical benefit.
   ii. The member is not experiencing treatment failure (e.g., clinical pubertal progression, lack of growth deceleration, continued excessive bone age advancement).

B. Salivary gland tumors

Authorization of 12 months may be granted for continued treatment of salivary gland tumors in members requesting authorization who are experiencing clinical benefit to therapy and who have not experienced an unacceptable toxicity.

C. Prostate cancer

Authorization of 12 months may be granted for continued treatment of prostate cancer in members requesting authorization who are experiencing clinical benefit to therapy (e.g., serum testosterone less than 50 ng/dL) and who have not experienced an unacceptable toxicity.

D. Other indications

All members (including new members) requesting authorization for continuation of therapy for the specified indications below must meet all initial authorization criteria:

1. Stimulation test for CPP diagnosis
2. Advancing puberty and growth failure
3. Inhibition of premature LH surge
4. Oocyte maturation and ovulation trigger

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QUANTITY LIMIT CRITERIA

DRUG CLASS	**LIDOCAINE, LIDOCAINE-PRILOCAINE, LIDOCAINE-TETRACAINE DERMATOLOGICAL TOPICAL**
BRAND NAME* (generic)	
	(lidocaine HCl 2% gel)
	(lidocaine HCl-collagen-aloe vera 2% gel)
	(lidocaine HCl 4% gel)
	(lidocaine HCl urethral/mucosal 2% gel)
	(lidocaine HCl urethral/mucosal 2% gel prefilled syringe)
	(lidocaine HCl 4% solution)
	(lidocaine 5% ointment)
	(lidocaine 2.5% and prilocaine 2.5% cream)
	PLIAGLIS (lidocaine and tetracaine 7-7% cream)
	SYNERA (lidocaine and tetracaine 70-70mg patch)
Status: CVS Caremark Criteria	
Type: Quantity Limit	***Ref # 1329-H***

** Products that are listed in the target drug box include both brand and generic and all dosages forms and strengths unless otherwise stated.*
** OTC products are included.*

FDA-APPROVED INDICATIONS

Lidocaine HCl 2% Gel

Lidocaine HCl 2% Gel is intended to be used under the supervision of a healthcare professional to be used as local management of skin wounds, including pressure ulcers, venous stasis ulcers, first and second degree burns, and superficial wounds and scrapes.

Lidocaine HCl-Collagen-Aloe Vera 2% Gel

Lidocaine-collagen-aloe vera 2% gel is indicated for the local management of painful skin wounds, including:

- Pressure ulcers
- Venous stasis ulcers
- Superficial wounds and scrapes
- 1st and 2nd degree burns

Lidocaine HCl 4% Gel

Lidocaine 4% Gel is indicated for the following:

- Stage I - IV pressure ulcers
- Venous stasis ulcers
- Ulcerations caused by mixed vascular etiologies
- Diabetic skin ulcers
- First and second degree burns
- Post-surgical incisions, cuts and abrasions

Lidocaine HCl Urethral/Mucosal 2% Gel
Lidocaine HCl 2% jelly is indicated for prevention and control of pain in procedures involving the male and female urethra, for topical treatment of painful urethritis, and as an anesthetic lubricant for endotracheal intubation (oral and nasal).

Lidocaine HCl Urethral/Mucosal 2% Gel Prefilled Syringe
Lidocaine HCl jelly USP, 2% is indicated for prevention and control of pain in procedures involving the male and female urethra, for topical treatment of painful urethritis, and as an anesthetic lubricant for endotracheal intubation (oral and nasal).

Lidocaine HCl 4% Topical Solution
Lidocaine HCl 4% topical solution is indicated for the production of topical anesthesia of accessible mucous membranes of the oral and nasal cavities and proximal portions of the digestive tract.

Lidocaine 5% Ointment
Lidocaine 5% ointment is indicated for production of anesthesia of accessible mucous membranes of the oropharynx. It is also useful as an anesthetic lubricant for intubation and for the temporary relief of pain associated with minor burns, including sunburn, abrasions of the skin, and insect bites.

Lidocaine 2.5% and Prilocaine 2.5% Cream
Lidocaine and Prilocaine cream USP, 2.5%/2.5% (a eutectic mixture of lidocaine 2.5% and prilocaine 2.5%) is indicated as a topical anesthetic for use on:

- normal intact skin for local analgesia.
- genital mucous membranes for superficial minor surgery and as pretreatment for infiltration anesthesia.

Lidocaine and prilocaine cream is not recommended in any clinical situation when penetration or migration beyond the tympanic membrane into the middle ear is possible because of the ototoxic effects observed in animal studies.

Pliaglis (lidocaine and tetracaine 7-7% cream)
Pliaglis is indicated for use on intact skin in adults to provide topical local analgesia for superficial dermatological procedures such as dermal filler injection, pulsed dye laser therapy, facial laser resurfacing, and laser-assisted tattoo removal.

Synera (lidocaine and tetracaine 70-70mg patch)
Synera is a combination amide and ester local anesthetic indicated for use on intact skin to provide local dermal analgesia for superficial venous access and superficial dermatological procedures such as excision, electrodessication and shave biopsy of skin lesions.

RATIONALE
Lidocaine 2.5% and prilocaine 2.5% cream is indicated as a topical anesthetic for use on either normal intact skin for local analgesia, or genital mucous membranes for superficial minor surgery and as pretreatment for infiltration anesthesia. Lidocaine HCl urethral/mucosal 2% gel is indicated for prevention and control of pain in procedures involving the male and female urethra, for topical treatment of painful urethritis, and as an anesthetic lubricant for endotracheal intubation (oral and nasal). Lidocaine 2% gel and Lidocaine-collagen-aloe vera 2% gel is indicated for the local management of painful skin wounds, including: pressure ulcers, venous stasis ulcers, superficial wounds and scrapes, 1st and 2nd degree burns. Lidocaine HCl 4% gel is indicated for any of the following: Stage I - IV pressure ulcers, Venous stasis ulcers, Ulcerations caused by mixed vascular etiologies, Diabetic skin ulcers, First and second degree burns, Post-surgical incisions, cuts and abrasions. Lidocaine 5% ointment is indicated for production of anesthesia of accessible mucous membranes of the

oropharynx. It is also useful as an anesthetic lubricant for intubation and for the temporary relief of pain associated with minor burns, including sunburn, abrasions of the skin, and insect bites. Lidocaine HCl 4% topical solution is indicated for the production of topical anesthesia of accessible mucous membranes of the oral and nasal cavities and proximal portions of the digestive tract. Pliaglis cream (lidocaine and tetracaine 7-7% cream) is indicated for use on intact skin in adults to provide topical local analgesia for superficial dermatological procedures such as dermal filler injection, pulsed dye laser therapy, facial laser resurfacing, and laser-assisted tattoo removal. Synera (lidocaine and tetracaine 70-70mg patch) is a combination amide and ester local anesthetic indicated for use on intact skin to provide local dermal analgesia for superficial venous access and superficial dermatological procedures such as excision, electrodessication and shave biopsy of skin lesions.

Lidocaine 2% gel, Lidocaine 4% gel, and Lidocaine HCl-collagen-aloe vera 2% gel are available as Medical Devices. A medical device is an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including a component part or accessory which is:

- recognized in the official National Formulary, or the United States Pharmacopoeia, or any supplement to them
- intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, or
- intended to affect the structure or any function of the body,

and which does not achieve any of its primary intended purposes through chemical action within or on the body and which is not dependent upon being metabolized for the achievement of any of its primary intended purposes.[13]

When Lidocaine topical products are used concomitantly with other products containing lidocaine, the total dose contributed by all formulations must be kept in mind. Although the incidence of adverse effects with topical Lidocaine is low, caution should be exercised, particularly when employing large amounts, since the incidence of adverse effects is directly proportional to the total dose of the local anesthetic agent administered. Life-threatening adverse events have been reported when topical anesthetics, like lidocaine, are used improperly.[11,12] Therefore, these products will be limited to a quantity sufficient for acute use.

Since manufacturer package sizes may vary, it is the discretion of the dispensing pharmacy to fill quantities per package size up to these quantity limits. In such cases the filling limit and day supply may be less than what is indicated.

If the patient is requesting more than the initial quantity limit the claim will reject with a message indicating that a prior authorization is required.

Lidocaine HCl 2% gel
Apply 7T Lido Gel to the wound and skin surrounding the wound 3-4 times daily.
Lidocaine HCl 2% gel is available as a Medical Device (K020540) 7T Lido gel in 85gm.

Lidocaine HCl-collagen-aloe vera 2% gel
Apply Lidotrex to the wound and skin surrounding the wound 3-4 times daily.
Lidocaine HCl-collagen-aloe vera 2% gel is available as a Medical Device (K020540) Lidotrex gel in 28.33gm.

Lidocaine HCl 4% gel
Apply a thin layer of LDO Plus to the wound surface and the skin immediately surrounding the wound 3-4 times daily.
Lidocaine HCl 4% gel is available as a Medical Device (K092086) LDO Plus in 30mL and as Astero gel in 30mL and 90mL.
Lidocaine HCl 4% gel is also available in other various package sizes. However, these package sizes will not be accommodated in the criteria.

Lidocaine HCl urethral/mucosal 2% gel
No more than 600mg (30mL) of lidocaine HCl should be given in any 12 hour period.
For children less than ten years who have a normal lean body mass and a normal lean body development, the maximum dose may be determined by the application of one of the standard pediatric drug formulas (e.g., Clark's rule). For example, in a child of five years weighing 50lbs., the dose of lidocaine hydrochloride should not exceed 75 to 100 mg when calculated according to Clark's rule. In any case, the maximum amount of Lidocaine HCl administered should not exceed 4.5mg/kg (2mg/lb) of body weight.
<u>For Surface Anesthesia of the Male Adult Urethra:</u>

Slowly instill approximately 15mL (300mg of lidocaine HCl) into the urethra or until the patient has a feeling of tension. An additional dose of not more than 15mL (300mg) can be instilled for adequate anesthesia. A total dose of 30mL (600mg) is usually required to fill and dilate the male urethra. Prior to catheterization, smaller volumes of 5 to 10 mL (100 to 200 mg) are usually adequate for lubrication.
For Surface Anesthesia of the Female Adult Urethra:
Slowly instill 3 to 5 mL (60 to 100 mg of lidocaine HCl) of the jelly into the urethra. If desired, some jelly may be deposited on a cotton swab and introduced into the urethra.
Lubrication for Endotracheal Intubation:
Apply a moderate amount of jelly to the external surface of the endotracheal tube shortly before use.
Lidocaine HCL urethral/mucosal 2% gel is available in 5mL and 30mL

Lidocaine HCl urethral/mucosal 2% gel prefilled syringe (20mg per mL)
No more than 600 mg of lidocaine HCl should be given in any 12 hour period.
For children less than ten years who have a normal lean body mass and a normal lean body development, the maximum dose may be determined by the application of one of the standard pediatric drug formulas (e.g., Clark's rule). For example, in a child of five years weighing 50lbs, the dose of lidocaine hydrochloride should not exceed 75 to 100 mg when calculated according to Clark's rule. In any case, the maximum amount administered should not exceed 4.5mg/kg of body weight.
For Surface Anesthesia of the Male Adult Urethra
The jelly is instilled by an easy syringe-like action, until the patient has a feeling of tension or until about 15mL (i.e., 300mg of lidocaine HCl) is instilled. Additional jelly (about 15mL) can be instilled for adequate anesthesia. A total dose of 30mL (i.e., 600mg) is usually required to fill and dilate the male urethra. Prior to catheterization, smaller volumes of 5 to 10mL (100 to 200 mg) are usually adequate for lubrication.
For Surface Anesthesia of the Female Adult Urethra
Slowly instill 3 to 5 mL (60 to 100 mg of lidocaine HCl) of the jelly into the urethra. If desired, some jelly may be deposited on a cotton swab and introduced into the urethra.
Lubrication for Endotracheal Intubation
Apply a moderate amount of jelly to the external surface of the endotracheal tube shortly before use.
Lidocaine HCL urethral/mucosal 2% gel prefilled syringe is available in 10x6mL (60mL), 10x11mL (110mL), 25x5mL (125mL).
Lidocaine HCl urethral/mucosal 2% gel is also available in other various package sizes. However, these package sizes will not be accommodated in the criteria.

Lidocaine HCl 4% solution
For normal healthy adults, the maximum recommended dose of Lidocaine Hydrochloride Topical Solution, 4% should be such that the dose of lidocaine HCl is kept below 300mg [7.5mL] and in any case should not exceed 4.5 mg/kg (2mg/lb) body weight.
For children less than ten years who have a normal lean body mass and normal body development, the maximum dose may be determined by the application of one of the standard pediatric drug formulas (e.g., Clark's rule). For example, in a child of five years weighing 50 lbs, the dose of lidocaine HCl should not exceed 75 to 100 mg when calculated according to Clark's rule. In any case, the maximum dose of Lidocaine Hydrochloride Topical Solution, 4% with epinephrine should not exceed 7 mg/kg (3.2 mg/lb) of body weight. When used without epinephrine, the amount of Lidocaine Hydrochloride Topical Solution, 4% administered should be such that the dose is kept below 300 mg and in any case should not exceed 4.5 mg/kg (2 mg/lb) of body weight.
When used as a spray, or when applied by means of cotton applicators or packs, as when instilled into a cavity, the suggested dosage of Lidocaine Hydrochloride Topical Solution, 4% is 1 to 5 mL (40 to 200 mg lidocaine HCl), i.e., 0.6 to 3 mg/kg or 0.3 to 1.5 mg/lb body weight.
Lidocaine 4% solution is available in 50mL.

Lidocaine 5% ointment
Dosage for Adults: A single application should not exceed 5gm of lidocaine ointment, 5%, containing 250mg of lidocaine base (equivalent chemically to approximately 300mg of lidocaine hydrochloride). This is roughly equivalent to squeezing a six (6) inch length of ointment from the tube. In a 70kg adult this dose equals 3.6mg/kg (1.6mg/lb) lidocaine base. No more than one-half tube, approximately 17 to 20 gm of ointment or 850 to 1000 mg lidocaine base, should be administered in any one day.
Dosage for children: It is difficult to recommend a maximum dose of any drug for children since this varies as a function of age and weight. For children less than ten years who have a normal lean body mass and a normal lean body

development, the maximum dose may be determined by the application of one of the standard pediatric drug formulas (e.g., Clark's rule). For example a child of five years weighing 50 lbs., the dose of lidocaine should not exceed 75 to 100 mg when calculated according to Clark's rule. In any case, the maximum amount of lidocaine administered should not exceed 4.5 mg/kg (2 mg/lb) of body weight.
Lidocaine 5% ointment is available in 30gm, 35.44gm, and 50gm.
Lidocaine 5% ointment is also available in other various package sizes. However, these package sizes will not be accommodated in the criteria.

Lidocaine 2.5% and prilocaine 2.5% cream
Minor Dermal Procedures
For minor procedures such as intravenous cannulation and venipuncture, apply 2.5gm of lidocaine and prilocaine cream (1/2 the 5gm tube) over 20 to 25 cm^2 of skin surface for at least 1 hour. In controlled clinical trials using lidocaine and prilocaine cream, two sites were usually prepared in case there was a technical problem with cannulation or venipuncture at the first site.
Major Dermal Procedures
For more painful dermatological procedures involving a larger skin area such as split thickness skin graft harvesting, apply 2gm of lidocaine and prilocaine cream per 10cm^2 of skin and allow to remain in contact with the skin for at least 2 hours.
Adult Male Genital Skin
As an adjunct prior to local anesthetic infiltration, apply a thick layer of lidocaine and prilocaine cream (1gm/10cm^2) to the skin surface for 15 minutes. Local anesthetic infiltration should be performed immediately after removal of lidocaine and prilocaine cream. Dermal analgesia can be expected to increase for up to 3 hours under occlusive dressing and persist for 1 to 2 hours after removal of the cream.
Adult Female Patients -Genital Mucous Membranes
For minor procedures on the female external genitalia, such as removal of condylomata acuminata, as well as for use as pretreatment for anesthetic infiltration, apply a thick layer (5 to10 grams) of lidocaine and prilocaine cream for 5 to 10 minutes.
Pediatric Patients -Intact Skin
The following are the maximum recommended doses, application areas and application times for lidocaine and prilocaine cream based on a child's age and weight:

Age and Body Weight Requirements	Maximum Total Dose	Maximum Application Area	Maximum Application Time
0 up to 3 months or < 5 kg	1 gm	10 cm^2	1 hour
3 up to 12 months and >5 kg	2 gm	20 cm^2	4 hours
1 to 6 years and > 10 kg	10 gm	100 cm^2	4 hours
7 to 12 years and > 20 kg	20 gm	200 cm^2	4 hours

Lidocaine 2.5% and prilocaine 2.5% cream is available in 5gm and 30gm.
Lidocaine 2.5% and prilocaine 2.5% cream is also available in other various package sizes. However, these package sizes will not be accommodated in the criteria.

Pliaglis (lidocaine and tetracaine 7-7% cream)
For superficial dermatological procedures such as dermal filler injection, non-ablative laser facial resurfacing, or pulsed-dye laser therapy, apply Pliaglis Cream to intact skin for 20-30 minutes prior to the procedure. See Table for instructions on the amount to apply.
For superficial dermatological procedures such as laser-assisted tattoo removal, apply Pliaglis Cream to intact skin for 60 minutes prior to the procedure. See Table for instructions on the amount to apply.
Using the ruler on the applicator included in the carton, squeeze out and measure the amount of Pliaglis that approximates the amount required to achieve proper coverage.

Surface Area of Treatment Site ($inch^2$)	Length of Pliaglis for 1 mm Thickness (inch)	Weight of Pliaglis Dispensed (g)
2	1	1
3	2	3
6	5	5

12	9	11
16	12	13
23	18	20
31	24	26
39	30	33
47	36	40
54	42	46
62	48	53

Lidocaine and tetracaine 7-7% cream is available in 30gm.

Synera (lidocaine and tetracaine 70-70mg patch)
Venipuncture or Intravenous Cannulation: Prior to venipuncture or intravenous cannulation, apply Synera to intact skin for 20 to 30 minutes.
Superficial Dermatological Procedures: For superficial dermatological procedures such as superficial excision or shave biopsy, apply Synera to intact skin for 30 minutes prior to the procedure.
Simultaneous or sequential application of multiple Synera patches is not recommended. However, application of one additional patch at a new location to facilitate venous access is acceptable after a failed attempt.
Lidocaine and tetracaine 70-70mg patch is available as 1 patch and box of 10 patches.

REFERENCES

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Written by:	UM Development (CT)
Date Written:	01/2016
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Reviewed:	Medical Affairs (WF) 01/2016; (AN) 01/2017, (AN) 09/2017, (AN) 09/2018, (AN) 03/2019, CHART: 10/2019, 11/2019, CHART 09/24/2020, 09/30/2021 External Review: 03/2016, 04/2017, 02/2018, 02/2019, 04/2019 (FYI), 02/2020, 12/2020, 12/2021

LIMIT CRITERIA

This quantity limit should accumulate across all products and strengths up to highest quantity listed depending on the order the claims are processed. Accumulation does not apply if limit is coded for daily dose.

PLEASE NOTE: Since manufacturer package sizes may vary, it is the discretion of the dispensing pharmacy to fill quantities per package size up to these quantity limits. In such cases the filling limit and day supply may be less than what is indicated.

Product	1 Month Limit*	3 Month Limit*
Lidocaine HCl 2% gel	30 gm or mL / 25 days	Does Not Apply*
Lidocaine HCl-collagen-aloe vera 2% gel	30 gm or mL / 25 days	Does Not Apply*
Lidocaine HCl 4% gel	30 mL / 25 days	Does Not Apply*
Lidocaine HCl urethral/mucosal 2% gel	60 mL / 25 days	Does Not Apply*
Lidocaine HCl urethral/mucosal 2% gel prefilled syringe	60 mL / 25 days	Does Not Apply*
Lidocaine HCl 4% topical solution	50 mL / 25 days	Does Not Apply*
Lidocaine 5% ointment	50 gm / 25 days	Does Not Apply*
Lidocaine-Prilocaine 2.5-2.5% cream	30 gm / 25 days	Does Not Apply*
Pliaglis 7-7% cream Lidocaine-tetracaine 7-7% cream	30 gm / 25 days	Does Not Apply*
Synera 70-70mg patch Lidocaine-tetracaine 70-70mg patch	2 patches / 25 days	Does Not Apply*

** The duration of 25 days is used for a 30-day fill period to allow time for refill processing.*
** These products are for short-term acute use; therefore, the mail limit will be the same as the retail limit. The intent is for prescriptions of the requested product to be filled one month at a time, even if at mail order; there should be no 3 month supplies filled.*

PRIOR AUTHORIZATION CRITERIA

DRUG CLASS	**LIDOCAINE, LIDOCAINE-PRILOCAINE, LIDOCAINE-TETRACAINE DERMATOLOGICAL TOPICAL**
BRAND NAME* (generic)	
	(lidocaine HCl 2% gel)
	(lidocaine HCl-collagen-aloe vera 2% gel)
	(lidocaine HCl 4% gel)
	(lidocaine HCl urethral/mucosal 2% gel)
	(lidocaine HCl urethral/mucosal 2% gel prefilled syringe)
	(lidocaine HCl 4% solution)
	(lidocaine 5% ointment)
	(lidocaine 2.5% and prilocaine 2.5% cream)
	PLIAGLIS (lidocaine and tetracaine 7-7% cream)
	SYNERA (lidocaine and tetracaine 70-70mg patch)
Status: CVS Caremark Criteria	
Type: Post Limit Prior Authorization	***Ref # 1330-J***

** Products that are listed in the target drug box include both brand and generic and all dosages forms and strengths unless otherwise stated.*
** OTC products are included.*

FDA-APPROVED INDICATIONS

Lidocaine HCl 2% Gel

Lidocaine HCl 2% gel is intended to be used under the supervision of a healthcare professional to be used as local management of skin wounds, including pressure ulcers, venous stasis ulcers, first and second degree burns, and superficial wounds and scrapes.

Lidocaine HCl-Collagen-Aloe Vera 2% Gel

Lidocaine-collagen-aloe vera 2% gel is indicated for the local management of painful skin wounds, including:

- Pressure ulcers
- Venous stasis ulcers
- Superficial wounds and scrapes
- 1st and 2nd degree burns

Lidocaine HCl 4% Gel

Lidocaine 4% Gel is indicated for the following:

- Stage I - IV pressure ulcers
- Venous stasis ulcers
- Ulcerations caused by mixed vascular etiologies
- Diabetic skin ulcers
- First and second degree burns
- Post-surgical incisions, cuts and abrasions

Lidocaine HCl Urethral/Mucosal 2% Gel
Lidocaine HCl 2% jelly is indicated for prevention and control of pain in procedures involving the male and female urethra, for topical treatment of painful urethritis, and as an anesthetic lubricant for endotracheal intubation (oral and nasal).

Lidocaine HCl Urethral/Mucosal 2% Gel Prefilled Syringe
Lidocaine HCl jelly USP, 2% is indicated for prevention and control of pain in procedures involving the male and female urethra, for topical treatment of painful urethritis, and as an anesthetic lubricant for endotracheal intubation (oral and nasal).

Lidocaine HCl 4% Topical Solution
Lidocaine HCl 4% topical solution is indicated for the production of topical anesthesia of accessible mucous membranes of the oral and nasal cavities and proximal portions of the digestive tract.

Lidocaine 5% Ointment
Lidocaine 5% ointment is indicated for production of anesthesia of accessible mucous membranes of the oropharynx. It is also useful as an anesthetic lubricant for intubation and for the temporary relief of pain associated with minor burns, including sunburn, abrasions of the skin, and insect bites.

Lidocaine 2.5% and Prilocaine 2.5% Cream
Lidocaine and Prilocaine cream USP, 2.5%/2.5% (a eutectic mixture of lidocaine 2.5% and prilocaine 2.5%) is indicated as a topical anesthetic for use on:

- normal intact skin for local analgesia.
- genital mucous membranes for superficial minor surgery and as pretreatment for infiltration anesthesia.

Lidocaine and prilocaine cream is not recommended in any clinical situation when penetration or migration beyond the tympanic membrane into the middle ear is possible because of the ototoxic effects observed in animal studies.

Pliaglis (lidocaine and tetracaine 7-7% cream)
Pliaglis is indicated for use on intact skin in adults to provide topical local analgesia for superficial dermatological procedures such as dermal filler injection, pulsed dye laser therapy, facial laser resurfacing, and laser-assisted tattoo removal.

Synera (lidocaine and tetracaine 70-70mg patch)
Synera is a combination amide and ester local anesthetic indicated for use on intact skin to provide local dermal analgesia for superficial venous access and superficial dermatological procedures such as excision, electrodessication and shave biopsy of skin lesions.

COVERAGE CRITERIA

The requested product will be covered with prior authorization when the following criteria are met:

- Lidocaine-prilocaine 2.5-2.5% cream is being prescribed as a topical anesthetic for use on either:
    A) Normal intact skin for local analgesia
    B) Genital mucous membranes for superficial minor surgery or as pretreatment for infiltration anesthesia

OR

- Lidocaine 5% ointment is being prescribed for any of the following:
    A) Production of anesthesia of accessible mucous membranes of the oropharynx
    B) As an anesthetic lubricant for intubation
    C) Temporary relief of pain associated with minor burns, including sunburn, abrasions of the skin, or insect bites

OR

- Lidocaine urethral/mucosal 2% gel is being prescribed for any of the following:
    A) Prevention and control of pain in procedures involving the urethra
    B) Topical treatment of painful urethritis
    C) As an anesthetic lubricant for endotracheal intubation (oral or nasal)

OR

- Lidocaine-tetracaine 7-7% cream (Pliaglis) is being prescribed for use on intact skin in adults to provide topical local analgesia for superficial dermatological procedures such as dermal filler injection, pulsed dye laser therapy, facial laser resurfacing, or laser-assisted tattoo removal

OR

- Lidocaine 4% topical solution is being prescribed for the production of topical anesthesia of accessible mucous membranes of the oral or nasal cavities or proximal portions of the digestive tract

OR

- Lidocaine-tetracaine 70-70mg patch (Synera) is being prescribed for use on intact skin to provide local dermal analgesia for superficial venous access or superficial dermatological procedures such as excision, electrodessication or shave biopsy of skin lesions

OR

- Lidocaine 2% gel or Lidocaine-collagen-aloe vera 2% gel is being prescribed for the local management of painful skin wounds for any of the following:
    A) Pressure ulcers
    B) Venous stasis ulcers
    C) Superficial wounds or scrapes
    D) 1st or 2nd degree burns
    AND
    - The patient experienced an inadequate treatment response, intolerance, or contraindication to all available FDA-approved drugs and over-the-counter (OTC) products for their medical condition

OR

- Lidocaine 4% gel is being prescribed for any of the following:
    A) Stage I - IV pressure ulcers
    B) Venous stasis ulcers
    C) Ulcerations caused by mixed vascular etiologies
    D) Diabetic skin ulcers
    E) First or second degree burns
    F) Post-surgical incisions, cuts or abrasions
    AND
    - The patient experienced an inadequate treatment response, intolerance, or contraindication to all available FDA-approved drugs and over-the-counter (OTC) products for their medical condition

AND

The requested product will not be used as part of a compound.

Quantity Limits apply.

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Lidocaine 2.5% and prilocaine 2.5% cream is indicated as a topical anesthetic for use on either normal intact skin for local analgesia, or genital mucous membranes for superficial minor surgery and as pretreatment for infiltration anesthesia. Lidocaine HCl urethral/mucosal 2% gel is indicated for prevention and control of pain in procedures involving the male and female urethra, for topical treatment of painful urethritis, and as an anesthetic lubricant for endotracheal intubation (oral and nasal). Lidocaine HCl 2% gel and Lidocaine-collagen-aloe vera 2% gel is indicated for the local management of painful skin wounds, including: pressure ulcers, venous stasis ulcers, superficial wounds and scrapes, 1st and 2nd degree burns. Lidocaine HCl 4% gel is indicated for any of the following: Stage I - IV pressure ulcers, Venous stasis ulcers, Ulcerations caused by mixed vascular etiologies, Diabetic skin ulcers, First and second degree burns, Post-surgical incisions, cuts and abrasions. Lidocaine 5% ointment is indicated for production of anesthesia of accessible mucous membranes of the oropharynx. It is also useful as an anesthetic lubricant for intubation and for the temporary relief of pain associated with minor burns,

including sunburn, abrasions of the skin, and insect bites. Lidocaine HCl 4% topical solution is indicated for the production of topical anesthesia of accessible mucous membranes of the oral and nasal cavities and proximal portions of the digestive tract. Pliaglis cream (lidocaine and tetracaine 7-7% cream) is indicated for use on intact skin in adults to provide topical local analgesia for superficial dermatological procedures such as dermal filler injection, pulsed dye laser therapy, facial laser resurfacing, and laser-assisted tattoo removal. Synera (lidocaine and tetracaine 70-70mg patch) is a combination amide and ester local anesthetic indicated for use on intact skin to provide local dermal analgesia for superficial venous access and superficial dermatological procedures such as excision, electrodessication and shave biopsy of skin lesions.

When Lidocaine topical products are used concomitantly with other products containing lidocaine, the total dose contributed by all formulations must be kept in mind. Although the incidence of adverse effects with topical Lidocaine is low, caution should be exercised, particularly when employing large amounts, since the incidence of adverse effects is directly proportional to the total dose of the local anesthetic agent administered. Life-threatening adverse events have been reported when topical anesthetics, like lidocaine, are used improperly.[11,12] Therefore, these products will be limited to a quantity sufficient for acute use. For Lidocaine 5% ointment, Lidocaine 4% solution, Lidocaine urethral/mucosal 2% gel, Lidocaine-Prilocaine 2.5-2.5% cream, Pliaglis (lidocaine-tetracaine 7-7% cream), and Synera (lidocaine-tetracaine 70-70mg patch), Post Limit quantities for approval are set to at least two times the initial quantity limit to allow for additional quantities, if needed.

Since manufacturer package sizes may vary, it is the discretion of the dispensing pharmacy to fill quantities per package size up to these quantity limits. In such cases the filling limit and day supply may be less than what is indicated.

Lidocaine 2% gel, Lidocaine 4% gel, and Lidocaine HCl-collagen-aloe vera 2% gel are available as Medical Devices and will be limited to a quantity sufficient for acute use. In addition, if the patient has experienced an inadequate treatment response, intolerance, or contraindication to all available FDA-approved drugs and over-the-counter (OTC) products for the patient's medical condition, the prior authorization will be approved. A medical device is an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including a component part or accessory which is:

- recognized in the official National Formulary, or the United States Pharmacopoeia, or any supplement to them
- intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, or
- intended to affect the structure or any function of the body,

and which does not achieve any of its primary intended purposes through chemical action within or on the body and which is not dependent upon being metabolized for the achievement of any of its primary intended purposes.[14]

Pharmaceutical compounding is the combining, mixing, or altering of ingredients to create a customized medication that is not otherwise commercially available. Compounded products are not FDA-approved. This means that FDA does not verify the safety, or effectiveness of compounded products. Consumers and health professionals rely on the drug approval process to ensure that drugs are safe and effective and made in accordance with Federal quality standards. Compounded products also lack an FDA finding of manufacturing quality before such drugs are marketed.[13] Approval will not be given if these products are being used as part of a compounded product. Compounded products should be submitted with a compound indicator.

Lidocaine HCl 2% gel
Apply 7T Lido Gel to the wound and skin surrounding the wound 3-4 times daily.
Allowing for 1 to 3 weeks for wound healing, and utilizing the Rule of 9's suggested AAD estimation, 85 gm or mL may be sufficient for approximately 4%BSA up to 3 weeks.
0.25gm per application over 1%BSA x 4 times daily x 21 days x 4%BSA = 85 total gm
Lidocaine HCl 2% gel is available as a Medical Device (K020540) 7T Lido gel in 85gm.

Lidocaine HCl-collagen-aloe vera 2% gel
Apply Lidotrex to the wound and skin surrounding the wound 3-4 times daily.
Allowing for 1 to 3 weeks for wound healing, and utilizing the Rule of 9's suggested AAD estimation, 85 gm or mL may be sufficient for approximately 4%BSA up to 3 weeks.
0.25gm per application over 1%BSA x 4 times daily x 21 days x 4%BSA = 85 total gm
Lidocaine HCl-collagen-aloe vera 2% gel is available as a Medical Device (K020540) Lidotrex gel in 28.33gm.

Lidocaine HCl 4% gel
Apply a thin layer of LDO Plus to the wound surface and the skin immediately surrounding the wound 3-4 times daily. Allowing for 1 to 3 weeks for wound healing, and utilizing the Rule of 9's suggested AAD estimation, 90gm may be sufficient for approximately 4%BSA up to 3 weeks.
0.25gm per application over 1%BSA x 4 times daily x 21 days x 4%BSA = 90 total gm
Lidocaine HCl 4% gel is available as a Medical Device (K092086) LDO Plus in 30mL and as Astero gel in 30mL and 90mL.
Lidocaine HCl 4% gel is also available in other various package sizes. However, these package sizes will not be accommodated in the criteria.

Lidocaine HCl urethral/mucosal 2% gel
No more than 600mg (30mL) of lidocaine HCl should be given in any 12 hour period.
For children less than ten years who have a normal lean body mass and a normal lean body development, the maximum dose may be determined by the application of one of the standard pediatric drug formulas (e.g., Clark's rule). For example, in a child of five years weighing 50lbs., the dose of lidocaine hydrochloride should not exceed 75 to 100 mg when calculated according to Clark's rule. In any case, the maximum amount of Lidocaine HCl administered should not exceed 4.5mg/kg (2mg/lb) of body weight.
For Surface Anesthesia of the Male Adult Urethra:
Slowly instill approximately 15mL (300mg of lidocaine HCl) into the urethra or until the patient has a feeling of tension. An additional dose of not more than 15mL (300mg) can be instilled for adequate anesthesia. A total dose of 30mL (600mg) is usually required to fill and dilate the male urethra. Prior to catheterization, smaller volumes of 5 to 10 mL (100 to 200 mg) are usually adequate for lubrication.
For Surface Anesthesia of the Female Adult Urethra:
Slowly instill 3 to 5 mL (60 to 100 mg of lidocaine HCl) of the jelly into the urethra. If desired, some jelly may be deposited on a cotton swab and introduced into the urethra.
Lubrication for Endotracheal Intubation:
Apply a moderate amount of jelly to the external surface of the endotracheal tube shortly before use.
125mL is sufficient for at least 4 procedures.
Lidocaine HCL urethral/mucosal 2% gel is available in 5mL and 30mL.

Lidocaine HCl urethral/mucosal 2% gel prefilled syringe (20mg per mL)
No more than 600 mg of lidocaine HCl should be given in any 12 hour period.
For children less than ten years who have a normal lean body mass and a normal lean body development, the maximum dose may be determined by the application of one of the standard pediatric drug formulas (e.g., Clark's rule). For example, in a child of five years weighing 50lbs, the dose of lidocaine hydrochloride should not exceed 75 to 100 mg when calculated according to Clark's rule. In any case, the maximum amount administered should not exceed 4.5mg/kg of body weight.
For Surface Anesthesia of the Male Adult Urethra
The jelly is instilled by an easy syringe-like action, until the patient has a feeling of tension or until about 15mL (i.e., 300mg of lidocaine HCl) is instilled. Additional jelly (about 15mL) can be instilled for adequate anesthesia. A total dose of 30mL (i.e., 600mg) is usually required to fill and dilate the male urethra. Prior to catheterization, smaller volumes of 5 to 10mL (100 to 200 mg) are usually adequate for lubrication.
For Surface Anesthesia of the Female Adult Urethra
Slowly instill 3 to 5 mL (60 to 100 mg of lidocaine HCl) of the jelly into the urethra. If desired, some jelly may be deposited on a cotton swab and introduced into the urethra.
Lubrication for Endotracheal Intubation
Apply a moderate amount of jelly to the external surface of the endotracheal tube shortly before use.
125mL is sufficient for at least 4 procedures.
Lidocaine HCL urethral/mucosal 2% gel prefilled syringe is available in 10x6mL (60mL), 10x11mL (110mL), 25x5mL (125mL).
Lidocaine HCl urethral/mucosal 2% gel is also available in other various package sizes. However, these package sizes will not be accommodated in the criteria.

Lidocaine HCl 4% solution

For normal healthy adults, the maximum recommended dose of Lidocaine Hydrochloride Topical Solution, 4% should be such that the dose of lidocaine HCl is kept below 300 mg [7.5mL] and in any case should not exceed 4.5 mg/kg (2mg/lb) body weight.
For children less than ten years who have a normal lean body mass and normal body development, the maximum dose may be determined by the application of one of the standard pediatric drug formulas (e.g., Clark's rule). For example, in a child of five years weighing 50 lbs, the dose of lidocaine HCl should not exceed 75 to 100 mg when calculated according to Clark's rule. In any case, the maximum dose of Lidocaine Hydrochloride Topical Solution, 4% with epinephrine should not exceed 7 mg/kg (3.2 mg/lb) of body weight. When used without epinephrine, the amount of Lidocaine Hydrochloride Topical Solution, 4% administered should be such that the dose is kept below 300 mg and in any case should not exceed 4.5 mg/kg (2 mg/lb) of body weight.
When used as a spray, or when applied by means of cotton applicators or packs, as when instilled into a cavity, the suggested dosage of Lidocaine Hydrochloride Topical Solution, 4% is 1 to 5 mL (40 to 200 mg lidocaine HCl), i.e., 0.6 to 3 mg/kg or 0.3 to 1.5 mg/lb body weight.
100mL is sufficient for at least 13 procedures.
Lidocaine 4% solution is available in 50mL.

Lidocaine 5% ointment
Dosage for Adults: A single application should not exceed 5 gm of lidocaine ointment, 5%, containing 250 mg of lidocaine base (equivalent chemically to approximately 300 mg of lidocaine hydrochloride). This is roughly equivalent to squeezing a six (6) inch length of ointment from the tube. In a 70 kg adult this dose equals 3.6 mg/kg (1.6 mg/lb) lidocaine base. No more than one-half tube, approximately 17 to 20 gm of ointment or 850 to 1000 mg lidocaine base, should be administered in any one day.
For children less than ten years who have a normal lean body mass and a normal lean body development, the maximum dose may be determined by the application of one of the standard pediatric drug formulas (e.g., Clark's rule). For example a child of five years weighing 50 lbs., the dose of lidocaine should not exceed 75 to 100 mg when calculated according to Clark's rule. In any case, the maximum amount of lidocaine administered should not exceed 4.5 mg/kg (2 mg/lb) of body weight.
100gm is sufficient for at least 20 procedures, or at least 5 days.
Lidocaine 5% ointment is available in 30gm, 35.44gm, and 50gm.
Lidocaine 5% ointment is also available in other various package sizes. However, these package sizes will not be accommodated in the criteria.

Lidocaine 2.5% and prilocaine 2.5% cream
Minor Dermal Procedures
For minor procedures such as intravenous cannulation and venipuncture, apply 2.5gm of lidocaine and prilocaine cream (1/2 the 5gm tube) over 20 to 25 cm^2 of skin surface for at least 1 hour. In controlled clinical trials using lidocaine and prilocaine cream, two sites were usually prepared in case there was a technical problem with cannulation or venipuncture at the first site.
Major Dermal Procedures
For more painful dermatological procedures involving a larger skin area such as split thickness skin graft harvesting, apply 2gm of lidocaine and prilocaine cream per 10cm^2 of skin and allow to remain in contact with the skin for at least 2 hours.
Adult Male Genital Skin
As an adjunct prior to local anesthetic infiltration, apply a thick layer of lidocaine and prilocaine cream (1gm/10cm^2) to the skin surface for 15 minutes. Local anesthetic infiltration should be performed immediately after removal of lidocaine and prilocaine cream. Dermal analgesia can be expected to increase for up to 3 hours under occlusive dressing and persist for 1 to 2 hours after removal of the cream.
Adult Female Patients -Genital Mucous Membranes
For minor procedures on the female external genitalia, such as removal of condylomata acuminata, as well as for use as pretreatment for anesthetic infiltration, apply a thick layer (5 to10 grams) of lidocaine and prilocaine cream for 5 to 10 minutes.
Pediatric Patients -Intact Skin
The following are the maximum recommended doses, application areas and application times for lidocaine and prilocaine cream based on a child's age and weight:

Age and Body Weight Requirements	Maximum Total Dose	Maximum Application Area	Maximum Application Time
0 up to 3 months	1 gm	10 cm^2	1 hour

or < 5 kg			
3 up to 12 months and >5 kg	2 gm	20 cm^2	4 hours
1 to 6 years and > 10 kg	10 gm	100 cm^2	4 hours
7 to 12 years and > 20 kg	20 gm	200 cm^2	4 hours

60gm is sufficient for treatment area of at least 300cm^2, or at least 6 procedures.
Lidocaine 2.5% and prilocaine 2.5% cream is available in 5gm and 30gm.
Lidocaine 2.5% and prilocaine 2.5% cream is also available in other various package sizes. However, these package sizes will not be accommodated in the criteria.

Pliaglis (lidocaine and tetracaine 7-7% cream)
For superficial dermatological procedures such as dermal filler injection, non-ablative laser facial resurfacing, or pulsed-dye laser therapy, apply Pliaglis Cream to intact skin for 20-30 minutes prior to the procedure. See Table for instructions on the amount to apply.
For superficial dermatological procedures such as laser-assisted tattoo removal, apply Pliaglis Cream to intact skin for 60 minutes prior to the procedure. See Table for instructions on the amount to apply.
Using the ruler on the applicator included in the carton, squeeze out and measure the amount of Pliaglis that approximates the amount required to achieve proper coverage.

Surface Area of Treatment Site ($inch^2$)	Length of Pliaglis for 1 mm Thickness (inch)	Weight of Pliaglis Dispensed (g)
2	1	1
3	2	3
6	5	5
12	9	11
16	12	13
23	18	20
31	24	26
39	30	33
47	36	40
54	42	46
62	48	53

60gm is sufficient for treatment area of at least 62 $inches^2$.
Lidocaine and tetracaine 7-7% cream is available in 30gm.

Synera (lidocaine and tetracaine 70-70mg patch)
Venipuncture or Intravenous Cannulation: Prior to venipuncture or intravenous cannulation, apply Synera to intact skin for 20 to 30 minutes.
Superficial Dermatological Procedures: For superficial dermatological procedures such as superficial excision or shave biopsy, apply Synera to intact skin for 30 minutes prior to the procedure.
Simultaneous or sequential application of multiple Synera patches is not recommended. However, application of one additional patch at a new location to facilitate venous access is acceptable after a failed attempt.
10 patches are sufficient for at least 5 procedures.
Lidocaine and tetracaine 70-70mg patch is available in 1 patch and 10 patches.

REFERENCES

1. 7T Lido (lidocaine 2% gel) [package insert]. Los Angeles, CA: 7T Pharma, LLC; October 2018.
2. Glydo (lidocaine 2% jelly urethral/mucosal prefilled syringe) [package insert]. Schaumburg, IL: Sagent Pharmaceuticals. March 2020.
3. Lidotrex (lidocaine-collagen-aloe vera 2% gel) [package insert]. Ripley, MS: Sterling-Knight Pharmaceuticals, LLC; March 2018.
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5. Lidocaine urethral/mucosal 2% gel [package insert]. Lake Forest, IL: Akorn, Inc.; February 2020.
6. Lidocaine HCl 4% topical solution [package insert]. Buena, NJ: Teligent Pharma, Inc; November 2019.

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9. Pliaglis [package insert]. Hawthorne, NY: Taro Pharma; August 2020.
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11. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. http://online.lexi.com/. Accessed August 2021.
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13. Human Drug Compounding. Available at: https://www.fda.gov/drugs/guidance-compliance-regulatory-information/human-drug-compounding. Accessed September 2020.
14. Medical Devices. Available at: https://www.fda.gov/medical-devices. Accessed August 2021.

Written by:	UM Development (CT)
Date Written:	01/2016
Revised:	01/2017; 09/2017 (operational update to denial reason); (TM) 09/2017, (TM) 09/2018, (removed brand Emla d/c), (TM) 02/2019 (add Lidotrex), (TM) 09/2019 (add q9, revised quantities), (TM) 10/2019 (updated urethral/mucosal, & qtys), (TM) 09/2020 (no clinical changes), (PM) 08/2021 (updated denial reasons), (TM) 08/2021 (no clinical changes)
Reviewed:	Medical Affairs (WF) 01/2016; (AN) 01/2017, (AN) 09/2017, (AN) 09/2018, (AN) 03/2019, CHART: 10/2019, 11/2019, CHART 09/24/2020, 09/30/2021 External Review: 03/2016, 04/2017, 02/2018, 02/2019, 04/2019 (FYI), 02/2020, 12/2020, 12/2021

CRITERIA FOR APPROVAL

1	Is this request for Lidocaine-prilocaine 2.5-2.5 percent cream as a topical anesthetic for use on either A) normal intact skin for local analgesia, B) genital mucous membranes for superficial minor surgery or as pretreatment for infiltration anesthesia? [If yes, then skip to question 12.]	Yes	No
2	Is this request for Lidocaine 5 percent ointment for any of the following: A) production of anesthesia of accessible mucous membranes of the oropharynx, B) as an anesthetic lubricant for intubation, C) temporary relief of pain associated with minor burns, including sunburn, abrasions of the skin, or insect bites? [If yes, then skip to question 12.]	Yes	No
3	Is this request for Lidocaine urethral/mucosal 2 percent gel for any of the following: A) prevention and control of pain in procedures involving the urethra, B) topical treatment of painful urethritis, C) as an anesthetic lubricant for endotracheal intubation (oral or nasal)? [If yes, then skip to question 12.]	Yes	No
4	Is this request for Lidocaine-tetracaine 7-7 percent cream (Pliaglis) for use on intact skin in adults to provide topical local analgesia for superficial dermatological procedures such as dermal filler injection, pulsed dye laser therapy, facial laser resurfacing, or laser-assisted tattoo removal? [If yes, then skip to question 12.]	Yes	No
5	Is this request for Lidocaine 4 percent topical solution for production of topical anesthesia of accessible mucous membranes of the oral or nasal cavities or proximal portions of the digestive tract? [If yes, then skip to question 12.]	Yes	No
6	Is this request for Lidocaine-tetracaine 70-70mg patch (Synera) for use on intact skin to provide local dermal analgesia for superficial venous access or superficial dermatological procedures such as excision, electrodessication or shave biopsy of skin lesions? [If yes, then skip to question 12.]	Yes	No

7	Is this request for Lidocaine 2 percent gel or Lidocaine-collagen-aloe vera 2 percent gel for the local management of painful skin wounds for any of the following: A) pressure ulcers, B) venous stasis ulcers, C) superficial wounds or scrapes, D) first or second degree burns? [If yes, then skip to question 9.]	Yes	No
8	Is this request for Lidocaine 4 percent gel for any of the following: A) stage I - IV pressure ulcers, B) venous stasis ulcers, C) ulcerations caused by mixed vascular etiologies, D) diabetic skin ulcers, E) first or second degree burns, F) post-surgical incisions, cuts or abrasions? [If no, then no further questions.]	Yes	No
9	Has the patient experienced an inadequate treatment response to all available FDA-approved drugs and over-the counter (OTC) products for their medical condition? [If yes, then skip to question 12.]	Yes	No
10	Has the patient experienced an intolerance to all available FDA-approved drugs and over-the counter (OTC) products for their medical condition? [If yes, then skip to question 12.]	Yes	No
11	Does the patient have a contraindication that would prohibit a trial of all available FDA-approved drugs and over-the counter (OTC) products for their medical condition? [If no, then no further questions.]	Yes	No
12	Will the requested product be used as part of a compound? [If yes, then no further questions.]	Yes	No
13	Does the patient require more than the plan allowance of any of the following per month: A) 100 gm or mL of Lidocaine ointment or Lidocaine solution, B) 125 mL of Lidocaine urethral/mucosal gel, C) 60 gm of Lidocaine-prilocaine cream or Lidocaine-tetracaine cream (Pliaglis), D) 10 patches of Lidocaine-tetracaine patch (Synera), E) 85 gm or mL of Lidocaine HCl 2 percent gel or Lidocaine-collagen-aloe vera 2 percent gel, F) 90 mL of Lidocaine HCl 4 percent gel? [RPh Note: If yes, then deny and enter a partial approval per Post Limit Quantity Chart.]	Yes	No

Guidelines for Approval							
Duration of Approval **3 Months**							
Quantity for Approval **See Post Limit Quantity Chart**							
Set 1 - Lidocaine-prilocaine 2.5-2.5 percent cream		**Set 2 -** Lidocaine 5 percent ointment		**Set 3 -** Lidocaine urethral/mucosal 2 percent gel		**Set 4 -** Lidocaine-tetracaine 7-7 percent cream (Pliaglis)	
Yes to question(s)	**No to question(s)**	**Yes to question(s)**	**No to question(s)**	**Yes to question(s)**	**No to question(s)**	**Yes to question(s)**	**No to question(s)**
1	12	2	1	3	1	4	1
	13		12		2		2
			13		12		3
					13		12
							13
Duration of Approval **3 Months**							
Quantity for Approval							

See Post Limit Quantity Chart							
Set 5 - Lidocaine 4 percent topical solution		**Set 6 -** Lidocaine-tetracaine 70-70mg patch (Synera)		**Set 7 -** Lidocaine 2 percent gel or Lidocaine-collagen-aloe vera 2 percent gel		**Set 8 -** Lidocaine 4 percent gel	
Yes to question(s)	**No to question(s)**	**Yes to question(s)**	**No to question(s)**	**Yes to question(s)**	**No to question(s)**	**Yes to question(s)**	**No to question(s)**
5	1	6	1	7	1	8	1
	2		2	9	2	9	2
	3		3		3		3
	4		4		4		4
	12		5		5		5
	13		12		6		6
			13		12		7
					13		12
							13
Duration of Approval **3 Months**							
Quantity for Approval **See Post Limit Quantity Chart**							
Set 9 - Lidocaine 2 percent gel or Lidocaine-collagen-aloe vera 2 percent gel		**Set 10 -** Lidocaine 4 percent gel		**Set 11 -** Lidocaine 2 percent gel or Lidocaine-collagen-aloe vera 2 percent gel		**Set 12 -** Lidocaine 4 percent gel	
Yes to question(s)	**No to question(s)**	**Yes to question(s)**	**No to question(s)**	**Yes to question(s)**	**No to question(s)**	**Yes to question(s)**	**No to question(s)**
7	1	8	1	7	1	8	1
10	2	10	2	11	2	11	2
	3		3		3		3
	4		4		4		4
	5		5		5		5
	6		6		6		6
	9		7		9		7
	12		9		10		9
	13		12		12		10
			13		13		12
							13

Mapping Instructions			
	Yes	**No**	**DENIAL REASONS – DO NOT USE FOR MEDICARE PART D**
1.	Go to 12	Go to 2	
2.	Go to 12	Go to 3	
3.	Go to 12	Go to 4	
4.	Go to 12	Go to 5	
5.	Go to 12	Go to 6	
6.	Go to 12	Go to 7	
7.	Go to 9	Go to 8	
8.	Go to 9	Deny	You do not meet the requirements of your plan. Your plan covers additional quantities of this product when it is used for the FDA-approved use. Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]
9.	Go to 12	Go to 10	
10.	Go to 12	Go to 11	
11.	Go to 12	Deny	You do not meet the requirements of your plan.

			Your plan covers additional quantities of this medical device when you meet these conditions: - You have tried all available FDA-approved drugs for your medical condition and they either did not work for you or you cannot use them - You have tried all available over-the-counter (OTC) products for your medical condition and they either did not work for you or you cannot use them Your request has been denied based on the information we have. [Short Description: No inadequate response, intolerance or contraindication to FDA-approved drugs and OTC products]
12.	Deny	Go to 13	You do not meet the requirements of your plan. Your plan covers additional quantities of this product when it is not being used as part of a compound. Your request has been denied based on the information we have. [Short Description: Being used in a compound.]
13.	Deny RPh Note: For the denial verbiage, only include the requested product. Remove all the other products from the verbiage.	Approve, 3 months, See Post Limit Quantity Chart	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to: - 60 grams per month of Lidocaine-prilocaine 2.5-2.5 percent cream - 125 mL per month of Lidocaine HCl urethral/mucosal 2 percent gel - 100 grams per month of Lidocaine 5 percent ointment - 100 mL per month of Lidocaine HCl 4 percent solution - 60 grams per month of Lidocaine-tetracaine 7-7 percent cream (Pliaglis) - 10 patches per month of Lidocaine-tetracaine 70-70mg patch (Synera) - 85 gm or mL per month of Lidocaine HCl 2 percent gel - 85 gm or mL per month of Lidocaine-collagen-aloe vera 2 percent gel - 90 mL per month of Lidocaine HCl 4 percent gel Your request has been partially approved. You have been approved for the maximum quantity that your plan covers. Your request for additional quantities of the requested product and strength has been denied. [Short Description: Over max quantity]

POST LIMIT QUANTITY

PLEASE NOTE: Since manufacturer package sizes may vary, it is the discretion of the dispensing pharmacy to fill quantities per package size up to these quantity limits. In such cases the filling limit and day supply may be less than what is indicated.

Product	1 Month Limit *	3 Month Limit*
Lidocaine HCl 2% gel	85 gm or mL / 25 days	Does Not Apply*
Lidocaine HCl-collagen-aloe vera 2% gel	85 gm or mL / 25 days	Does Not Apply*
Lidocaine HCl 4% gel	90 mL / 25 days	Does Not Apply*
Lidocaine HCl urethral/mucosal 2% gel	125 mL / 25 days	Does Not Apply*
Lidocaine HCl urethral/mucosal 2% gel prefilled syringe	125 mL / 25 days	Does Not Apply*
Lidocaine HCl 4% topical solution	100 mL / 25 days	Does Not Apply*

Lidocaine 5% ointment	100 gm / 25 days	Does Not Apply*
Lidocaine-Prilocaine 2.5-2.5% cream	60 gm / 25 days	Does Not Apply*
Pliaglis 7-7% cream Lidocaine-tetracaine 7-7% cream	60 gm / 25 days	Does Not Apply*
Synera 70-70mg patch Lidocaine-tetracaine 70-70mg patch	10 patches / 25 days	Does Not Apply*

** The duration of 25 days is used for a 30-day fill period to allow time for refill processing.*
** These products are for short-term acute use; therefore, the mail limit will be the same as the retail limit. The intent is for prescriptions of the requested product to be filled one month at a time, even if at mail order; there should be no 3 month supplies filled.*

PRIOR AUTHORIZATION CRITERIA

BRAND NAME
(generic)

LIDODERM
(lidocaine patch 5%)

ZTLIDO
(lidocaine topical system)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization with Quantity Limit

POLICY

FDA-APPROVED INDICATIONS

Lidoderm
Lidoderm is indicated for relief of pain associated with post-herpetic neuralgia. It should be applied only to **intact skin**.

ZTLido
ZTLido (lidocaine topical system) 1.8% is indicated for relief of pain associated with post-herpetic neuralgia (PHN) in adults.

Compendial Uses
Pain associated with diabetic neuropathy[4]
Pain associated with cancer-related neuropathy[4,5]

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for any of the following: A) Pain associated with post-herpetic neuralgia, B) Pain associated with diabetic neuropathy, C) Pain associated with cancer-related neuropathy (including treatment-related neuropathy [e.g., neuropathy associated with radiation treatment or chemotherapy])

Quantity Limits apply.
90 patches/ 25 days
270 patches/ 75 days

REFERENCES

1. Lidoderm [package insert]. Malvern, PA: Endo Pharmaceuticals Inc.; January 2020.
2. ZTLido [package insert]. Palo Alto, CA: Scilex Pharmaceuticals Inc.; April 2021.
3. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2022; Accessed September 6, 2022.
4. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed September 6, 2022.
5. National Comprehensive Cancer Network (NCCN) Guidelines: Adult Cancer Pain V2.2022. National Comprehensive Cancer Network. Available from URL: http://www.nccn.org/professionals/physician_gls/PDF/pain.pdf. Accessed September 2022.
6. Vadalouca A, Raptis E, Moka E, et al. Pharmacological Treatment of Neuropathic Cancer Pain: A Comprehensive Review of the Current Literature. World Institute of Pain. *Pain Practice.* 2011; 12(3):219-251.
7. Derry S, Wiffen PJ, Moore RA, et al. Topical lidocaine for neuropathic pain in adults (Review). *Cochrane Database Syst Rev* 2014. doi: 10.1002/14651858.CD010958.

8. Dworkin RH, O'Connor AB, Backonja M, et al. Pharmacologic Management of Neuropathic Pain: Evidence-based recommendations. Pain. 2007;132(3):237-251.
9. Saguil A, Kane S, Mercado M, et al. Herpes Zoster and Postherpetic Neuralgia: Prevention and Management. Am Fam Physician. 2017;96(10):656-663.

QUANTITY LIMIT CRITERIA

BRAND NAME*
(generic)

LIDODERM
(lidocaine patch 5%)

ZTLIDO
(lidocaine topical system)

Status: CVS Caremark Criteria
Type: Quantity Limit ***Ref # 2971-H***

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Lidoderm
Lidoderm is indicated for relief of pain associated with post-herpetic neuralgia. It should be applied only to **intact skin**.

ZTLido
ZTLido (lidocaine topical system) 1.8% is indicated for relief of pain associated with post-herpetic neuralgia (PHN) in adults.

Compendial Uses
Pain associated with diabetic neuropathy[4,5,8]
Pain associated with cancer-related neuropathy[4,6,7]

RATIONALE

Lidoderm (lidocaine patch 5%) is indicated for relief of pain associated with post-herpetic neuralgia (PHN).[1] ZTLido (lidocaine topical system) 1.8% is indicated for relief of pain associated with post-herpetic neuralgia (PHN) in adults.[2]

Because of the difference in bioavailability of ZTLido compared with Lidoderm (lidocaine 5% patch), a different dosage strength is required to be administered to the patient. One ZTLido (lidocaine topical system) 1.8% provides equivalent lidocaine exposure to one Lidoderm (lidocaine patch 5%). In a single-dose, crossover study conducted in 53 healthy volunteers, ZTLido (lidocaine topical system) 1.8% demonstrated equivalent exposure (AUC) and peak concentration (C_{max}) of lidocaine to Lidoderm (lidocaine patch 5%).[2]

Lidocaine 5% patches were well tolerated and reduced pain in patients with diabetic neuropathy in an open-label, flexible-dosing, 3-week study with a 5-week extension. The study included 56 patients with clinically defined painful diabetic polyneuropathy of longer than a 3 months' duration. Results determined that 5% lidocaine patches for up to 18 hours per day are well tolerated in patients with painful diabetic polyneuropathy, significantly improve pain and quality-of-life ratings, and may allow tapering of concomitant analgesic therapy.[5] Additionally, the American Academy of Neurology recommends that the Lidoderm patch may be considered for the treatment of painful diabetic neuropathy.[8] Because ZTLido patches provide an equivalent dose of lidocaine as Lidoderm patches, coverage is available for Lidoderm (lidocaine patches) 5% and ZTLido (lidocaine topical system) 1.8% for pain associated with diabetic neuropathy.

Neuropathic cancer pain (NCP) may be cancer-related, namely resulting from nervous system tumor invasion, surgical nerve damage during tumor removal, radiation-induced nerve damage and chemotherapy-related neuropathy, or may be of benign origin, unrelated to cancer.[7] Additional analgesic medications or therapies may be necessary in patients with cancer-related pain, particularly when opioid analgesics are ineffective or produce inadequate pain relief. According to the

National Comprehensive Cancer Network (NCCN) guidelines for adult cancer pain, a topical agent such as lidocaine can be used as an adjunctive treatment for neuropathic pain.[4,6]

Lidoderm or ZTLido should be applied to intact skin to cover the most painful area. Apply the prescribed number of patches (maximum of 3), only once for up to 12 hours within a 24-hour period. Patches may be cut into smaller sizes with scissors prior to removal of the release liner. Excessive dosing by applying more than the recommended quantity of the requested drug or applying for longer than the recommended wearing time could result in increased absorption of lidocaine and high blood concentrations, leading to serious adverse effects. Therefore, the quantity limit is set to 90 patches per month.[1-4]

If the patient is requesting more than the initial quantity limit, the claim will reject with a message indicating that quantity limits are exceeded.

REFERENCES

1. Lidoderm [package insert]. Malvern, PA: Endo Pharmaceuticals Inc.; January 2020.
2. ZTLido [package insert]. Palo Alto, CA: Scilex Pharmaceuticals Inc.; April 2021.
3. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2021; Accessed September 2, 2021.
4. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed September 2, 2021.
5. Barbano RL, Herrmann DN, Hart-Gouleau S, et al: Effectiveness, tolerability, and impact on quality of life of the 5% lidocaine patch in diabetic polyneuropathy. *Arch Neurol.* 2004; 61:914-918.
6. National Comprehensive Cancer Network (NCCN) Guidelines: Adult Cancer Pain V2.2021. National Comprehensive Cancer Network. Available from URL: http://www.nccn.org/professionals/physician_gls/PDF/pain.pdf. Accessed September 2021.
7. Vadalouca A, Raptis E, Moka E, et al. Pharmacological Treatment of Neuropathic Cancer Pain: A Comprehensive Review of the Current Literature. World Institute of Pain. *Pain Practice.* 2011; 12(3):219-251.
8. Bril V., England J., Franklin G.M., et al. Evidence-based guideline: Treatment of painful diabetic neuropathy. *Neurology.* 2011;76;1758-1765. Available at www.neurology.org. Accessed September 2021.
9. Derry S, Wiffen PJ, Moore RA, et al. Topical lidocaine for neuropathic pain in adults (Review). *Cochrane Database Syst Rev* 2014. doi: 10.1002/14651858.CD010958.

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Date Written:	06/2019
Revised:	09/2019 (no clinical changes); (CJM) 09/2020 (no clinical changes), (DFW) 09/2021 (added accumulation statement)
Reviewed:	Medical Affairs (GAD) 06/2019, (CHART) 10/10/19; (CHART) 09/24/20, (CHART) 09/30/2021 External Review: 10/2019, 02/2020, 12/2020, 12/2021

LIMIT CRITERIA

Limits should accumulate across all drugs and strengths up to highest quantity listed depending on the order the claims are processed.

Drug	1 Month Limit*	3 Month Limit*
Lidoderm 5% (lidocaine patch 5%)	90 patches / 25 days	270 patches / 75 days
ZTLido 1.8% (lidocaine topical system 1.8%)	90 patches / 25 days	270 patches / 75 days

**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*

Reference number
6064-A

SPECIALTY GUIDELINE MANAGEMENT

LITFULO (ritlecitinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Litfulo is indicated for the treatment of severe alopecia areata in adults and adolescents 12 years and older.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
A. Initial requests: Chart notes or medical record documentation supporting more than 50% scalp hair loss (e.g., Severity of Alopecia Tool [SALT] score of 50 or higher).
B. Continuation requests: Chart notes or medical record documentation supporting positive clinical response (e.g., increased scalp hair coverage, 80% total scalp hair coverage [SALT score of 20 or less]).

III. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with a dermatologist.

IV. CRITERIA FOR INITIAL APPROVAL

Alopecia areata
Authorization of 12 months may be granted for members 12 years of age or older for treatment of severe alopecia areata when both of the following criteria are met:
A. Member has more than 50% scalp hair loss (e.g., Severity of Alopecia Tool [SALT] score of 50 or higher).
B. Other forms of alopecia have been ruled out (e.g., androgenetic alopecia, trichotillomania, telogen effluvium, chemotherapy-induced hair loss, tinea capitis).

V. CONTINUATION OF THERAPY

Alopecia areata
Authorization of 12 months may be granted for all members 12 years of age or older (including new members) who are using the requested medication for severe alopecia areata and who achieve or maintain a positive clinical response as evidenced by an improvement in signs and symptoms of the condition from baseline (e.g., increased scalp hair coverage, 80% total scalp hair coverage [SALT score of 20 or less]).

VI. OTHER

Member has had a documented negative tuberculosis (TB) test (which can include a tuberculosis skin test [PPD], an interferon-release assay [IGRA], or a chest x-ray)* within 6 months of initiating therapy for persons who are naïve to biologic drugs or targeted synthetic drugs associated with an increased risk of TB.

* If the screening testing for TB is positive, there must be further testing to confirm there is no active disease. Do not administer the requested medication to members with active TB infection. If there is latent disease, TB treatment must be started before initiation of the requested medication.

Member cannot use the requested medication concomitantly with any other biologic drug, targeted synthetic drug, or potent immunosuppressant such as azathioprine or cyclosporine.

VII. DOSAGE AND ADMINISTRATION

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

VIII. REFERENCES

1. Litfulo [package insert]. New York, NY: Pfizer Inc.; June 2023.
2. King B, Zhang X, Harcha WG, et al. Efficacy and safety of ritlecitinib in adults and adolescents with alopecia areata: a randomised, double-blind, multicentre, phase 2b-3 trial. *Lancet*. 2023;401:1518-1529.
3. Testing for TB Infection. Centers for Disease Control and Prevention. Retrieved on July 3, 2023 from: https://www.cdc.gov/tb/topic/basics/risk.htm.

Reference number(s)
1896-A

SPECIALTY GUIDELINE MANAGEMENT

LONSURF (trifluridine and tipiracil)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
1. Lonsurf is indicated for the treatment of adult patients with metastatic colorectal cancer previously treated with fluoropyrimidine-, oxaliplatin- and irinotecan-based chemotherapy, an anti-VEGF biological therapy, and if RAS wild-type, an anti-EGFR therapy.

2. Lonsurf is indicated for the treatment of adult patients with metastatic gastric or gastroesophageal junction adenocarcinoma previously treated with at least two prior lines of chemotherapy that included a fluoropyrimidine, a platinum, either a taxane or irinotecan, and if appropriate, HER2/neu-targeted therapy.

B. Compendial Uses
1. Advanced or metastatic colon cancer
2. Advanced or metastatic rectal cancer
3. Esophageal and esophagogastric junction cancers
4. Gastric cancer

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Colorectal Cancer (CRC)
Authorization of 12 months may be granted for treatment of advanced or metastatic colorectal cancer, including appendiceal adenocarcinoma and anal adenocarcinoma, when the member has progressed on previous treatment with all the following regimens unless the member has a contraindication or intolerance:
1. Fluoropyrimidine-, oxaliplatin- and irinotecan-based chemotherapy; AND
2. An anti-vascular endothelial growth factor (VEGF) therapy; AND
3. If RAS wild type, an anti-epidermal growth factor receptor (EGFR) therapy, such as Erbitux (cetuximab) or Vectibix (panitumumab), for rectal cancer, appendiceal adenocarcinoma, anal adenocarcinoma, or left-sided colon cancer.

B. Gastric or Gastroesophageal Junction Adenocarcinoma
Authorization of 12 months may be granted for treatment of unresectable locally advanced, recurrent, or metastatic gastric or gastroesophageal junction adenocarcinoma when the member has been previously treated with at least two prior lines of chemotherapy.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

IV. REFERENCES

1. Lonsurf [package insert]. Princeton, NJ: Taiho Oncology, Inc.; December 2019.
2. The NCCN Drugs & Biologics Compendium® © 2022 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed July 8, 2022.
3. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines): Anal Carcinoma. Version 1.2022. Accessed July 12, 2022. https://www.nccn.org/professionals/physician_gls/pdf/anal.pdf
4. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines): Colon Cancer. Version 1.2022. Accessed September 12, 2022. https://www.nccn.org/professionals/physician_gls/pdf/colon.pdf

Reference number(s)
2787-A

SPECIALTY GUIDELINE MANAGEMENT

LORBRENA (lorlatinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication
Lorbrena is indicated for the treatment of adult patients with metastatic non-small cell lung cancer (NSCLC) whose tumors are anaplastic lymphoma kinase (ALK)-positive as detected by an FDA-approved test.

B. Compendial Uses
1. Single-agent therapy for recurrent, advanced or metastatic NSCLC in patients with:
   a. ALK rearrangement-positive tumors
   b. ROS1 rearrangement-positive tumors, following disease progression on crizotinib, entrectinib or ceritinib
2. Inflammatory myofibroblastic tumor (IMT) with ALK translocation
3. Erdheim-Chester disease with ALK fusion

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: Chart documentation indicating ALK mutation status or ROS1 rearrangement status (where applicable).

III. CRITERIA FOR INITIAL APPROVAL

A. Non-Small Cell Lung Cancer (NSCLC)
1. Authorization of 12 months may be granted for treatment of ALK rearrangement-positive advanced or metastatic NSCLC (including brain metastases from NSCLC) as a single-agent.

2. Authorization of 12 months may be granted for treatment of advanced or metastatic NSCLC as a single-agent therapy when all of the following criteria are met:
   a. The disease is ROS1 rearrangement-positive
   b. The disease has progressed on any of the following: ceritinib, crizotinib, or entrectinib.

B. Inflammatory Myofibroblastic Tumor (IMT)
Authorization of 12 months may be granted for treatment of ALK-positive IMT as a single agent.

C. Erdheim-Chester Disease
Authorization of 12 months may be granted for treatment of ALK-positive Erdheim-Chester disease as a single agent.

IV. CONTINUATION OF THERAPY

A. Non-Small Cell Lung Cancer (NSCLC)
Authorization of 12 months may be granted for continued treatment of non-small cell lung cancer (NSCLC) in members requesting reauthorization when there is no evidence of unacceptable toxicity while on the current regimen.

B. Inflammatory Myofibroblastic Tumor (IMT) and Erdheim-Chester Disease
Authorization of 12 months may be granted for continued treatment of inflammatory myofibroblastic tumor or Erdheim-Chester disease in members requesting reauthorization when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

V. REFERENCES

1. Lorbrena [package insert]. New York, NY: Pfizer, Inc.; March 2021.
2. The NCCN Drugs & Biologics Compendium® © 2022 National Comprehensive Cancer Network, Inc. Available at: https://www.nccn.org. Accessed July 14, 2022.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME
(generic)

LOTRONEX
(alosetron)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

FDA-APPROVED INDICATIONS

Lotronex is indicated only for women with severe diarrhea-predominant irritable bowel syndrome (IBS) who have:

- chronic IBS symptoms (generally lasting six months or longer),
- had anatomic or biochemical abnormalities of the gastrointestinal tract excluded, and
- not responded adequately to conventional therapy.

Diarrhea-predominant IBS is severe if it includes diarrhea and one or more of the following:

- frequent and severe abdominal pain/discomfort,
- frequent bowel urgency or fecal incontinence,
- disability or restriction of daily activities due to IBS.

Because of infrequent but serious gastrointestinal adverse reactions associated with Lotronex, the indication is restricted to those patients for whom the benefit-to-risk balance is most favorable.

Clinical studies have not been performed to adequately confirm the benefits of Lotronex in men.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for a biological female or a person that self-identifies as a female with a diagnosis of severe diarrhea-predominant irritable bowel syndrome (IBS)

AND

- The patient has experienced chronic irritable bowel syndrome (IBS) symptoms lasting at least 6 months

AND

- Gastrointestinal tract abnormalities have been ruled out

AND

- The patient has had an inadequate response to conventional therapy

REFERENCES

1. Lotronex [package insert]. Roswell, GA: Sebela Pharmaceuticals Inc.; July 2016.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2022; Accessed August 31, 2022.
3. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed August 31, 2022.

Reference number(s)
4766-A

SPECIALTY GUIDELINE MANAGEMENT

LUMAKRAS (sotorasib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication
Lumakras is indicated for the treatment of adult patients with KRAS G12C-mutated locally advanced or metastatic non-small cell lung cancer (NSCLC), as determined by an FDA-approved test, who have received at least one prior systemic therapy.

B. Compendial Uses
1. Recurrent, advanced, or metastatic KRAS G12C-mutated NSCLC
2. Pancreatic adenocarcinoma
3. Colorectal cancer

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: Documentation of the presence of KRAS G12C mutation in tumor or plasma specimens.

III. CRITERIA FOR INITIAL APPROVAL

A. Non-Small Cell Lung Cancer (NSCLC)
Authorization of 12 months may be granted for treatment of KRAS G12C-mutated recurrent, advanced or metastatic NSCLC in members who have received at least one prior systemic therapy, as a single agent.

B. Pancreatic Adenocarcinoma
Authorization of 12 months may be granted for treatment of recurrent, locally advanced or metastatic pancreatic adenocarcinoma when all of the following criteria are met:
1. The tumor or plasma specimen is positive for the KRAS G12C mutation.
2. The member has an ECOG (Eastern Cooperative Oncology Group) performance status of 0-2
3. The requested medication will be used as a single agent

C. Colorectal Cancer
Authorization of 12 months may be granted for treatment of advanced or metastatic colorectal cancer, including appendiceal adenocarcinoma and anal adenocarcinoma, when all of the following criteria are met:
1. The tumor or plasma specimen is positive for the KRAS G12C mutation.

2. The requested medication will be used as a single agent, or in combination with cetuximab (Erbitux) or panitumumab (Vectibix).
3. The member previously received treatment with chemotherapy.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

V. REFERENCES

1. Lumakras [package insert]. Thousand Oaks, CA: Amgen Inc.; January 2023.
2. The NCCN Drugs & Biologics Compendium® © 2023 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed October 10, 2023.
3. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines): Colon Cancer. Version 3.2023. Accessed October 6, 2023. https://www.nccn.org/professionals/physician_gls/pdf/colon.pdf
4. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines): Anal Carcinoma. Version 3.2023. Accessed October 6, 2023. https://www.nccn.org/professionals/physician_gls/pdf/anal.pdf

Reference number(s)
4448-A

SPECIALTY GUIDELINE MANAGEMENT

LUPKYNIS (voclosporin)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Lupkynis is a calcineurin-inhibitor immunosuppressant indicated in combination with a background immunosuppressive therapy regimen for the treatment of adult patients with active lupus nephritis (LN).

Limitations of Use
Safety and efficacy of Lupkynis have not been established in combination with cyclophosphamide. Use of Lupkynis is not recommended in this situation.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
A. Initial requests: Medical records (e.g., chart notes, lab reports) documenting the presence of autoantibodies relevant to SLE (e.g., ANA, anti-ds DNA, anti-Sm, antiphospholipid antibodies, complement proteins), or kidney biopsy supporting the diagnosis.
B. Continuation requests: Medical records (e.g., chart notes, lab reports) documenting disease stability or improvement.

III. EXCLUSIONS

Coverage will not be provided for members using Lupkynis in combination with cyclophosphamide.

IV. CRITERIA FOR INITIAL APPROVAL

Active lupus nephritis
Authorization of 12 months may be granted for the treatment of active lupus nephritis when all of the following criteria are met:
1. Prior to initiating therapy, the member is positive for autoantibodies relevant to SLE (e.g., ANA, anti-ds DNA, anti-Sm, antiphospholipid antibodies, complement proteins) or lupus nephritis was confirmed on kidney biopsy.
2. Member has clinically active lupus renal disease and is receiving background therapy with mycophenolate mofetil (MMF) with corticosteroids.

3. Member must have an eGFR > 45ml/min per 1.73 m^2.

V. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section IV who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition.

VI. REFERENCES

1. Lupkynis [package insert]. Rockville, MD: Aurinia Pharma U.S., Inc,; January 2021.
2. Rovin BH, Solomons N, Pendergraft WF 3rd, Dooley MA, Tumlin J, Romero-Diaz J, Lysenko L, Navarra SV, Huizinga RB; AURA-LV Study Group. A randomized, controlled double-blind study comparing the efficacy and safety of dose-ranging voclosporin with placebo in achieving remission in patients with active lupus nephritis. Kidney Int. 2019 Jan;95(1):219-231.
3. Rovin BH, Adler SG, Barratt J, et al. Kidney Disease: Improving Global Outcomes (KDIGO) Golmerular Disease Work Group. KDIGO 2021 Clinical Practice Guideline for the Management of Glomerular Diseases. *Kidney Int.* 2021 Oct; 100(4S):S1-S276.
4. Gordon C, Amissah-Arthru MB, Gayed M, et al. The British Society for Rheumatology guideline for the management of systemic lupus erythematosus in adults. *Rheumatology (Oxford)*. 2018; 57(1):e1-e45.

Reference number
1810-A

SPECIALTY GUIDELINE MANAGEMENT

LYNPARZA (olaparib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Ovarian Cancer
   a. First-Line Maintenance Treatment of *BRCA*-mutated Advanced Ovarian Cancer
      Lynparza is indicated for the maintenance treatment of adult patients with deleterious or suspected deleterious germline or somatic *BRCA*-mutated (g*BRCA*m or s*BRCA*m) advanced epithelial ovarian, fallopian tube or primary peritoneal cancer who are in complete or partial response to first-line platinum-based chemotherapy. Select patients for therapy based on an FDA-approved companion diagnostic for Lynparza.

   b. Maintenance Treatment of Recurrent Ovarian Cancer
      Lynparza is indicated for the maintenance treatment of adult patients with recurrent epithelial ovarian, fallopian tube or primary peritoneal cancer, who are in complete or partial response to platinum-based chemotherapy.

   c. First-Line Maintenance Treatment of HRD-positive Advanced Ovarian Cancer in Combination with Bevacizumab
      Lynparza is indicated in combination with bevacizumab for maintenance treatment of adult patients with advanced epithelial ovarian, fallopian tube or primary peritoneal cancer who are in complete or partial response to first line platinum-based chemotherapy and whose cancer is associated with homologous recombination deficiency (HRD) positive status defined by either
      i. A deleterious or suspected deleterious BRCA mutation, and/or
      ii. Genomic instability
      Select patients for therapy based on an FDA-approved companion diagnostic for Lynparza.

2. Breast Cancer
   a. Lynparza is indicated for the adjuvant treatment of adult patients with deleterious or suspected deleterious gBRCAm human epidermal growth factor receptor 2 (HER2)-negative high risk early breast cancer who have been treated with neoadjuvant or adjuvant chemotherapy. Select patients for therapy based on an FDA-approved companion diagnostic for Lynparza.

   b. Lynparza is indicated for the treatment of adult patients with deleterious or suspected deleterious *gBRCAm*, HER2-negative metastatic breast cancer, who have been treated with chemotherapy in the neoadjuvant, adjuvant, or metastatic setting. Patients with hormone receptor (HR)-positive breast cancer should have been treated with a prior endocrine therapy or be considered inappropriate for endocrine therapy. Select patients for therapy based on an FDA-approved companion diagnostic for Lynparza.

3. Pancreatic Adenocarcinoma
   Lynparza is indicated for the maintenance treatment of adult patients with deleterious or suspected deleterious *gBRCAm* metastatic pancreatic adenocarcinoma whose disease has not progressed on at

least 16 weeks of a first-line platinum-based chemotherapy regimen. Select patients for therapy based on an FDA-approved companion diagnostic for Lynparza.

4. Prostate Cancer
   a. Lynparza is indicated for the treatment of adult patients with deleterious or suspected deleterious germline or somatic homologous recombination repair (HRR) gene-mutated metastatic castration-resistant prostate cancer (mCRPC) who have progressed following prior treatment with enzalutamide or abiraterone. Select patients for therapy based on an FDA-approved companion diagnostic for Lynparza.

   b. Lynparza is indicated in combination with abiraterone and prednisone or prednisolone for the treatment of adult patients with deleterious or suspected deleterious BRCA-mutated (BRCAm) metastatic castration-resistant prostate cancer (mCRPC). Select patients for therapy based on an FDA-approved companion diagnostic for Lynparza

B. Compendial Uses
   1. Breast cancer
      a. Recurrent or metastatic HER2-negative, BRCA 1/2-germline mutated breast cancer
      b. Recurrent or metastatic HER2-positive, BRCA 1/2-germline mutated breast cancer
      c. Adjuvant therapy for early-stage, HER2-negative, BRCA 1/2-germline mutated breast cancer with high-risk of recurrence, after completion of neoadjuvant/adjuvant chemotherapy and local treatment
   2. Ovarian cancer, Fallopian tube cancer, Primary peritoneal cancer
      c. As a single-agent maintenance therapy for patients with BRCA1/2 germline or somatic mutations who are in complete or partial response after primary treatment for stage II-IV disease
      d. In combination with bevacizumab for maintenance therapy for stage II-IV disease if in complete or partial response after primary therapy that includes bevacizumab.
   3. Uterine Leiomyosarcoma (uLMS)

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
A. Documentation of laboratory report confirming BRCA mutation status, where applicable.
B. Documentation of laboratory report confirming germline or somatic HRR gene mutation, where applicable.
C. Documentation of hormone receptor (HR) and human epidermal growth factor receptor 2 (HER2) status, where applicable.

III. CRITERIA FOR INITIAL APPROVAL

A. Epithelial Ovarian, Fallopian Tube, or Primary Peritoneal Cancer
Authorization of 12 months may be granted for the maintenance treatment of epithelial ovarian, fallopian tube, or primary peritoneal cancer that is in a complete or partial response to chemotherapy when any of the following criteria are met:
1. Member has completed two or more lines of platinum-based therapy for recurrent disease and will be using the requested medication as a single agent
2. Member has a deleterious or suspected deleterious germline or somatic BRCA mutation and will be using the requested medication as a single agent or in combination with bevacizumab for advanced (stage II-IV) disease

3. Member has received primary therapy that includes bevacizumab for advanced (stage II-IV) disease and will be using the requested medication in combination with bevacizumab

B. Breast Cancer

1. Authorization of 12 months may be granted for the treatment of breast cancer with no response to preoperative systemic therapy, or for recurrent or metastatic breast cancer as a single agent in members with deleterious or suspected deleterious germline BRCA mutations.

2. Authorization of 12 months may be granted for use as adjuvant therapy for the treatment of HER2-negative, germline BRCA mutated breast cancer after completion of neoadjuvant/adjuvant chemotherapy in any of the following settings:
   a. Hormone receptor-negative breast cancer with any residual disease; OR
   b. Hormone receptor-negative breast cancer with either tumor size ≥2 cm or any involved axillary nodes; OR
   c. Hormone receptor-positive breast cancer with ≥4 positive lymph nodes; OR
   d. Hormone receptor-positive breast cancer with any residual disease and a CPS+EG (clinical stage, pathologic stage, estrogen receptor status and tumor grade) score ≥3 following preoperative therapy

C. Pancreatic Adenocarcinoma

Authorization of 12 months may be granted for the maintenance treatment of deleterious or suspected deleterious germline BRCA-mutated metastatic pancreatic adenocarcinoma as a single agent, in members whose disease has not progressed on at least 16 weeks of a first-line platinum-based chemotherapy regimen.

D. Prostate Cancer

Authorization of 12 months may be granted for treatment of metastatic castration-resistant prostate cancer (mCRPC) when either of the following criteria are met:

1. The requested medication will be used as a single agent (concurrent use with a GnRH analog is allowed) and all of the following criteria are met:
   a. Member has deleterious or suspected deleterious germline or somatic homologous recombination repair (HRR) gene mutation, which includes BRCA1, BRCA2, ATM, BARD1, BRIP1, CDK12, CHEK1, CHEK2, FANCL, PALB2, RAD51B, RAD51C, RAD51D, RAD54L
   b. Member has progressed on prior androgen receptor-directed therapy
   c. Member is receiving therapy concurrently with a gonadotropin-releasing hormone (GnRH) analog or has had a bilateral orchiectomy
2. The requested medication will be used in combination with abiraterone and prednisone or prednisolone and all of the following criteria are met:
   a. Member has deleterious or suspected deleterious BRCA mutation
   b. Member is receiving therapy concurrently with a gonadotropin-releasing hormone (GnRH) analog or has had a bilateral orchiectomy

E. Uterine Leiomyosarcoma

Authorization of 12 months may be granted for treatment of BRCA altered uterine leiomyosarcoma (uLMS) as second-line therapy when used as a single agent.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

a. For the first-line maintenance treatment of BRCA-mutated advanced ovarian cancer in a complete response, the maximum treatment duration is 2 years.
b. For the first-line maintenance treatment of advanced ovarian cancer in combination with bevacizumab in a complete response, the maximum treatment duration is 2 years.
c. For use as adjuvant treatment of early-stage, HER2-negative, BRCA-mutated breast cancer with high-risk of recurrence, the maximum treatment duration is 1 year.

V. REFERENCES

1. Lynparza® Tablets [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; May 2023.
2. The NCCN Drugs & Biologics Compendium® © 2022 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed December 6, 2022.

QUANTITY LIMIT CRITERIA

BRAND NAME*
(generic)

LYRICA
(pregabalin)

LYRICA CR
(pregabalin extended-release)

Status: CVS Caremark Criteria
Type: Quantity Limit ***Ref # 134-H***

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Lyrica
Lyrica is indicated for:
- Management of neuropathic pain associated with diabetic peripheral neuropathy
- Management of postherpetic neuralgia
- Adjunctive therapy for the treatment of partial onset seizures in patients 1 month of age and older
- Management of fibromyalgia
- Management of neuropathic pain associated with spinal cord injury

Lyrica CR
Lyrica CR is indicated for the management of:
- Neuropathic pain associated with diabetic peripheral neuropathy
- Postherpetic neuralgia

Efficacy of Lyrica CR has not been established for the management of fibromyalgia or as adjunctive therapy for adult patients with partial onset seizures.

Compendial Uses
Lyrica
- Cancer-Related Neuropathic Pain[4,5]
- Cancer Treatment-Related Neuropathic Pain[4,5]

RATIONALE

Lyrica (pregabalin) is indicated for the management of neuropathic pain associated with diabetic peripheral neuropathy (DPN), the management of postherpetic neuralgia (PHN), adjunctive therapy for the treatment of partial onset seizures in patients 1 month of age and older, the management of fibromyalgia (FM), and the management of neuropathic pain associated with spinal cord injury.[1] Lyrica CR (pregabalin extended-release) is indicated for the management of neuropathic pain associated with diabetic peripheral neuropathy (DPN) and the management of postherpetic neuralgia (PHN).[2]

In 2017, the International League Against Epilepsy (ILAE) presented a revised operational classification of seizure types, changing the term “partial” to “focal”. The new classification does not represent a fundamental change but allows greater flexibility and transparency in naming seizure types.[6]

Neuropathic Pain Associated with Diabetic Peripheral Neuropathy
Lyrica[1]

The maximum recommended dose of Lyrica (pregabalin) is 100 mg three times a day (300 mg/day) in patients with creatinine clearance of at least 60 mL/min. Begin dosing at 50 mg three times a day (150 mg/day). The dose may be increased to 300 mg/day within 1 week based on efficacy and tolerability. Although Lyrica was also studied at 600 mg/day, there is no evidence that this dose confers additional significant benefit, and this dose was less well tolerated. In view of the dose-dependent adverse reactions, treatment with doses above 300 mg/day is not recommended.

Lyrica CR[2]
The maximum recommended dose of Lyrica CR (pregabalin extended-release) is 330 mg once daily. Begin dosing at 165 mg once daily and increase to 330 mg once daily within 1 week based on individual patient response and tolerability. Although Lyrica was studied at 600 mg/day, there was no evidence that this dose conferred additional significant benefit and this dose was less well tolerated. In view of the dose-dependent adverse reactions with Lyrica, treatment with doses above 330 mg/day is not recommended for Lyrica CR.

Postherpetic Neuralgia
Lyrica[1]
The recommended dose of Lyrica (pregabalin) is 75 to 150 mg two times a day, or 50 to 100 mg three times a day (150 to 300 mg/day) in patients with creatinine clearance of at least 60 mL/min. Begin dosing at 75 mg two times a day, or 50 mg three times a day (150 mg/day). The dose may be increased to 300 mg/day within 1 week based on efficacy and tolerability. Patients who do not experience sufficient pain relief following 2 to 4 weeks of treatment with 300 mg/day, and who are able to tolerate Lyrica (pregabalin), may be treated with up to 300 mg two times a day, or 200 mg three times a day (600 mg/day). In view of the dose-dependent adverse reactions and the higher rate of treatment discontinuation due to adverse reactions, reserve dosing above 300 mg/day for those patients who have on-going pain and are tolerating 300 mg daily.

Lyrica CR[2]
The maximum recommended dose of Lyrica CR (pregabalin extended-release) is 660 mg once daily. Begin dosing at 165 mg once daily and increase to 330 mg once daily within 1 week based on individual patient response and tolerability. Patients who do not experience sufficient pain relief following 2 to 4 weeks of treatment with 330 mg once daily and who are able to tolerate Lyrica CR, may be treated with up to 660 mg once daily. In view of the dose-dependent adverse reactions and the higher rate of treatment discontinuation due to adverse reactions, dosing above 330 mg/day should be reserved only for those patients who have on-going pain and are tolerating 330 mg daily.

Adjunctive Therapy for Partial-Onset Seizures (i.e., focal-onset seizures)
Lyrica[1]
The recommended dosage for adult and pediatric patients 1 month of age and older is included in the table below. Administer the total daily dosage orally in two or three divided doses. In pediatric patients, the recommended dosing regimen is dependent upon body weight. Based on clinical response and tolerability, dosage may be increased, approximately weekly.

Recommended Dosage for Adults and Pediatric Patients 1 month and Older		
Age and Body Weight	Recommended Initial Dosage (administer in two to three divided doses)	Recommended Maximum Dosage (administer in two to three divided doses)
Adults (17 years and older)	150 mg/day	600 mg/day
Pediatric patients weighing 30 kg or more	2.5 mg/kg/day	10 mg/kg/day (not to exceed 600 mg/day)
Pediatric patients weighing less than 30 kg	3.5 mg/kg/day	14 mg/kg/day

Both the efficacy and adverse event profiles of Lyrica (pregabalin) have been shown to be dose-related.
The effect of dose escalation rate on the tolerability of Lyrica (pregabalin) has not been formally studied.
The efficacy of adjunctive Lyrica (pregabalin) in patients taking gabapentin has not been evaluated in controlled trials. Consequently, dosing recommendations for the use of Lyrica (pregabalin) with gabapentin cannot be offered.

Management of Fibromyalgia
Lyrica[1]
The recommended dose of Lyrica (pregabalin) for fibromyalgia is 300 to 450 mg/day. Begin dosing at 75 mg two times a day (150 mg/day). The dose may be increased to 150 mg two times a day (300 mg/day) within 1 week based on efficacy and tolerability. Patients who do not experience sufficient benefit with 300 mg/day may be further increased to 225 mg two

times a day (450 mg/day). Although Lyrica (pregabalin) was also studied at 600 mg/day, there is no evidence that this dose confers additional benefit, and this dose was less well tolerated. In view of the dose-dependent adverse reactions, treatment with doses above 450 mg/day is not recommended.

Neuropathic Pain Associated with Spinal Cord Injury

Lyrica[1]

The recommended dose range of Lyrica (pregabalin) for the treatment of neuropathic pain associated with spinal cord injury is 150 to 600 mg/day. The recommended starting dose is 75 mg two times a day (150 mg/day). The dose may be increased to 150 mg two times a day (300 mg/day) within 1 week based on efficacy and tolerability. Patients who do not experience sufficient pain relief after 2 to 3 weeks of treatment with 150 mg two times a day and who tolerate Lyrica (pregabalin) may be treated with up to 300 mg two times a day.

Renal Impairment and Conversion[1,2]

In view of dose-dependent adverse reactions and since pregabalin is eliminated primarily by renal excretion, adjust the dose in patients with reduced renal function. The use of Lyrica (pregabalin) in pediatric patients with compromised renal function has not been studied. Base the dose adjustment in patients with renal impairment on creatinine clearance (CLcr), as indicated in Table 1 (Lyrica) and Table 2 (Lyrica CR). Next, determine the recommended total daily dose based on indication, for a patient with normal renal function (CLcr ≥ 60mL/min). Then refer to Table 1 (Lyrica) or Table 2 (Lyrica CR) to determine the corresponding renal adjusted dose.

For patients undergoing hemodialysis, adjust the pregabalin daily dose based on renal function. In addition to the daily dose adjustment, administer a supplemental dose immediately following every 4-hour hemodialysis treatment (See Table 1).

Table 1. *Lyrica* (Pregabalin) Dosage Adjustment Based on Renal Function

Creatinine Clearance (CLcr) (mL/min)	Total Pregabalin Daily Dose (mg/day)*				Dose Regimen
≥60	150	300	450	600	BID or TID
30–60	75	150	225	300	BID or TID
15–30	25–50	75	100–150	150	QD or BID
<15	25	25–50	50–75	75	QD
Supplementary dosage following hemodialysis (mg)†					
Patients on the 25mg QD regimen: take one supplemental dose of 25mg or 50mg Patients on the 25–50mg QD regimen: take one supplemental dose of 50mg or 75mg Patients on the 50–75mg QD regimen: take one supplemental dose of 75mg or 100mg Patients on the 75mg QD regimen: take one supplemental dose of 100mg or 150mg					

TID= Three divided doses; BID = Two divided doses; QD = Single daily dose.

* Total daily dose (mg/day) should be divided as indicated by dose regimen to provide mg/dose.

† Supplementary dose is a single additional dose.

Table 2. *Lyrica CR* (Pregabalin Extended-Release) Dosage Adjustment Based on Renal Function

Creatinine Clearance (CLcr) (mL/min)	Total Pregabalin Extended-Release Daily Dose (mg/day)*				Dose Regimen
≥60	165	330	495[a]	660[b]	Once a day
30–60	82.5	165	247.5[c]	330	Once a day
Less than 30/hemodialysis	Dose with Lyrica				

a. 495 mg = 3 x 165 mg tablets taken once daily
b. 660 mg = 2 x 330 mg tablets taken once daily
c. 247.5 mg = 3 x 82.5 mg tablets taken once daily

Conversion from Lyrica Capsules or Oral Solution to Lyrica CR	
Lyrica Total Daily Dose (dosed 2 or 3 times daily)	Lyrica CR Dose (dosed once a day)
75 mg	82.5 mg

150 mg	165 mg
225 mg	247.5 mg[a]
300 mg	330 mg
450 mg	495 mg[b]
600 mg	660 mg[c]

a. 247.5 mg = 3 × 82.5 mg tablets taken once a day
b. 495 mg = 3 × 165 mg tablets taken once a day
c. 660 mg = 2 × 330 mg tablets taken once a day

Cancer-related Pain

Lyrica[4,5]

Frequently used as an adjuvant for the neuropathic component of the pain, the starting dose for pregabalin is 75 mg twice a day, with increasing dose increments of 50%-100% every 3 days to a maximum daily dose of 600 mg. Slower titration is needed for the elderly or medically frail. Dose adjustment is required for those with renal insufficiency.[5]

Presently, there is limited clinical data regarding off-label uses and doses that exceed the FDA recommended maximum dose of 600 mg per day of Lyrica (pregabalin) and 660 mg per day of Lyrica CR (pregabalin extended-release).[1-4]

Lyrica (pregabalin) is available in several strengths and may be dosed two or three times daily. To allow for dosing intervals and dose titrations, the following limits will be set for Lyrica (pregabalin) per month at: 120 capsules for 25 mg, 50 mg, 75 mg, 100 mg, and 150 mg strengths, 90 capsules for the 200 mg strength, 60 capsules for the 225 mg and 300 mg strengths, and 900 mL for the 20 mg/mL oral solution. Lyrica CR (pregabalin extended-release) is available in 82.5 mg, 165 mg, and 330 mg tablets and is dosed once daily. To allow for dose titrations and dosage adjustments based on renal function, the following limits will be set for Lyrica CR (pregabalin extended-release) per month at 90 tablets for 82.5 mg and 165 mg strengths, and 60 tablets for the 330 mg strength.

If the patient is requesting more than the initial quantity limit, the system will reject with a message indicating that quantity limits are exceeded.

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Written by:	UM Development (JG)
Date Written:	08/2005
Revised:	UM Development (NB) 11/2006, 06/2007; (CT) 05/2008, 05/2009, 01/2010 (05/2009(2) Lyrica oral soln added), 05/2010, (TM) 06/2011, 03/2012, 06/2012 (update PI), 09/2012, (TM) 03/2013, (PL) 09/2013, 05/2014, (JH) 05/2015; (KM) 05/2016 (no clinical changes), 05/2017, 09/2017 (added cancer treatment pain), 10/2017 (added Lyrica CR); (DS) 05/2018 (no clinical changes), 05/2019, (TM) 05/2020, 05/2021 (no clinical changes), (DFW) 05/2022 (no clinical changes)
Reviewed:	Medical Affairs 08/2005, 11/2006, 06/2007; (WF) 05/2008, 05/2009; (KP) 01/2010, 05/2010, 06/2011, 03/2012, 06/2012, (LB) 09/2012, (LS) 03/2013, (LCB) 05/2014, (DNC) 05/2015; (AN) 09/2017; (DNC) 10/2017, 05/2019, CHART 05/28/2020, 05/27/2021, 05/26/2022 External Review 12/2005, 12/2006, 10/2007, 08/2008, 10/2009, 01/2010, 12/2010, 10/2011, 08/2012, 10/2012, 06/2013, 10/2013, 02/2014, 10/2014, 10/2015, 02/2016, 10/2016, 10/2017, 12/2017, 10/2018, 10/2019, 10/2020, 08/2021, 08/2022

LIMIT CRITERIA

Limits do not accumulate together; patient is allowed the maximum limit for each drug and strength

Drug	1 Month Limit*	3 Month Limit*
Lyrica (pregabalin) capsules 25 mg, 50 mg, 75 mg, 100 mg, 150 mg	120 capsules / 25 days	360 capsules / 75 days
Lyrica (pregabalin) capsules 200 mg	90 capsules / 25 days	270 capsules / 75 days
Lyrica (pregabalin) capsules 225 mg, 300 mg	60 capsules / 25 days	180 capsules / 75 days
Lyrica (pregabalin) oral solution 20 mg/mL	900 mL / 25 days	2700 mL / 75 days
Lyrica CR (pregabalin extended-release) 82.5 mg	90 tablets / 25 days	270 tablets / 75 days
Lyrica CR (pregabalin extended-release) 165 mg	90 tablets / 25 days	270 tablets / 75 days
Lyrica CR (pregabalin extended-release) 330 mg	60 tablets / 25 days	180 tablets / 75 days

**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*

STEP THERAPY CRITERIA

BRAND NAME
(generic)

GRALISE
(gabapentin extended-release tablet)

HORIZANT
(gabapentin enacarbil extended-release tablet)

LYRICA
(pregabalin)

LYRICA CR
(pregabalin extended-release)

Status: CVS Caremark Criteria
Type: Initial Step Therapy; Post Step Therapy Prior Authorization

POLICY

FDA-APPROVED INDICATIONS

Gralise
Gralise is indicated for the management of postherpetic neuralgia.

Gralise is not interchangeable with other gabapentin products because of differing pharmacokinetic profiles that affect the frequency of administration.

Horizant
Treatment of Restless Legs Syndrome
Horizant is indicated for the treatment of moderate-to-severe primary Restless Legs Syndrome (RLS) in adults.
Horizant is not recommended for patients who are required to sleep during the daytime and remain awake at night.
Management of Postherpetic Neuralgia
Horizant is indicated for the management of postherpetic neuralgia (PHN) in adults.

Lyrica
Lyrica is indicated for:
- Management of neuropathic pain associated with diabetic peripheral neuropathy
- Management of postherpetic neuralgia
- Adjunctive therapy for the treatment of partial-onset seizures in patients 1 month of age and older
- Management of fibromyalgia
- Management of neuropathic pain associated with spinal cord injury

Lyrica CR
Lyrica CR is indicated for the management of:
- Neuropathic pain associated with diabetic peripheral neuropathy
- Postherpetic neuralgia

Efficacy of Lyrica CR has not been established for the management of fibromyalgia or as adjunctive therapy for adult patients with partial onset seizures.

Compendial Uses
Lyrica
- Cancer-Related Neuropathic Pain[10,14]
- Cancer Treatment-Related Neuropathic Pain[10,14]

INITIAL STEP THERAPY
For Lyrica, Lyrica CR, or Gralise
If the patient has filled a prescription for at least a 30 day supply of gabapentin immediate-release within the past 120 days under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit. If the patient does not meet the initial step therapy criteria, then the system will reject with a message indicating that a prior authorization (PA) is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

For Horizant
If the patient has filled a prescription for at least a 30 day supply of any of the following: pramipexole immediate-release, ropinirole immediate-release, or gabapentin immediate-release within the past 120 days under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit. If the patient does not meet the initial step therapy criteria, then the system will reject with a message indicating that a prior authorization (PA) is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

COVERAGE CRITERIA
The requested drug will be covered with prior authorization when the following criteria are met:
- Lyrica (pregabalin immediate-release) is being prescribed for one of the following: A) Management of fibromyalgia, B) Management of neuropathic pain associated with spinal cord injury, C) Adjunctive therapy for partial-onset seizures (i.e., focal-onset seizures) in a patient 1 month to up to 3 years of age, D) Cancer-related neuropathic pain, E) Cancer treatment-related neuropathic pain **AND**
    - If the request is for Lyrica (pregabalin) oral solution, the patient meets one of the following: A) has difficulty swallowing oral solid dosage forms (e.g., capsules), B) requires a dose that cannot be obtained using the commercially available capsules

OR
- Lyrica (pregabalin immediate-release) is being prescribed for one of the following: A) Adjunctive therapy for partial-onset seizures (i.e., focal-onset seizures) in a patient 3 years of age or older, B) Management of postherpetic neuralgia, C) Management of neuropathic pain associated with diabetic peripheral neuropathy **AND**
    - The patient has experienced an inadequate treatment response, intolerance, or has a contraindication to gabapentin immediate-release **AND**
        - If the request is for Lyrica (pregabalin) oral solution, the patient meets one of the following: A) has difficulty swallowing oral solid dosage forms (e.g., capsules), B) requires a dose that cannot be obtained using the commercially available capsules

OR
- Lyrica CR (pregabalin extended-release), Gralise (gabapentin extended-release), or Horizant (gabapentin enacarbil extended-release) is being prescribed for the management of postherpetic neuralgia **AND**
    - The patient has experienced an inadequate treatment response, intolerance, or has a contraindication to gabapentin immediate-release

OR
- Lyrica CR (pregabalin extended-release) is being prescribed for the management of neuropathic pain associated with diabetic peripheral neuropathy **AND**
    - The patient has experienced an inadequate treatment response, intolerance, or has a contraindication to TWO of the following: A) gabapentin immediate-release, B) pregabalin immediate-release, C) duloxetine, D) venlafaxine, E) a tricyclic antidepressant

OR
- Horizant (gabapentin enacarbil extended-release) is being prescribed for the treatment of Restless Legs Syndrome **AND**

- The patient has experienced an inadequate treatment response, intolerance, or has a contraindication to ANY of the following: A) pramipexole immediate-release, B) ropinirole immediate-release

REFERENCES

1. Cymbalta [package insert]. Indianapolis, IN: Lilly USA, LLC; September 2021.
2. Gralise [package insert]. Newark, CA: Depomed, Inc.; April 2020.
3. Horizant [package insert]. Atlanta, GA: Arbor Pharmaceuticals, April 2020.
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5. Lyrica CR [package insert]. New York, NY: Parke-Davis; June 2020.
6. Pramipexole [package insert]. East Windsor, NJ: Aurobindo Pharma USA, Inc.; July 2021.
7. Ropinirole [package insert]. Bedminster, NJ: Alembic Pharmaceuticals, Inc. August 2021.
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13. Price R, Smith D, Franklin D et. al. Oral and Topical Treatment of Painful Diabetic Polyneuropathy: Practice Guideline Update Summary. Report of the AAN Guideline Subcommittee. *Neurology* 2022; 98:31-43.
14. NCCN Guidelines. Version 1.2022 Adult Cancer Pain. Available at http://www.nccn.org/professionals/physician_gls/pdf/pain.pdf. Accessed April 2022.
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16. Winkelman J, Armstrong M, Allen R, et al. Practice guideline summary: Treatment of Restless Legs Syndrome in Adults. *Neurology.* 2016;87:2585–2593.

Reference number(s)
2975-A

SPECIALTY GUIDELINE MANAGEMENT

MAVENCLAD (cladribine)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Mavenclad is indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include relapsing-remitting disease and active secondary progressive disease, in adults. Because of its safety profile, use of Mavenclad is generally recommended for patients who have had an inadequate response to, or are unable to tolerate, an alternative drug indicated for the treatment of MS.

Limitations of Use
Mavenclad is not recommended for use in patients with clinically isolated syndrome (CIS) because of its safety profile.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Multiple Sclerosis

A. Initial requests
Authorization of 45 days may be granted for treatment of relapsing forms of multiple sclerosis (including relapsing-remitting and secondary progressive disease for those who continue to experience relapses) and when all of the following criteria are met:
1. Inadequate response or unable to tolerate an alternative drug indicated for the treatment of multiple sclerosis.
2. Member does not have clinically isolated syndrome (CIS).
3. Member has not received 2 courses (i.e., 4 cycles) of Mavenclad.

B. Subsequent requests
Authorization of 45 days may be granted for treatment of relapsing forms of multiple sclerosis (including relapsing-remitting and secondary progressive disease for those who continue to experience relapses) and when all of the following criteria are met:
1. Member has not received 2 courses (i.e., 4 cycles) of Mavenclad.
2. The member has not received Mavenclad in the last 43 weeks.

III. OTHER CRITERIA

Members will not use Mavenclad concomitantly with other disease modifying multiple sclerosis agents (Note: Ampyra and Nuedexta are not disease modifying).

IV. REFERENCES

1. Mavenclad [package insert]. Rockland, MA: EMD Serono; April 2019.
2. Giovannoni, G., Comi, G., Cook, S., et al. A Placebo-Controlled Trial of Oral Cladribine for Relapsing Multiple Sclerosis. N Engl J Med 2010;362:416-426.

Reference number(s)
2242-A, 2678-A

SPECIALTY GUIDELINE MANAGEMENT

MAVYRET (glecaprevir and pibrentasvir)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Mavyret is indicated for the treatment of adult and pediatric patients 3 years and older with:

A. Chronic hepatitis C virus (HCV) genotype 1, 2, 3, 4, 5 or 6 infection without cirrhosis or with compensated cirrhosis (Child-Pugh A)
B. HCV genotype 1 infection, who previously have been treated with a regimen containing an HCV NS5A inhibitor or an NS3/4A protease inhibitor (PI), but not both.

All other indications are considered experimental/investigational and not medically necessary.

II. EXCLUSIONS

Coverage will not be provided for members with decompensated cirrhosis/moderate or severe hepatic impairment (Child Turcotte Pugh Class B or C).

Note: When the requested drug is being used in a combination therapy regimen, exclusions to the other antiviral drugs also apply.

III. CRITERIA FOR INITIAL APPROVAL

A. Hepatitis C virus infection, without ribavirin

1. Genotype 1 infection

i. Authorization of up to 8 weeks total may be granted for treatment-naive members without cirrhosis or with compensated cirrhosis.
ii. Authorization of up to 12 weeks total may be granted for treatment-naïve members with compensated cirrhosis and HIV coinfection.
iii. Authorization of up to 16 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who failed prior treatment with an NS5A inhibitor (excluding glecaprevir/pibrentasvir) and who have not received an NS3/4A protease inhibitor.
iv. Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who failed prior treatment with an NS3/4A protease inhibitor (e.g., simeprevir, boceprevir or telaprevir in combination with peginterferon and ribavirin, simeprevir with sofosbuvir) and who have not received an NS5A inhibitor.
v. Authorization of up to 8 weeks total may be granted for members without cirrhosis who failed prior treatment with an interferon-based regimen with or without ribavirin (RBV) and who have not received an NS3/4A protease inhibitor or NS5A inhibitor.

vi. Authorization of up to 12 weeks total may be granted for members with compensated cirrhosis who failed prior treatment with an interferon-based regimen with or without RBV and who have not received an NS3/4A protease inhibitor or NS5A inhibitor.
vii. Authorization of up to 16 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who failed prior treatment with a sofosbuvir-based regimen (e.g., sofosbuvir and ribavirin with or without interferon, sofosbuvir/ledipasvir [Harvoni], sofosbuvir/velpatasvir [Epclusa]) and who have not had prior exposure to an NS5A inhibitor plus NS3/4A protease inhibitor regimen (e.g., elbasvir/grazoprevir [Zepatier]).

2. Genotype 3 infection
i. Authorization of up to 8 weeks total may be granted for treatment-naive members without cirrhosis or with compensated cirrhosis.
ii. Authorization of up to 12 weeks total may be granted for treatment-naïve members with compensated cirrhosis and HIV coinfection.
iii. Authorization of up to 16 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who failed prior treatment with an interferon-based regimen with or without RBV and who have not received an NS3/4A protease inhibitor or NS5A inhibitor.
iv. Authorization of up to 16 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who failed prior treatment with a sofosbuvir-based regimen (e.g., sofosbuvir and ribavirin with or without interferon) without sofosbuvir/NS5A inhibitor experience (e.g., sofosbuvir/ledipasvir [Harvoni], sofosbuvir/velpatasvir [Epclusa]) or prior exposure to a NS5A inhibitor plus NS3/4A protease inhibitor regimen (e.g., elbasvir/grazoprevir [Zepatier]).

3. Genotype 2, 4, 5, or 6 infection
i. Authorization of up to 8 weeks total may be granted for treatment-naive members without cirrhosis or with compensated cirrhosis.
ii. Authorization of up to 12 weeks total may be granted for treatment-naïve members with compensated cirrhosis and HIV coinfection.
iii. Authorization of up to 8 weeks total may be granted for members without cirrhosis who failed prior treatment with an interferon-based regimen with or without RBV and who have not received an NS3/4A protease inhibitor or NS5A inhibitor.
iv. Authorization of up to 12 weeks total may be granted for members with compensated cirrhosis who failed prior treatment with an interferon-based regimen with or without RBV and who have not received an NS3/4A protease inhibitor or NS5A inhibitor.
v. Authorization of up to 16 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who failed prior treatment with a sofosbuvir-based regimen (e.g., sofosbuvir and ribavirin with or without interferon, sofosbuvir/ledipasvir [Harvoni], sofosbuvir/velpatasvir [Epclusa]) and who have not had prior exposure to an NS5A inhibitor plus NS3/4A protease inhibitor regimen (e.g., elbasvir/grazoprevir [Zepatier]).

4. Unknown genotype/genotype could not be determined
Authorization of up to 8 weeks total may be granted for members with unknown or undetermined genotype without cirrhosis who are treatment-naïve and do not have any of the following characteristics:
i. HIV or HBsAG positive
ii. Current pregnancy
iii. Known or suspected hepatocellular carcinoma
iv. Prior liver transplantation

Note: Genotype testing is required for members with any of the characteristics listed.

5. Recurrent HCV infection post liver transplantation

i. Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis and recurrent HCV genotype 1, 2, 3, 4, 5 or 6 infection post liver transplantation.
ii. Authorization of up to 16 weeks total may be granted for members with recurrent HCV genotype 1 infection post liver transplantation without cirrhosis or with compensated cirrhosis who failed prior treatment with an NS5A inhibitor (excluding glecaprevir/pibrentasvir) and who have not received an NS3/4A protease inhibitor.
iii. Authorization of up to 16 weeks total may be granted for members with recurrent HCV genotype 3 infection post liver transplantation without cirrhosis or with compensated cirrhosis who failed prior treatment with PEG-IFN and RBV and who have not received an NS3/4A protease inhibitor or NS5A inhibitor.
iv. Authorization of up to 16 weeks total may be granted for members with recurrent HCV genotype 3 infection post liver transplantation without cirrhosis or with compensated cirrhosis who failed prior treatment with sofosbuvir (Sovaldi) and RBV with or without PEG-IFN and who have not received an NS3/4A protease inhibitor or NS5A inhibitor.

6. Kidney transplant recipients

i. Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who have HCV genotype 1, 2, 3, 4, 5 or 6 infection and are treatment-naïve or who have not failed prior treatment with a direct-acting antiviral.
ii. Authorization of up to 16 weeks total may be granted for members with HCV genotype 1 infection without cirrhosis or with compensated cirrhosis who failed prior treatment with an NS5A inhibitor (excluding glecaprevir/pibrentasvir) and who have not received an NS3/4A protease inhibitor.
iii. Authorization of up to 16 weeks total may be granted for members with HCV genotype 3 infection without cirrhosis or with compensated cirrhosis who failed prior treatment with PEG-IFN and RBV and who have not received an NS3/4A protease inhibitor or NS5A inhibitor.
iv. Authorization of up to 16 weeks total may be granted for members with HCV genotype 3 infection without cirrhosis or with compensated cirrhosis who failed prior treatment with sofosbuvir (Sovaldi) and RBV with or without PEG-IFN and who have not received an NS3/4A protease inhibitor or NS5A inhibitor.

7. Organ recipient from HCV-viremic donor

i. Authorization of up to 12 weeks total may be granted for members who have received a liver transplant from an HCV-viremic donor.
ii. Authorization of up to 8 weeks total may be granted for members who have received a non-liver organ transplant from an HCV-viremic donor when treatment is initiated in the first week after transplant.
iii. Authorization of up to 12 weeks total may be granted for members who have received a non-liver organ transplant from an HCV-viremic donor when treatment is initiated more than one week after transplant.

B. Hepatitis C virus infection, in combination with Sovaldi and ribavirin
Genotype 1, 2, 3, 4, 5, or 6 infection

1. Authorization of up to 16 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who failed prior treatment with glecaprevir/pibrentasvir (Mavyret). An additional 8 weeks may be granted following failure with sofosbuvir (Sovaldi) and Mavyret.
2. Authorization of up to 16 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who failed prior treatment with sofosbuvir/velpatasvir/voxilaprevir (Vosevi). Authorization of up to 24 weeks may be granted for members with extremely difficult cases (e.g., genotype 3 with cirrhosis).

C. HCV and HIV Coinfection

Authorization may be granted for members with HCV and HIV coinfection when the criteria for approval of the requested regimen in Sections A or B above are met.

IV. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

V. REFERENCES

1. Mavyret [package insert]. North Chicago, IL: AbbVie Inc.; June 2021.
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Reference number(s)
2973-A

SPECIALTY GUIDELINE MANAGEMENT

MAYZENT (siponimod)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Mayzent is indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease and active secondary progressive disease, in adults.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Relapsing forms of multiple sclerosis
Authorization of 12 months may be granted to members who have been diagnosed with a relapsing form of multiple sclerosis (including relapsing-remitting and secondary progressive disease for those who continue to experience relapse).

B. Clinically isolated syndrome
Authorization of 12 months may be granted to members for the treatment of clinically isolated syndrome.

III. CONTINUATION OF THERAPY

For all indications: Authorization of 12 months may be granted for members who are experiencing disease stability or improvement while receiving Mayzent.

IV. OTHER CRITERIA

Members will not use Mayzent concomitantly with other disease modifying multiple sclerosis agents (Note: Ampyra and Nuedexta are not disease modifying).

V. REFERENCES

1. Mayzent [package insert]. East Hanover, NJ: Novaritis; January 2021.

Reference number(s)
1681-A

SPECIALTY GUIDELINE MANAGEMENT

MEKINIST (trametinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met, and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
1. Mekinist is indicated, as a single agent in BRAF-inhibitor treatment-naïve patients or in combination with dabrafenib, for the treatment of patients with unresectable or metastatic melanoma with BRAF V600E or V600K mutations as detected by an FDA-approved test.
2. Mekinist is indicated, in combination with dabrafenib, for the adjuvant treatment of patients with melanoma with BRAF V600E or V600K mutations as detected by an FDA-approved test, and involvement of lymph node(s), following complete resection.
3. Mekinist is indicated, in combination with dabrafenib, for the treatment of patients with metastatic non-small cell lung cancer (NSCLC) with BRAF V600E mutation as detected by an FDA-approved test.
4. Mekinist is indicated, in combination with dabrafenib, for the treatment of patients with locally advanced or metastatic anaplastic thyroid cancer (ATC) with BRAF V600E mutation and no satisfactory locoregional treatment options.
5. Mekinist is indicated, in combination with dabrafenib, for the treatment of adult and pediatric patients 6 years of age and older with unresectable or metastatic solid tumors with BRAF V600E mutation who have progressed following prior treatment and have no satisfactory alternative treatment options.

   Limitations of Use: Mekinist is not indicated for treatment of patients with colorectal cancer because of known intrinsic resistance to BRAF inhibition.

B. Compendial Uses
1. Melanoma (including brain metastases), BRAF V600 activating mutation-positive
2. Glioma, BRAF V600 activating mutation-positive
3. Meningioma, BRAF V600 activating mutation-positive
4. Astrocytoma, BRAF V600 activating mutation-positive
5. Uveal melanoma as a single agent
6. Brain cancer and neurofibromatosis type 1
7. Non-small cell lung cancer (NSCLC)
8. Ovarian cancer/fallopian tube cancer/primary peritoneal cancer
9. Hepatobiliary Cancers
   i. Gallbladder Cancer
   ii. Extrahepatic Cholangiocarcinoma
   iii. Intrahepatic Cholangiocarcinoma
10. Histiocytic Neoplasms
    i. Erdheim-Chester Disease
    ii. Langerhans Cell Histiocytosis
    iii. Rosai-Dorfman Disease
11. Thyroid Carcinoma

i. Anaplastic carcinoma
ii. Papillary carcinoma
iii. Follicular carcinoma
iv. Hurthle cell carcinoma

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of BRAF mutation documentation is necessary to initiate the prior authorization review for applicable indications as outlined in section III.

III. CRITERIA FOR INITIAL APPROVAL

A. Melanoma

Authorization of 12 months may be granted for treatment of melanoma in any of the following settings:

1. Unresectable or metastatic cutaneous melanoma with a BRAF V600 activating mutation as a single agent or in combination with dabrafenib (Tafinlar).
2. Brain metastases from melanoma with a BRAF V600E activating mutation in combination with dabrafenib (Tafinlar).
3. Adjuvant treatment of resected stage III cutaneous melanoma with a BRAF V600 activating mutation in combination with dabrafenib (Tafinlar).
4. Limited resectable local satellite/in-transit recurrent disease in combination with dabrafenib (Tafinlar).
5. Uveal melanoma as a single agent for distant metastatic disease.

B. Non-Small Cell Lung Cancer (NSCLC)

Authorization of 12 months may be granted for treatment of BRAF V600E mutation-positive advanced or metastatic NSCLC in combination with dabrafenib (Tafinlar).

C. Thyroid Cancer

Authorization of 12 months may be granted for treatment of thyroid carcinoma when any of the following criteria are met:

1. Member has progressive and/or symptomatic BRAF V600E mutation-positive follicular, Hürthle cell, or papillary thyroid carcinoma that is not amenable to radioactive iodine (RAI) therapy in combination with dabrafenib (Tafinlar).
2. Member has locally advanced, metastatic, or borderline resectable BRAF V600E mutation-positive anaplastic thyroid carcinoma and the requested medication will be used in combination with dabrafenib (Tafinlar).

D. Central Nervous System Cancer

Authorization of 12 months may be granted for treatment of central nervous system cancer in a member with either of the following:

1. BRAF V600 mutation-positive gliomas, meningiomas, or astrocytomas
2. Brain cancer and neurofibromatosis type 1

E. Ovarian Cancer, Fallopian Tube Cancer, and Primary Peritoneal Cancer

Authorization of 12 months may be granted for treatment of persistent or recurrent epithelial ovarian cancer, fallopian tube cancer, primary peritoneal cancer, carcinosarcoma (malignant mixed Mullerian tumors), clear cell carcinoma of the ovary, grade 1 endometrioid carcinoma, low-grade serous ovarian

carcinoma/ ovarian borderline epithelial tumors (low malignant potential) or mucinous carcinoma of the ovary.

F. Hepatobiliary Cancers
Authorization of 12 months may be granted for subsequent treatment of progressive BRAF-V600E mutated unresectable or metastatic gallbladder cancer, extrahepatic cholangiocarcinoma, or intrahepatic cholangiocarcinoma in combination with dabrafenib (Tafinlar).

G. Histiocytic Neoplasms
Authorization of 12 months may be granted for treatment of Erdheim-Chester disease, Langerhans cell histiocytosis, or Rosai-Dorfman disease as a single agent.

H. Solid Tumors
Authorization of 12 months may be granted for treatment of unresectable or metastatic solid tumors when all of the following criteria are met:
1. The tumors are BRAF V600E mutation positive.
2. The disease has progressed following prior treatment and there are no satisfactory alternative treatment options.
3. The member is 6 years of age or older.
4. The requested medication will not be used for the treatment of colorectal cancer.
5. The requested medication will be used in combination with dabrafenib (Tafinlar).

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continuation of therapy for an indication outlined in section III when there is no evidence of unacceptable toxicity or disease progression or recurrence while on the current regimen. For patients using Mekinist for adjuvant treatment of cutaneous melanoma, only 12 months of therapy total will be approved.

V. REFERENCES

1. Mekinist [package insert]. East Hanover, NJ: Novartis Pharmaceutical Corporation; June 2022.
2. The NCCN Drugs & Biologics Compendium® © 2022 National Comprehensive Cancer Network, Inc. Available at: https://www.nccn.org. Accessed November 17, 2022.
3. Usubalieva A, Pierson CR, Kavran CA, et al. Primary Meningeal Pleomorphic Xanthoastrocytoma With Anaplastic Features: A Report of 2 Cases, One With *BRAFV600E* Mutation and Clinical Response to the *BRAF* Inhibitor Dabrafenib. *J Neuropathol Exp Neurol*. 2015;74(10):960-969. doi:10.1097/NEN.0000000000000240.
4. Mordechai O, Postovsky S, Vlodavsky E, et al. Metastatic Rhabdoid Meningioma with *BRAF* V600E Mutation and Good Response to Personalized Therapy: Case Report and Review of the Literature. *Pediatr Hematol Oncol*. 2015; 32:3, 207-211, DOI: 10.3109/08880018.2014.936058
5. Lassaletta, A, Guerreiro Stucklin, A, Ramaswamy, V, et al. Profound clinical and radiological response to BRAF inhibition in a 2-month-old diencephalic child with hypothalamic/chiasmatic glioma. *Pediatric Blood and Cancer*. 2016; 63: 2038-2041. doi:10.1002/pbc.26086.
6. Meletath SK, Pavlick D, Brennan T, et al. Personalized Treatment for a Patient with a BRAF V600E Mutation using Dabrafenib and a Tumor Treatment Fields Device in a High-Grade Glioma Arising from Ganglioglioma. *J Natl Compr Canc Netw.* 2016;14(11):1345-1350.
7. Knight T, Shatara M, Carvalho L, et al. Dramatic response to trametinib in a male child with neurofibromatosis type 1 and refractory astrocytoma. *Pediatr Blood Cancer*. 2019; 66(1):e27474.
8. See WL, Tan IL, Mukherjee J, et al. Sensitivity of Glioblastomas to Clinically Available MEK Inhibitors Is Defined by Neurofibromin 1 Deficiency. *Cancer Res*. 2012;72(13):3350.

Reference number
2612-A

SPECIALTY GUIDELINE MANAGEMENT

MEKTOVI (binimetinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met, and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication
Mektovi is indicated, in combination with encorafenib, for the treatment of patients with unresectable or metastatic melanoma with a BRAF V600E or V600K mutation, as detected by an FDA-approved test.

B. Compendial Uses
1. Glioma, BRAF V600 activating mutation-positive
2. Meningioma, BRAF V600 activating mutation-positive
3. Astrocytoma, BRAF V600 activating mutation-positive
4. Cutaneous melanoma
5. Langerhans cell histiocytosis

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of BRAF mutation documentation is necessary to initiate the prior authorization review, where applicable.

III. CRITERIA FOR INITIAL APPROVAL

A. Cutaneous Melanoma
Authorization of 12 months may be granted for treatment of cutaneous melanoma with a BRAF V600 activating mutation (e.g., V600E or V600K) in any of the following settings:
1. Unresectable or metastatic disease when used in combination with encorafenib (Braftovi).
2. Adjuvant treatment of resected stage III disease in combination with encorafenib (Braftovi) when the member has had an unacceptable toxicity to dabrafenib (Tafinlar) in combination with trametinib (Mekinist) or dabrafenib/trametinib are less desirable based on side-effect profiles.
3. Limited resectable local satellite/in-transit recurrent disease in combination with encorafenib (Braftovi) when the member has had an unacceptable toxicity to dabrafenib (Tafinlar) in combination with trametinib (Mekinist) or dabrafenib/trametinib are less desirable based on side-effect profiles

B. Central Nervous System Cancer
Authorization of 12 months may be granted for treatment of BRAF V600 mutation-positive (e.g., BRAF V600E or V600K) gliomas, meningiomas, or astrocytomas.

Reference number(s)
1991-A, 1992-A

SPECIALTY GUIDELINE MANAGEMENT

MENOPUR (menotropins for injection)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Menopur is indicated for development of multiple follicles and pregnancy in ovulatory women as part of an assisted reproductive technology (ART) cycle.

All other indications are considered experimental/investigational and not medically necessary.

II. MEDICAL BENEFIT ALIGNMENT

Specialty Guideline Management coverage review will be bypassed for drug(s) being requested for a procedure that has been approved under a member's medical benefit plan. Such members will be exempt from the requirements in Sections III. A medical authorization number and confirmation of the approved procedure(s) will be required.

NOTE: Some plans may opt-out of medical benefit alignment. Members receiving coverage under such plans must meet the requirements in Sections III.

III. CRITERIA FOR INITIAL APPROVAL

Follicle stimulation
Authorization of 12 months may be granted for members undergoing ovulation induction or assisted reproductive technology (ART) who meet any of the following criteria:
A. Member has completed three or more previous cycles of clomiphene
B. Member has a risk factor for poor ovarian response to clomiphene
C. Member has a contraindication or exclusion to clomiphene
D. Member is 37 years of age or older

IV. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

V. REFERENCES

1. Menopur [package insert]. Parsippany, NJ: Ferring Pharmaceuticals Inc.; May 2018.

CVS caremark

2. Practice Committee of the American Society for Reproductive Medicine. Evidence-based treatments for couples with unexplained infertility: a guideline. *Fertil & Steril.* 2020. 113(2):305-322.

C. Langerhans Cell Histiocytosis
Authorization of 12 months may be granted as a single agent for treatment of Langerhans cell histiocytosis.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

V. REFERENCES

1. Mektovi [package insert]. Boulder, CO: Array BioPharma, Inc.; October 2020.
2. The NCCN Drugs & Biologics Compendium® © 2022 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed November 14, 2022.
3. Usubalieva A, Pierson CR, Kavran CA, et al. Primary Meningeal Pleomorphic Xanthoastrocytoma With Anaplastic Features: A Report of 2 Cases, One With *BRAFV600E* Mutation and Clinical Response to the *BRAF* Inhibitor Dabrafenib. *Journal of neuropathology and experimental neurology*. 2015;74(10):960-969. doi:10.1097/NEN.0000000000000240.
4. Mordechai O, Postovsky S, Vlodavsky E, et al. Metastatic Rhabdoid Meningioma with *BRAF* V600E Mutation and Good Response to Personalized Therapy: Case Report and Review of the Literature. *Pediatric Hematology and Oncology*. 2015; 32:3, 207-211, DOI: 10.3109/08880018.2014.936058
5. Lassaletta, A, Guerreiro Stucklin, A, Ramaswamy, V, et al. Profound clinical and radiological response to BRAF inhibition in a 2-month-old diencephalic child with hypothalamic/chiasmatic glioma. *Pediatric Blood and Cancer*. 2016; 63: 2038-2041. doi:10.1002/pbc.26086.
6. Meletah SK, Pavlick D, Brennan T, et al. Personalized Treatment for a Patient with a BRAF V600E Mutation using Dabrafenib and a Tumor Treatment Fields Device in a High-Grade Glioma Arising from Ganglioglioma. *Journal of the National Comprehensive Cancer Network.* 2016; 14(11): 1345-1350.

QUANTITY LIMIT PRIOR AUTHORIZATION CRITERIA

BRAND NAME
(generic)

METHERGINE TABLET
(methylergonovine)

Status: CVS Caremark Criteria
Type: Quantity Limit; Post Limit Prior Authorization

POLICY

FDA-APPROVED INDICATIONS
Following delivery of placenta, for routine management of uterine atony, hemorrhage and subinvolution of the uterus. For control of uterine hemorrhage in the second stage of labor following delivery of the anterior shoulder.

INITIAL QUANTITY LIMIT**

LIMIT CRITERIA
This limit is coded for daily dose. Accumulation does not apply if limit is coded for daily dose.

Drug	Daily Limit
Methergine (methylergonovine)	4 tablets/day

***If the patient is requesting more than the initial quantity limit, then the claim will reject with a message indicating that the daily dose has been exceeded: "Quantity Limit Exceeded. Daily dose allowance of 4 per day."*

DURATION LIMIT*

Drug	Duration Limit (per 6 months)
Methergine (methylergonovine)	7-day supply

**If the patient is requesting more than a cumulative 7-day supply within the past 6 months, then the claim will reject with a message indicating that a prior authorization is required: "MAX 7DS per 180 days. PA req call 800-XXX-XXXX." [Note: Benefits coding to populate correct PA phone number.]*

The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

COVERAGE CRITERIA
The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for the management of uterine atony, hemorrhage or subinvolution of the uterus following delivery of the placenta OR for control of uterine hemorrhage in the second stage of labor
  AND
- There is a valid medical reason why the patient requires additional quantities within a six-month time period

Quantity Limits apply.

Daily limit: 4 tablets / day, Duration limit: 14-day supply / 6 months

REFERENCES

1. Methergine [package insert]. Baltimore, Maryland: Lupin Pharma; January 2016.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2022; Accessed November 18, 2022.
3. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed November 18, 2022.

QUANTITY LIMIT PRIOR AUTHORIZATION CRITERIA

BRAND NAME
(generic)

METROCREAM
(metronidazole cream 0.75%)

METROGEL
(metronidazole gel 1%)

METROLOTION
(metronidazole lotion 0.75%)

(metronidazole gel 0.75%)

NORITATE
(metronidazole cream 1%)

Status: CVS Caremark Criteria
Type: Quantity Limit; Post Limit Prior Authorization

POLICY

FDA-APPROVED INDICATIONS
MetroCream
MetroCream (metronidazole topical cream) Topical Cream is indicated for topical application in the treatment of inflammatory papules and pustules of rosacea.
MetroGel
MetroGel is indicated for the topical treatment of inflammatory lesions of rosacea.
MetroLotion
MetroLotion Topical Lotion is indicated for topical application in the treatment of inflammatory papules and pustules of rosacea.
Metronidazole gel 0.75%
Metronidazole gel is indicated for topical application in the treatment of inflammatory papules and pustules of rosacea.
Noritate
Noritate is indicated for the topical treatment of inflammatory lesions and erythema of rosacea.

INITIAL QUANTITY LIMIT**

LIMIT CRITERIA
Limits should accumulate across all drugs and strengths up to highest quantity listed depending on the order the claims are processed. Accumulation does not apply if limit is coded for daily dose.

PLEASE NOTE: Since manufacturer package sizes may vary, it is the discretion of the dispensing pharmacy to fill quantities per package size up to these quantity limits. In such cases the filling limit and day supply may be less than what is indicated.

Drug	1 Month Limit*	3 Month Limit*
MetroCream (metronidazole cream 0.75%)	60 gm / 25 days	180 gm / 75 days

MetroGel (metronidazole gel 1%)	60 gm / 25 days	180 gm / 75 days
MetroLotion (metronidazole lotion 0.75%)	60 mL / 25 days	180 mL / 75 days
(metronidazole gel 0.75%)	60 gm / 25 days	180 gm / 75 days
Noritate (metronidazole cream 1%)	60 gm / 25 days	180 gm / 75 days

**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*

**If the patient is requesting more than the initial quantity limit, the claim will reject with a message indicating that a prior authorization is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for the treatment of rosacea

AND

- The requested drug is not being used in a footbath

Quantity Limits apply.

**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*

REFERENCES

1. MetroCream [package insert]. Fort Worth, TX: Galderma Laboratories, L.P; January 2017.
2. MetroGel [package insert]. Fort Worth, TX: Galderma Laboratories, L.P; March 2022.
3. MetroLotion [package insert]. Fort Worth, TX: Galderma Laboratories, L.P; February 2017.
4. Metronidazole gel 0.75% [package insert]. Mason, OH: Prasco Laboratories; September 2014.
5. Noritate [package insert]. Bridgewater, NJ: Bausch Health US, LLC; June 2020.
6. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2023; Accessed January 23, 2023.
7. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed January 23, 2023.
8. Eichenfield L, Tom W, Berger T, et al. Guidelines of Care for the Management of Atopic Dermatitis Section 2. Management and Treatment of Atopic Dermatitis with Topical Therapies. *J Am Acad Dermatol* 2014; 71:116-32. https://www.aad.org/practicecenter/quality/clinical-guidelines/atopic-dermatitis. Accessed January 23, 2023.
9. Burn Triage and Treatment - Thermal Injuries. Available at: https://chemm.hhs.gov/burns.htm. Accessed January 23, 2023.

Reference number
2098-A

SPECIALTY GUIDELINE MANAGEMENT

ZAVESCA (miglustat)
Yargesa (miglustat)
miglustat (generic)
OPFOLDA (miglustat)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. miglustat (generic)/Yargesa/Zavesca:
      Indicated as monotherapy for the treatment of adult patients with mild to moderate type 1 Gaucher disease for whom enzyme replacement therapy is not a therapeutic option (e.g. due to allergy, hypersensitivity, or poor venous access).

   2. Opfolda:
      Indicated, in combination with Pombiliti, for the treatment of adult patients with late-onset Pompe disease (lysosomal acid alpha-glucosidase [GAA] deficiency) weighing greater than or equal to 40 kg and who are not improving on their current enzyme replacement therapy (ERT).

B. Compendial Uses
   Niemann-Pick disease, type C

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
A. Gaucher disease type 1: beta-glucocerebrosidase enzyme assay or genetic testing results supporting diagnosis.
B. Niemann-Pick disease, type C: genetic testing results showing mutations in *NPC1* or *NPC2* genes.
C. Late-onset Pompe disease:
   1. Initial requests: acid alpha-glucosidase enzyme assay or genetic testing results supporting diagnosis.
   2. Continuation requests: chart notes documenting a positive response to therapy (e.g., improvement, stabilization, or slowing of disease progression for motor function, walking capacity, respiratory function, muscle strength).

III. CRITERIA FOR INITIAL APPROVAL

A. Gaucher disease type 1 (miglustat (generic)/Yargesa/Zavesca only)
Authorization of 12 months may be granted for treatment of Gaucher disease type 1 when ALL of the following criteria are met:

1. The diagnosis of Gaucher disease was confirmed by enzyme assay demonstrating a deficiency of beta-glucocerebrosidase (glucosidase) enzyme activity or by genetic testing, and
2. The member has a documented inadequate response to, intolerable adverse events with, or a clinical reason to not use enzyme replacement therapy (e.g., allergy, hypersensitivity, poor venous access).

B. Niemann-Pick disease, type C (miglustat (generic)/Yargesa/Zavesca only)
Authorization of 12 months may be granted for treatment of Niemann-Pick disease, type C when the diagnosis was confirmed by genetic testing results showing mutations in *NPC1* or *NPC2* genes.

C. Late-onset Pompe disease (Opfolda only)
Authorization of 12 months may be granted for treatment of late-onset Pompe disease when all of the following criteria are met:
1. Member is 18 years of age or older.
2. Member weighs greater than or equal to 40 kg.
3. Diagnosis was confirmed by enzyme assay demonstrating a deficiency of acid alpha-glucosidase enzyme activity or by genetic testing.
4. The requested medication will be taken in combination with Pombiliti (cipaglucosidase alfa-atga).
5. Member is not improving on current enzyme replacement therapy (ERT) (e.g., Lumizyme, Nexviazyme).

IV. CONTINUATION OF THERAPY

A. Gaucher disease type 1 (miglustat (generic)/Yargesa/Zavesca only)
Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for Gaucher disease type 1 when all of the following criteria are met:
1. The diagnosis of Gaucher disease was confirmed by enzyme assay demonstrating a deficiency of beta-glucocerebrosidase (glucosidase) enzyme activity or by genetic testing.
2. Member is not experiencing an inadequate response or any intolerable adverse events from therapy.

B. Niemann-Pick disease, type C (miglustat (generic)/Yargesa/Zavesca only)
Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for Niemann-Pick disease, type C when all of the following criteria are met:
1. Member meets the criteria for initial approval.
2. Member is not experiencing an inadequate response or any intolerable adverse events from therapy.

C. Late-onset Pompe disease (Opfolda only)
Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for late-onset Pompe disease who are responding to therapy (e.g., improvement, stabilization, or slowing of disease progression for motor function, walking capacity, respiratory function, or muscle strength).

V. REFERENCES

1. Zavesca [package insert]. Titusville, NJ: Actelion Pharmaceuticals US, Inc.; August 2022.
2. miglustat [package insert]. Titusville, NJ: CoTherix, Inc.; July 2022.
3. Lexicomp Online, Lexi-Drugs Online. Waltham, MA: UpToDate, Inc.; Updated November 7, 2022. https://online.lexi.com. Accessed December 2, 2022.
4. National Organization for Rare Disorders. (2003). *NORD guide to rare disorders.* Philadelphia: Lippincott Williams & Wilkins.
5. Opfolda [package insert]. Philadelphia, PA: Amicus Therapeutics US, LLC; September 2023
6. Yargesa [package insert]. Parsippany, NJ: Edenbridge Pharmaceuticals, LLC; January 2022.

Reference number(s)
1618-A

SPECIALTY GUIDELINE MANAGEMENT

MIRCERA (methoxy polyethylene glycol-epoetin beta)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Mircera is indicated for the treatment of anemia associated with chronic kidney disease (CKD) in:

- Adult patients on dialysis and adult patients not on dialysis.
- Pediatric patients 5 to 17 years of age on hemodialysis who are converting from another erythropoiesis-stimulating agent (ESA) after their hemoglobin level was stabilized with an ESA.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Note: Requirements regarding hemoglobin level exclude values due to recent transfusion. All members must be assessed for iron deficiency anemia and have adequate iron stores (defined as a serum transferrin saturation [TSAT] level greater than or equal to 20% within the prior 3 months) or are receiving iron therapy before starting Mircera. Members may not use Mircera concomitantly with other erythropoiesis stimulating agents.

Anemia Due to Chronic Kidney Disease (CKD)
Authorization of 12 weeks may be granted for the treatment of anemia due to chronic kidney disease in members with pretreatment hemoglobin < 10 g/dL.

III. CONTINUATION OF THERAPY

Note: Requirements regarding current hemoglobin level exclude values due to recent transfusion. All members must be assessed for iron deficiency anemia and have adequate iron stores (defined as a serum transferrin saturation [TSAT] level greater than or equal to 20% with the prior 3 months) or are receiving iron therapy before continuation of treatment with Mircera. Members may not use Mircera concomitantly with other erythropoiesis stimulating agents.

Anemia Due to Chronic Kidney Disease (CKD)

1. Authorization of 12 weeks may be granted for continued treatment of anemia due to chronic kidney disease in members with current hemoglobin < 12 g/dL and the member has shown a response to therapy with a rise in hemoglobin of ≥ 1 g/dL after at least 12 weeks of ESA therapy.
2. Authorization of up to 12 weeks may be granted for continued treatment of anemia due to chronic kidney disease in members who have not completed 12 weeks of ESA therapy.

IV. REFERENCES

1. Mircera [package insert]. South San Francisco, CA: Hoffmann-La Roche Inc.; June 2018.
2. Kidney Disease: Improving Global Outcomes (KDIGO) Anemia Work Group. KDIGO Clinical Practice Guideline for Anemia in Chronic Kidney Disease. Kidney Int. 2012;Suppl 2:279-335.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME
(generic)

MOVANTIK
(naloxegol)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

POLICY

FDA-APPROVED INDICATIONS
Movantik is indicated for the treatment of opioid-induced constipation (OIC) in adult patients with chronic non-cancer pain, including patients with chronic pain related to prior cancer or its treatment who do not require frequent (e.g., weekly) opioid dosage escalation.

COVERAGE CRITERIA
The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for the treatment of opioid-induced constipation (OIC) in an adult patient with chronic non-cancer pain, including chronic pain related to prior cancer or its treatment who does not require frequent (e.g., weekly) opioid dosage escalation

REFERENCES

1. Movantik [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; April 2020.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2021; Accessed September 2, 2021.
3. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed September 2, 2021.

Reference number(s)
2990-A

SPECIALTY GUIDELINE MANAGEMENT

MULPLETA (lusutrombopag)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Mulpleta is indicated for the treatment of thrombocytopenia in adult patients with chronic liver disease who are scheduled to undergo a procedure.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review for thrombocytopenia in chronic liver disease: pretreatment platelet count.

III. EXCLUSIONS

Coverage will not be provided for members with the following exclusion: concomitant use of Mulpleta with other thrombopoietin receptor agonists (e.g., Doptelet, Promacta, Nplate) or with spleen tyrosine kinase inhibitors (e.g., Tavalisse).

IV. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with a hematologist, hepatologist or gastroenterologist

V. CRITERIA FOR INITIAL APPROVAL

Thrombocytopenia in chronic liver disease
Authorization of 30 days may be granted for treatment of thrombocytopenia in members with chronic liver disease when both of the following criteria are met:
1. Member has an untransfused platelet count of less than 50 x 10^9/L taken within 14 days of the request.
2. Member is scheduled to undergo a procedure.

VI. CONTINUATION OF THERAPY

Thrombocytopenia in chronic liver disease

Continuation of therapy, defined as use beyond the initial approval for same procedure, is not approvable. All members (including new members) requesting authorization due to newly scheduled procedure must meet all initial authorization criteria.

VII.REFERENCES

1. Mulpleta [package insert]. Florham Park, NJ: Shionogi Inc.; April 2020.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME
(generic)

MULTAQ
(dronedarone)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

POLICY

FDA-APPROVED INDICATIONS
Multaq is indicated to reduce the risk of hospitalization for atrial fibrillation in patients in sinus rhythm with a history of paroxysmal or persistent atrial fibrillation (AF).

COVERAGE CRITERIA
The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed to reduce the risk of hospitalization for atrial fibrillation in a patient with a history of paroxysmal or persistent atrial fibrillation (AF), i.e., non-permanent AF

REFERENCES

1. Multaq [package insert]. Bridgewater, NJ: Sanofi-Aventis U.S. LLC; November 2020.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2022; Accessed March 23, 2022.
3. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed March 23, 2022.
4. Multaq (dronedarone) Drug Safety Communication. Available at: https://www.fda.gov/drugs/drugsafety/ucm283933.htm. Accessed March 23, 2022.

QUANTITY LIMIT PRIOR AUTHORIZATION CRITERIA

BRAND NAME*
(generic)

(mupirocin calcium cream)

CENTANY OINTMENT
(mupirocin)

Status: CVS Caremark Criteria
Type: Quantity Limit; Post Limit Prior Authorization ***Ref # 2940-HJ***

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Mupirocin Calcium Cream
Mupirocin calcium cream is indicated for the treatment of secondarily infected traumatic skin lesions (up to 10 cm in length or 100 cm^2 in area) due to susceptible isolates of *Staphylococcus aureus (S. aureus) and Streptococcus pyogenes (S. pyogenes)*.

Centany Ointment
Centany ointment is indicated for the topical treatment of impetigo due to: *Staphylococcus aureus* and *Streptococcus pyogenes*.

Compendial Uses
Complication of catheter – Infectious disease, Exit site; Prophylaxis[5] (Centany only)
Superficial bacterial infection of skin[5]

INITIAL QUANTITY LIMIT***

LIMIT CRITERIA
Limits do not accumulate together; patient is allowed the maximum limit for each drug and strength

Drug	1 Month Limit*	3 Month Limit*
Mupirocin calcium cream	30 gm / 25 days	Does Not Apply**
Centany (mupirocin) ointment	30 gm / 25 days	Does Not Apply**

** The duration of 25 days is used for a 30-day fill period to allow time for refill processing.*
*** These drugs are for short-term acute use; therefore, the mail limit will be the same as the retail limit. The intent is for prescriptions of the requested drug to be filled one month at a time, even if filled at mail order; there should be no 3-month supplies filled.*

***If the patient is requesting more than the initial quantity limit, the claim will reject with a message indicating that a prior authorization is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The request is for mupirocin calcium CREAM **AND**

- The requested drug is being prescribed for the any of the following: A) treatment of secondarily infected traumatic skin lesions due to susceptible isolates of Staphylococcus aureus or Streptococcus pyogenes, B) superficial bacterial skin infections

OR

- The request is for mupirocin OINTMENT (Centany) **AND**
  - The requested drug is being prescribed for any of the following: A) impetigo due to Staphylococcus aureus or Streptococcus pyogenes, B) superficial bacterial skin infections, C) prophylaxis of catheter exit-site infections

AND

- The requested drug is not being used in a footbath

AND

- The requested drug is being prescribed to treat a body surface area that requires more than 30 grams in a one-month period

Quantity Limits apply.

RATIONALE

Centany Ointment

A small amount of Centany (mupirocin) ointment should be applied to the affected area three times daily or as directed by a physician. Patients not showing a clinical response within 3 to 5 days should be re-evaluated.

The initial quantity limit for Centany (mupirocin) ointment is set at 30 grams per month. The initial quantity limit should be sufficient to treat impetigo on 4% of a body surface area (BSA). Bullous and nonbullous impetigo can be treated with oral or topical antimicrobials, but oral therapy is recommended for patients with numerous lesions or in outbreaks affecting several people to help decrease transmission of infection.[6] Duration of treatment should last for up to 10 days.[3] A fingertip unit equals 0.5 grams, which treats a 2% BSA.[7,8] To calculate the initial quantity limit, one gram was used for a 4% BSA multiplied by three times daily dosing for up to a 10 days of treatment.

Mupirocin Calcium Cream

For the treatment of secondarily infected traumatic skin lesions, a small amount of mupirocin calcium cream should be applied to the affected area three times daily for 10 days. Patients not showing a clinical response within 3 to 5 days should be re-evaluated.

The initial quantity limit for mupirocin calcium cream is set at 30 grams per month. The initial quantity limit should be sufficient to treat secondarily infected traumatic skin lesions (up to 10 cm in length or 100 cm^2 in area). A fingertip unit equals 0.5 grams, which treats a 2% BSA.[7,8] To calculate the initial quantity limit for a single lesion, 0.5 gram was used for a 2% BSA multiplied by three times daily dosing for 10 days which is 15 grams. However, taking into consideration the largest package size and/or multiple lesions, 30 grams will be used as the initial quantity limit.

If the patient is requesting more than the initial quantity limit, the claim will reject with a message indicating that a prior authorization is required.

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Centany (mupirocin) ointment is indicated for the topical treatment of impetigo due to: *Staphylococcus aureus* and *Streptococcus pyogenes*. In addition, Centany (mupirocin) ointment is effective for the prophylaxis of catheter exit-site infections, as well as for the treatment of superficial bacterial infections of the skin.[4,5] Mupirocin calcium cream is indicated for the treatment of secondarily infected traumatic skin lesions (up to 10 cm in length or 100 cm^2 in area) due to susceptible isolates of *Staphylococcus aureus* (*S. aureus*) and *Streptococcus pyogenes* (*S. pyogenes*). Both mupirocin ointment and mupirocin calcium cream are also effective for the treatment of superficial bacterial infections of the skin.[5]

For patients with a body surface area that requires more than 30 grams of Centany (mupirocin) ointment or mupirocin calcium cream for treatment, the post limit approval quantity will be set at 60 grams per month, which provides two times more than the initial quantity limit. The duration of approval will be one month given impetigo, superficial bacterial infections of the skin, and secondarily infected traumatic skin lesions have short treatment course durations.[1-4] In studies

that examined the use of mupirocin for catheter exit site prophylaxis, dosing regimens used included once weekly, three times weekly or once daily application of mupirocin.[5] The International Society for Peritoneal Dialysis (ISPD) guidelines recommend daily topical application of antibiotic to the catheter exit site to prevent exit site infections caused by *S. aureus*. The optimal frequency of topical mupirocin, however, is not clearly defined.[9] Also, the CDC recommends the use of povidone iodine antiseptic ointment or bacitracin/gramicidin/ polymyxin B ointment at the hemodialysis catheter exit site after catheter insertion and at the end of each dialysis session, only if this ointment does not interact with the material of the hemodialysis catheter per manufacturer's recommendation.[10] Generally, the initial quantity limit of 30 grams per month would provide sufficient amount to apply a thin film to the cannula exit once daily.

The Post Limit prior authorization criteria do not approve topical antibiotics for use in a footbath, as this is not an FDA-approved use.

Mupirocin calcium cream is available in 15-gram and 30-gram tubes. Centany (mupirocin) ointment is available in 30-gram tubes. Generic mupirocin ointment is available in 15-gram and 22-gram tubes.

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Written by:	UM Development (JK)
Date Written:	04/2019
Revised:	(JK) 02/2020 (included compendial use of superficial bacterial skin infections for mupirocin calcium cream), (TM) 12/2020 (no clinical changes); (RZ) 08/2021 (no clinical changes)
Reviewed:	Medical Affairs (GAD) 04/2019; (CHART) 02/27/2020, 12/31/2020, 09/30/2021 External Review: 06/2019, 06/2020, 04/2021, 12/2021

CRITERIA FOR APPROVAL

1	Which drug is being requested (applies to brand or generic)? [Note: Please check the drug being requested (applies to brand or generic).] [] Mupirocin calcium CREAM (If checked, go to question 2) [] Mupirocin OINTMENT (Centany) (If checked, go to question 3)		
2	Is the requested drug being prescribed for the any of the following: A) treatment of secondarily infected traumatic skin lesions due to susceptible isolates of Staphylococcus aureus or Streptococcus pyogenes, B) superficial bacterial skin infections? [If yes, then skip to question 4.] [If no, then no further questions.]	Yes	No

3	Is the requested drug being prescribed for any of the following: A) impetigo due to Staphylococcus aureus or Streptococcus pyogenes, B) superficial bacterial skin infections, C) prophylaxis of catheter exit-site infections? [If no, then no further questions.]	Yes	No
4	Is the requested drug being used in a footbath? [If yes, then no further questions.]	Yes	No
5	Is the requested drug being prescribed to treat a body surface area that requires more than 30 grams in a one-month period? [If no, then no further questions.]	Yes	No
6	Does the patient require more than the plan allowance of 60 grams per month? [RPh Note: If yes, then deny and enter a partial approval for 60 grams / 25 days.]	Yes	No

Mapping Instructions			
	Yes	**No**	**DENIAL REASONS – DO NOT USE FOR MEDICARE PART D**
1.	1=2, 2=3		
2.	Go to 4	Deny	You do not meet the requirements of your plan. Your plan covers additional quantities of mupirocin calcium cream when it is being used for a skin infection caused by specific bacteria that are susceptible to the drug. Your request has been denied based on the information we have. [Short Description: No approvable diagnosis, cream]
3.	Go to 4	Deny	You do not meet the requirements of your plan. Your plan covers additional quantities of Centany (mupirocin) ointment when it is being used for a skin infection caused by specific bacteria that are susceptible to the drug. Your request has been denied based on the information we have. [Short Description: No approvable diagnosis, ointment]
4.	Deny	Go to 5	You do not meet the requirements of your plan. Your plan covers additional quantities of this drug when it is not being used in a footbath. Your request has been denied based on the information we have. [Short Description: Used in footbath]
5.	Go to 6	Deny	You do not meet the requirements of your plan. Your plan allows coverage of up to 30 grams per month of this drug without requiring a prior authorization. Your plan covers additional quantities of this drug when you need to treat a body surface area that requires more than 30 grams in a one-month period. Your request has been denied based on the information we have. [Short Description: No need for additional body surface area coverage]
6.	Deny	Approve, 1 month, 60 grams/25 days*	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 60 grams per month of the requested drug and strength. Your request has been partially approved. You have been approved for the maximum

			quantity that your plan covers for a duration of 1 month. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity]

** The duration of 25 days is used for a 30-day fill period to allow time for refill processing. These drugs are for short-term acute use; therefore, the mail limit will be the same as the retail limit. The intent is for prescriptions of the requested drug to be filled one month at a time, even if filled at mail order; there should be no 3-month supplies filled.*

Reference number
1674-A

SPECIALTY GUIDELINE MANAGEMENT

MYALEPT (metreleptin)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication
Myalept is indicated as an adjunct to diet as replacement therapy to treat the complications of leptin deficiency in patients with congenital or acquired generalized lipodystrophy.

Limitations of Use:
1. The safety and effectiveness of Myalept for the treatment of complications of partial lipodystrophy have not been established.
2. The safety and effectiveness of Myalept for the treatment of liver disease, including nonalcoholic steatohepatitis (NASH), have not been established.
3. Myalept is not indicated for use in patients with HIV-related lipodystrophy.
4. Myalept is not indicated for use in patients with metabolic disease, including diabetes mellitus and hypertriglyceridemia, without concurrent evidence of congenital or acquired generalized lipodystrophy.

B. Compendial Use
Partial lipodystrophy in patients with confirmed leptin deficiency and metabolic abnormalities

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: leptin level (for initial requests)

III. EXCLUSIONS

Coverage will not be provided for members with any of the following exclusions:
A. HIV-related lipodystrophy
B. Generalized obesity not associated with generalized lipodystrophy

IV. CRITERIA FOR INITIAL APPROVAL

Lipodystrophy
Authorization of 6 months may be granted for treatment of lipodystrophy when ALL of the following criteria are met:

A. Member has a diagnosis of congenital generalized lipodystrophy (i.e., Berardinelli-Seip syndrome), acquired generalized lipodystrophy (i.e., Lawrence syndrome), or partial lipodystrophy
B. Member has leptin deficiency confirmed by laboratory testing (i.e., less than 12 ng/ml)
C. Member has at least one complication of lipodystrophy (e.g., diabetes mellitus, hypertriglyceridemia, increased fasting insulin level)

V. CONTINUATION OF THERAPY

Lipodystrophy
Authorization of 12 months may be granted to members requesting continuation of treatment for lipodystrophy when the member has experienced an improvement from baseline in metabolic control (e.g., improved glycemic control, decrease in triglycerides, decrease in hepatic enzyme levels)

VI. REFERENCES

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PRIOR AUTHORIZATION CRITERIA

BRAND NAME
(generic)

MYFEMBREE
(relugolix/estradiol/norethindrone acetate)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

POLICY

FDA-APPROVED INDICATIONS

Heavy Menstrual Bleeding Associated with Uterine Leiomyomas
Myfembree is indicated for the management of heavy menstrual bleeding associated with uterine leiomyomas (fibroids) in premenopausal women.

Moderate to Severe Pain Associated with Endometriosis
Myfembree is indicated for the management of moderate to severe pain associated with endometriosis in premenopausal women.

Limitations of Use:
Use of Myfembree should be limited to 24 months due to the risk of continued bone loss that may not be reversible.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for the management of heavy menstrual bleeding associated with uterine leiomyomas (fibroids) in a premenopausal patient

OR

- The requested drug is being prescribed for the management of moderate to severe pain associated with endometriosis in a premenopausal patient
  AND
  - The patient has not received the maximum recommended treatment course of 12 months of Lupron Depot or Lupaneta Pack OR 6 months of Synarel or Zoladex

AND

- If the patient has previously received treatment with an elagolix-containing product (e.g., Oriahnn, Orilissa) or a relugolix-containing product (e.g., Myfembree), the patient has not already received ANY of the following: A) Greater than or equal to 24 cumulative months of treatment with elagolix-containing products (e.g., Oriahnn, Orilissa) and/or relugolix-containing products (e.g., Myfembree), B) Greater than or equal to 6 months of treatment with Orilissa 200 mg twice daily

Duration of Approval Limits apply.
Total additive duration: 24 months

REFERENCES

1. Lupaneta Pack [package insert]. North Chicago, IL: AbbVie Inc.; June 2015.
2. Lupron Depot [package insert]. North Chicago, IL: AbbVie Inc.; July 2022.
3. Myfembree [package insert]. Brisbane, CA: Myovant Sciences, Inc.; September 2022.
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PRIOR AUTHORIZATION CRITERIA

DRUG CLASS	**NAIL ANTIFUNGAL, TOPICAL**
BRAND NAME* **(generic)**	**JUBLIA** **(efinaconazole topical solution)**
	KERYDIN **(tavaborole topical solution)**
Status: CVS Caremark Criteria	
Type: Initial Prior Authorization	***Ref # 1325-A***

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Jublia
Jublia (efinaconazole) topical solution, 10% is an azole antifungal indicated for the topical treatment of onychomycosis of the toenail(s) due to Trichophyton rubrum and Trichophyton mentagrophytes.

Kerydin
Kerydin (tavaborole) topical solution, 5% is an oxaborole antifungal indicated for the treatment of onychomycosis of the toenails due to Trichophyton rubrum or Trichophyton mentagrophytes.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for onychomycosis of the toenail(s) due to Trichophyton rubrum or Trichophyton mentagrophytes

AND

- The patient's diagnosis has been confirmed with a fungal diagnostic test (e.g., potassium hydroxide [KOH] preparation, fungal culture, or nail biopsy)

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, or standards of medical practice. Jublia (efinaconazole) topical solution, 10% is an azole antifungal indicated for the topical treatment of onychomycosis of the toenail(s) due to Trichophyton rubrum and Trichophyton mentagrophytes. Kerydin (tavaborole) topical solution, 5% is an oxaborole antifungal indicated for the treatment of onychomycosis of the toenails due to Trichophyton rubrum or Trichophyton mentagrophytes.[1-4]

Jublia is to be applied to affected toenails once daily for 48 weeks, using the integrated flow-through brush applicator. When applying Jublia, the toenail, the toenail folds, toenail bed, hyponychium, and the undersurface of the toenail plate, are to be completely covered.[1] Kerydin is to be applied to affected toenails once daily for 48 weeks. Kerydin should be applied to the entire toenail surface and under the tip of each toenail being treated.[2]

Onychomycosis may be diagnosed by the presence of fungi by culture, microscopy (Potassium hydroxide [KOH] stain), or histological examination of the nail plate.[6] Microscopy is a commonly used method because it is inexpensive and easy to

perform; nail clippings or scrapings are placed in a drop of KOH and examined under a microscope for the presence of fungal elements.[7]

Per the CDC, oral antifungal therapy (terbinafine) is considered first line treatment for confirmed onychomycosis.[7] According to the Cochrane review, medication taken orally appears to cure the condition more quickly and effectively than topical treatment; there was high-quality evidence that oral azole (itraconazole) and terbinafine treatments were more effective for achieving mycological cure and clinical cure for onychomycosis compared to placebo, and when compared directly, terbinafine was probably more effective than azoles and likely not associated with excess adverse events (griseofulvin was associated with more adverse reactions than azoles and terbinafine).[6] Even though oral treatment is limited by drug interactions and risk of acute liver injury, topical lacquer treatments have negligible efficacy and low success rates due to the nail's physical properties.[5,6]

Jublia is the first topical triazole antifungal for the treatment of onychomycosis. In two randomized trials, complete cure rate, defined as no evidence of fungal infection at week 52, was demonstrated in 15.2% to 17.8% of patients receiving efinaconazole (N=1236) compared with 3.3% to 5.5% receiving placebo (N=415) for the treatment of onychomycosis of the toenail.[5]

In two randomized trials, complete cure rate for Kerydin, defined as no evidence of fungal infection at week 52, was demonstrated in 6.5% and 9.1% of patients receiving tavaborole (N=399, 396) compared with 0.5% and 1.5% receiving placebo (N=194, 205) for the treatment of onychomycosis of the toenail.[2]

Jublia and Kerydin represent alternative treatment options to oral antifungal agents for onychomycosis. Coverage is provided for confirmed cases of toenail onychomycosis due to Trichophyton infection.

REFERENCES

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Written by:	UM Development (CT)
Date Written:	06/2014
Revised:	(MS) 05/2015, (NB) 12/2015 (modified from standard for plan design alignment as an option for clients who request modeling); (KM) 05/2016 (coverage criteria bullet one changed from "and" to "or"); (JH) 04/2017 (no clinical changes); (KC) 04/2018, (ME) 02/2019 (no clinical changes); (NZ) 02/2020 (no clinical changes); (KC) 12/2020 (no clinical changes); (PM) 09/2021 (no clinical changes)
Reviewed:	Medical Affairs (LMS) 06/2014; (KU) 05/2015, (AD) 01/2016; (ME) 05/2016; (CHART) 02/27/20, 12/31/20, 09/30/21 External Review: 07/2014, 10/2015, 02/2016, 08/2016, 08/2017, 06/2018, 06/2019, 06/2020, 04/2021, 12/2021

CRITERIA FOR APPROVAL

1	Is the requested drug being prescribed for onychomycosis of the toenail(s) due to Trichophyton rubrum or Trichophyton mentagrophytes? [If no, then no further questions.]	Yes	No

2	Has the patient's diagnosis been confirmed with a fungal diagnostic test (e.g., potassium hydroxide [KOH] preparation, fungal culture, or nail biopsy)?	Yes	No

Mapping Instructions			
	Yes	**No**	**DENIAL REASONS – DO NOT USE FOR MEDICARE PART D**
1.	Go to 2	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have a specific fungal infection of the toenail(s). Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]
2.	Approve, 12 Months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you meet all of these conditions: - You have a specific fungal infection of the toenail(s) - You had a test to confirm your toenail fungus Your request has been denied based on the information we have. [Short Description: No confirmation of diagnosis]

PRIOR AUTHORIZATION CRITERIA

BRAND NAME*
(generic)

NAMENDA
(memantine hydrochloride)

Prior Authorization applies only to patients less than 30 years of age.

Status: CVS Caremark Criteria
Type: Initial Prior Authorization with Age Edit ***Ref # 511-B***

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Namenda, Namenda XR, and memantine hydrochloride oral solution are indicated for the treatment of moderate to severe dementia of the Alzheimer's type.

Compendial Uses
Vascular Dementia[4,6,7]

COVERAGE CRITERIA

The requested drug will be covered with prior authorization for patients less than 30 years of age when the following criteria are met:

- The patient has any of the following diagnoses: A) moderate to severe dementia of the Alzheimer's type, B) vascular dementia

AND

- If the request is for continuation of therapy, the medication continues to provide benefit to the patient
  [Note: If slowing decline of cognitive function is no longer a goal, or if the patient is rapidly declining, treatment with the medication is no longer appropriate.]
  OR
- If the request is NOT for continuation of therapy, the diagnosis is supported by a validated cognitive assessment within the past 12 months

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. These criteria only apply to patients less than 30 years of age. Namenda (memantine hydrochloride), Namenda XR (memantine hydrochloride extended release), and memantine hydrochloride oral solution are indicated for the treatment of moderate to severe dementia of the Alzheimer's type.[1-3]

Memantine may also be effective in the treatment of vascular dementia. In randomized trials, memantine significantly improved some symptom rating scores compared with placebo in patients with mild to moderate vascular dementia. According to Orgogozo et al, memantine 20 mg/day improved cognition consistently across different cognitive scales in patients with mild to moderate vascular dementia, with at least no deterioration in global functioning and behavior. Memantine was well tolerated and devoid of concerning side effects.[4,6,7]

The American College of Medical Genetics (ACMG) and the National Society of Genetic Counselors (NSGC) practice guidelines regarding genetic counseling and testing for Alzheimer disease (AD) provide clinicians with a framework for

assessing their patients' genetic risk for AD, identifying which individuals may benefit from genetic testing, and providing the key elements of genetic counseling for AD. Alzheimer disease currently affects more than 5 million Americans and although the majority of cases occur in the elderly, approximately 250,000 people have early-onset Alzheimer Disease (EOAD) with onset of symptoms before age 65 years. Per the guidelines, there are known deterministic (causative) genes in which pathogenic variants are associated with EOAD in patients as young as 30 years of age. Therefore, these criteria only apply to patients less than 30 years of age.[12,13]

The treatment of patients with dementia should be based on a thorough psychiatric, neurological, and general medical evaluation of the nature and cause of the cognitive deficits and associated noncognitive symptoms.[8] According to the Diagnostic and Statistical Manual of Mental Disorders 5th Edition (DSM-5), diagnostic criteria for Major Neurocognitive Disorder (dementia) or Mild Neurocognitive Disorder includes evidence of cognitive decline from a previous level of performance in one or more cognitive domains based on: 1) Concern of the individual, a knowledgeable informant, or the clinician that there has been a decline in cognitive function and 2) An impairment in cognitive performance, preferably documented by standardized neuropsychological testing or, in its absence, another quantified clinical assessment.[10] Tests commonly used in clinical studies to evaluate the efficacy of available therapies in the treatment of Alzheimer's dementia and the treatment of vascular dementia include but are not limited to, the Mini-Mental State Exam (MMSE) and the Alzheimer's Disease Assessment Scale—Cognitive Subscale (ADAS-Cog).[1-4,6-9,11] The decision to initiate therapy should be based on evaluation of the benefits and risks associated with an individual patient. In more advanced dementia, decision makers may not view stabilization or slowing of decline as a desirable goal if quality of life is judged to be poor. Memantine has known adverse events, and the decision to manage patients with dementia should balance harms against benefit.[11] Therefore, prior to initiating therapy with memantine, patients should receive a validated cognitive assessment within the past 12 months.

Ongoing assessment includes routine monitoring of the development and change in cognitive and noncognitive psychiatric symptoms and their response to intervention. In order to offer prompt treatment, enhance safety, and provide timely advice to the patient and family, it is usually necessary to see patients in routine follow-up at least every 3 to 6 months.[8] Currently, the available evidence is insufficient to determine the optimal duration of therapy of memantine. A beneficial effect (e.g., improvement, stabilization, slowing of decline), if any, would generally be observed within 3 months on the basis of duration of trials.[11] Therefore, if the request is for continuation of therapy, the medication must continue to provide benefit to the patient.

No medication treatment has been shown to delay the progression of neurodegeneration. If a patient is declining rapidly despite pharmacologic therapy (e.g., cholinesterase inhibitor), they may be considered a medication non-responder and the medication can be discontinued. Additionally, if slowing decline is no longer a goal, treatment with a memantine is no longer appropriate.[8,11]

REFERENCES

1. Namenda [package insert]. Madison, NJ: Allergan USA, Inc.; November 2018.
2. Namenda XR [package insert]. Madison, NJ: Allergan USA, Inc.; November 2019.
3. Memantine Hydrochloride Oral Solution [package insert]. Wall, NJ: Seton Pharmaceuticals; June 2021.
4. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed April 28, 2022.
5. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2022; Accessed April 28, 2022.
6. Orgogozo JM, Rigaud AS, Stoffler A, et al. Efficacy and Safety of Memantine in Patients with Mild to Moderate Vascular Dementia. *Stroke*. 2002;33:1834-39.
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9. Rabins P, Rovner B, Rummans T, et al. Guideline Watch (October 2014): Practice Guideline for the Treatment of Patients with Alzheimer's Disease and Other Dementias. 2014;1-26.
10. American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition. Arlington, VA, American Psychiatric Association, 2013.

11. Qaseem A, Snow V, Cross T, et al. Current Pharmacological Treatment of Dementia: A Clinical Practice Guideline from the American College of Physicians and the American Academy of Family Physicians. *Ann Intern Med.* 2008;148:370-78.
12. Goldman JS, Hahn SE, Catania JW, et al. Genetic Counseling and Testing for Alzheimer Disease: Joint Practice Guidelines of the American College of Medical Genetics and the National Society of Genetic Counselors. *Genet Med.* 2011;13(6):597-605.
13. Goldman JS, Hahn SE, Catania JW, et al. Addendum: Genetic Counseling and Testing for Alzheimer Disease: Joint Practice Guidelines of the American College of Medical Genetics and the National Society of Genetic Counselors. *Genet Med.* 2019;21(10):2404.

Written by:	UM Development (JG)
Date Written:	10/2003
Revised:	(NB) 10/2004; (JG) 10/2005; (NB) 06/2006, 07/2006; (AM) 09/2007 (converted to new non-MDC version), 05/2008, 05/2009 (TM) 05/2010; (RP) 07/2011, 06/2012, 06/2013, (SE) 02/2014; (SE/RP) 06/2014, (SE) 10/2014 (CMS requested changes); (RP) 05/2015; (JH) 05/2016 (no clinical changes), (SE) 06/2016 (created separate Med D); (RP) 05/2017, 05/2018 (no clinical changes); (DFW) 05/2019 (no clinical changes/removed MDC designation from title/document); (PM) 05/2020, 12/2020 (added continuation of therapy), 05/2021 (no clinical changes); (CJH) 05/2022 (no clinical changes)
Reviewed:	CRC: 10/2003; CDPR/Medical Affairs (MM): 10/2004, 10/2005, 06/2006, 07/2006; (WF): 09/2007, 05/2008, 05/2009, 05/2010; (KP) 07/2011, 06/2012; (SS) 06/2013, (KP) 02/2014; (LMS) 06/2014; (DNC) 05/2015; (ABM) 05/2017; (CHART) 05/28/20, 01/21/21, 05/27/21, 05/26/22 External Review: 12/2003, 12/2004, 02/2006, 12/2006, 02/2008, 08/2008, 10/2009, 09/2010, 10/2011, 10/2012, 10/2013, 03/2014, 10/2014, 10/2015, 10/2016, 10/2017, 10/2018, 10/2019, 10/2020, 04/2021, 10/2021, 08/2022

CRITERIA FOR APPROVAL

1	Does the patient have any of the following diagnoses: A) moderate to severe dementia of the Alzheimer's type, B) vascular dementia? [If yes, go to 2. If no, then no further questions.]	Yes	No
2	Is this request for continuation of therapy? [If yes, go to 3. If no, go to 4.]	Yes	No
3	Does the medication continue to provide benefit to the patient? [No further questions] [Note: If slowing decline of cognitive function is no longer a goal, or if the patient is rapidly declining, treatment with the medication is no longer appropriate.]	Yes	No
4	Is the diagnosis supported by a validated cognitive assessment within the past 12 months? [No further questions]	Yes	No

Mapping Instructions			
	Yes	**No**	**DENIAL REASONS**
1.	Go to 2	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have any of these conditions: - Moderate to severe dementia of the Alzheimer's type - Vascular dementia Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]
2.	Go to 3	Go to 4	

3.	Approve, 12 Months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when it continues to provide benefit to you. Your request has been denied based on the information we have. [Short Description: No continued benefit]
4.	Approve, 12 Months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have had an assessment in the past 12 months that supports your condition. Your request has been denied based on the information we have. [Short Description: No recent assessment]

Reference number(s)
2306-A

SPECIALTY GUIDELINE MANAGEMENT

NATPARA (parathyroid hormone)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Natpara is indicated as an adjunct to calcium and vitamin D to control hypocalcemia in patients with hypoparathyroidism.

Limitations of Use

- Because of the potential risk of osteosarcoma, Natpara is recommended only for patients who cannot be well-controlled on calcium supplements and active forms of vitamin D alone.
- Natpara was not studied in patients with hypoparathyroidism caused by calcium-sensing receptor mutations.
- Natpara was not studied in patients with acute post-surgical hypoparathyroidism.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

A. Initial requests:
   1. Lab results confirming serum parathyroid hormone concentrations below the lower limit of normal for the laboratory reference range on 2 separate days (at least 21 days apart) within the last 12 months.
   2. Lab results confirming magnesium levels within normal laboratory limits.
   3. Lab results confirming 25-hydroxyvitamin D concentration above the lower limit of normal laboratory range.
   4. Lab results confirming serum calcium is above 7.5 mg/dL prior to initiating therapy with the requested medication.

B. Continuation of therapy requests: Lab results confirming maintenance or normalization of calcium levels compared to baseline.

III. EXCLUSIONS

Coverage will not be provided for members with the following exclusion:
Acute postsurgical hypoparathyroidism (within 6 months of surgery) and expected recovery from the hypoparathyroidism.

IV. CRITERIA FOR INITIAL APPROVAL

Hypocalcemia - Hypoparathyroidism
Authorization of 12 months may be granted for treatment of hypocalcemia associated with hypoparathyroidism when all of the following criteria are met:

A. Member has hypocalcemia and concomitant serum parathyroid hormone concentrations below the lower limit of normal for the laboratory reference range on at least 2 separate dates at least 21 days apart within the last 12 months.
B. Member is receiving vitamin D metabolite/analog therapy with calcitriol greater than or equal to 0.25 mcg per day or alphacalcidol greater than or equal to 0.5 mcg/day (or equivalent).
C. Member is receiving supplemental calcium treatment greater than or equal to 1000 mg/day over and above normal dietary calcium intake.
D. Serum magnesium levels are within normal laboratory limits.
E. Serum 25-hydroxyvitamin D concentration is above the lower limit of normal laboratory range.
F. Serum calcium level is greater than 7.5 mg/dL prior to initiating therapy with the requested medication.

V. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section IV who are experiencing benefit from therapy as evidenced by maintenance or normalization of calcium levels compared to baseline.

VI. REFERENCES

1. Natpara [package insert]. Lexington, MA: Shire-NPS Pharmaceuticals, Inc.; July 2020.
2. Khan MI, Waguespack SG, Hu MI. Medical management of postsurgical hypoparathyroidism. *Endocr Pract*. 2011;17(Suppl 1): 18-25.

STEP THERAPY CRITERIA

BRAND NAME
(generic)

NATROBA
(spinosad)

Status: CVS Caremark Criteria
Type: Initial Step Therapy; Post Step Therapy Prior Authorization

POLICY

FDA-APPROVED INDICATIONS

Head Lice Infestations

Natroba is indicated for the topical treatment of head lice infestations in adult and pediatric patients 6 months of age and older.

Adjunctive Measures for Head Lice Infestations:

Natroba should be used in the context of an overall lice management program:

- Wash in hot water or dry-clean all recently worn clothing, hats, used bedding and towels.
- Wash personal care items such as combs, brushes and hair clips in hot water.
- A fine-tooth comb or special nit comb may be used to remove dead lice and nits.

Scabies Infestations

Natroba is indicated for the topical treatment of scabies infestations in adult and pediatric patients 4 years of age and older.

Adjunctive Measures for Scabies Infestations:

- Wash in hot water or dry-clean any bedding, clothing and towels used by anyone having scabies.

INITIAL STEP THERAPY*

**Include Rx and OTC products unless otherwise stated.*

If the patient has filled a prescription for at least a 1 day supply of permethrin 1% or permethrin 5% within the past 60 days under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit. If the patient does not meet the initial step therapy criteria, then the claim will reject with a message indicating that a prior authorization (PA) is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for the topical treatment of head lice in a patient that is 6 months of age or older
  AND
  - The patient has experienced an inadequate treatment response to permethrin 1%
    OR
  - The patient has experienced an intolerance to permethrin 1%
    OR
  - The patient has a contraindication that would prohibit a trial of permethrin 1%
    OR
  - There is a local pattern of known or suspected resistance to permethrin 1%

OR

- The requested drug is being prescribed for the topical treatment of scabies in a patient that is 4 years of age or older **AND**
  - The patient has experienced an inadequate treatment response to permethrin 5% **OR**
  - The patient has experienced an intolerance to permethrin 5% **OR**
  - The patient has a contraindication that would prohibit a trial of permethrin 5% **OR**
  - There is a local pattern of known or suspected resistance to permethrin 5%

REFERENCES

1. Natroba [package insert]. Brownsburg, IN: ParaPro LLC; April 2021.
2. Nix [package insert]. Tarrytown, NY: Insight Pharmaceuticals LLC.; April 2020.
3. Permethrin Cream 5% [package insert]. Parsippany, NJ: Actavis Pharma, Inc.; December 2019.
4. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2023; Accessed January 25, 2023.
5. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed January 25, 2023.
6. Devore CD, Schutze GE. Council on School Health and Committee on Infectious Diseases, American Academy of Pediatrics. Head lice. *Pediatrics*. 2015;135(5):e1355-65. Erratum in: *Pediatrics.* 2015;136(4):781-2.
7. Workowski K, Bachmann LH, Chan PA et. al. Centers for Disease Control and Prevention MMWR Sexually Transmitted Infections Treatment Guidelines, 2021. *MMWR Recomm Rep*. 2021;70(4):1-192.
8. Scabies. Centers for Disease Control and Prevention. Available at: https://www.cdc.gov/parasites/scabies/health_professionals/meds.html. Accessed January 26, 2023.
9. Gunning K, Kiraly B, Pippitt K. Lice and Scabies: Treatment Update. *Am Fam Physician.* 2019;99(10):635-642.

QUANTITY LIMIT CRITERIA

BRAND NAME*
(generic)

NAYZILAM
(midazolam nasal spray)

Status: CVS Caremark Criteria
Type: Quantity Limit ***Ref # 3489-H***

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Nayzilam is indicated for the acute treatment of intermittent, stereotypic episodes of frequent seizure activity (i.e., seizure clusters, acute repetitive seizures) that are distinct from a patient's usual seizure pattern in patients with epilepsy 12 years of age and older.

RATIONALE

Nayzilam is indicated for the acute treatment of intermittent, stereotypic episodes of frequent seizure activity (i.e., seizure clusters, acute repetitive seizures) that are distinct from a patient's usual seizure pattern in patients with epilepsy 12 years of age and older. Patients and caregivers should be instructed on what is and is not an intermittent and stereotypic episode of increased seizure activity (i.e., seizure cluster) that is appropriate for treatment, and the timing of administration in relation to the onset of the episode.[1]

The initial dose of Nayzilam is one spray (5 mg dose) administered into one nostril. If needed, one additional spray (5 mg dose) may be administered into the opposite nostril after 10 minutes if the patient has not responded to the initial dose. A second dose of Nayzilam should not be administered if the patient has trouble breathing or if there is excessive sedation that is uncharacteristic of the patient during a seizure cluster episode. Do not use more than 2 doses of Nayzilam to treat a single episode. It is recommended that Nayzilam be used to treat no more than 1 episode every three days and no more than 5 episodes per month.[1-3]

Nayzilam is supplied as a solution of midazolam. Each single-dose nasal spray unit delivers 5 mg of midazolam in 0.1 mL of solution. Nayzilam is supplied in boxes of 2 nasal spray units, each contained within an individual blister pack.[1] Because it is not recommended to treat more than 5 episodes per month and each episode could require up to 2 doses, the limit will be set at 5 boxes, 10 nasal spray units per month.

If the patient is requesting more than the initial quantity limit, then the claim will reject with a message indicating that quantity limits are exceeded.

REFERENCES

1. Nayzilam [package insert]. Smyrna, GA: UCB, Inc.; February 2021.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2022; Accessed April 7, 2022.
3. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed April 7, 2022.

Written by:	UM Development (DS)
Date Written:	01/2020
Revised:	05/2020 (no clinical changes), 05/2021 (no clinical changes), (DFW) 05/2022 (no clinical changes)
Reviewed:	Medical Affairs (CHART) 01/23/2020, 05/28/2020, 05/27/2021, 05/26/2022 External Review: 02/2020, 10/2020, 08/2021, 08/2022

LIMIT CRITERIA

Drug	1 Month Limit*	3 Month Limit*
Nayzilam (midazolam nasal spray)	10 units (5 boxes) / 25 days	30 units (15 boxes) / 75 days

**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*

PRIOR AUTHORIZATION CRITERIA

BRAND NAME*
(generic)

NAYZILAM
(midazolam nasal spray)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization with Quantity Limit ***Ref # 3102-C***

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Nayzilam is indicated for the acute treatment of intermittent, stereotypic episodes of frequent seizure activity (i.e., seizure clusters, acute repetitive seizures) that are distinct from a patient's usual seizure pattern in patients with epilepsy 12 years of age and older.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for the acute treatment of intermittent, stereotypic episodes of frequent seizure activity (i.e., seizure clusters, acute repetitive seizures) that are distinct from the patient's usual seizure pattern in a patient with epilepsy

AND

- The patient is 12 years of age or older

Quantity Limits apply.
**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Nayzilam is indicated for the acute treatment of intermittent, stereotypic episodes of frequent seizure activity (i.e., seizure clusters, acute repetitive seizures) that are distinct from a patient's usual seizure pattern in patients with epilepsy 12 years of age and older. Patients and caregivers should be instructed on what is and is not an intermittent and stereotypic episode of increased seizure activity (i.e., seizure cluster) that is appropriate for treatment, and the timing of administration in relation to the onset of the episode.[1]

The initial dose of Nayzilam is one spray (5 mg dose) administered into one nostril. If needed, one additional spray (5 mg dose) may be administered into the opposite nostril after 10 minutes if the patient has not responded to the initial dose. A second dose of Nayzilam should not be administered if the patient has trouble breathing or if there is excessive sedation that is uncharacteristic of the patient during a seizure cluster episode. Do not use more than 2 doses of Nayzilam to treat a single episode. It is recommended that Nayzilam be used to treat no more than 1 episode every three days and no more than 5 episodes per month.[1-3]

Nayzilam is supplied as a solution of midazolam. Each single-dose nasal spray unit delivers 5 mg of midazolam in 0.1 mL of solution. Nayzilam is supplied in boxes of 2 nasal spray units, each contained within an individual blister pack.[1] Because it is not recommended to treat more than 5 episodes per month and each episode could require up to 2 doses, the limit will be set at 5 boxes, 10 nasal spray units per month.

REFERENCES

1. Nayzilam [package insert]. Smyrna, GA: UCB, Inc.; February 2021.

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2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2022; Accessed April 7, 2022.
3. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed April 7, 2022.

Written by: UM Development (DS)
Date Written: 06/2019
Revised: 05/2020 (no clinical changes), 05/2021 (no clinical changes), (DFW) 05/2022 (no clinical changes)
Reviewed: Medical Affairs (GAD) 07/2019; (CHART) 05/28/2020, 05/27/2021, 05/26/2022
External Review: 10/2019, 10/2020, 08/2021, 08/2022

CRITERIA FOR APPROVAL

1	Is the requested drug being prescribed for the acute treatment of intermittent, stereotypic episodes of frequent seizure activity (i.e., seizure clusters, acute repetitive seizures) that are distinct from the patient's usual seizure pattern in a patient with epilepsy? [If yes, go to 2. If no, then no further questions.]	Yes	No
2	Is the patient 12 years of age or older? [If yes, go to 3. If no, then no further questions.]	Yes	No
3	Does the patient require more than the plan allowance of 10 nasal spray units (5 boxes) per month? [No further questions] [RPh Note: If yes, then deny and enter a partial approval for 10 nasal spray units (5 boxes) / 25 days or 30 nasal spray units (15 boxes) / 75 days of Nayzilam.] [Note: Coverage is provided up to an amount sufficient for treating up to five episodes per month at the maximum dose of the requested drug.]	Yes	No

Mapping Instructions			
	Yes	**No**	**DENIAL REASONS**
1.	Go to 2	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you meet all of the following: - You have epilepsy - The requested drug is being used for the acute treatment of intermittent, stereotypic episodes of frequent seizure activity (i.e., seizure clusters, acute repetitive seizures) that are distinct from your usual seizure pattern Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]
2.	Go to 3	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you are 12 years of age or older. Your request has been denied based on the information we have. [Short Description: No approvable age]

3.	Deny	Approve, 12 Months, 10 nasal spray units (5 boxes)/25 days or 30 nasal spray units (15 boxes)/75 days	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 10 nasal spray units/month of the requested drug and strength. Your request has been partially approved. You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity]

Reference number(s)
2178-A

SPECIALTY GUIDELINE MANAGEMENT

NERLYNX (neratinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

1. Nerlynx is indicated as a single agent for the extended adjuvant treatment of adult patients with early stage human epidermal growth factor receptor (HER)2-positive breast cancer, to follow adjuvant trastuzumab based therapy.
2. Nerlynx is indicated in combination with capecitabine, for the treatment of adult patients with advanced or metastatic HER2-positive breast cancer who have received two or more prior anti-HER2 based regimens in the metastatic setting.

Compendial Uses

1. Recurrent HER2-positive breast cancer in combination with capecitabine
2. Brain metastases from HER2-positive breast cancer in combination with capecitabine

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of human epidermal growth factor receptor 2 (HER2) status is necessary to initiate the prior authorization review.

III. CRITERIA FOR INITIAL APPROVAL

Breast cancer

A. Authorization of up to 12 months total may be granted for treatment of early stage HER2-positive breast cancer when Nerlynx will be initiated after completing adjuvant trastuzumab-based therapy when used as a single agent.
B. Authorization of 12 months may be granted for treatment of recurrent, advanced or metastatic (including brain metastases) HER2-positive breast cancer in combination with capecitabine.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication outlined in section III when there is no evidence of unacceptable toxicity or disease progression while on the current regimen. Adjuvant treatment of early stage breast cancer will be approved for a total of 12 months of therapy.

V. REFERENCES

1. Nerlynx [package insert]. Los Angeles, CA: Puma Biotechnology; June 2021.
2. Chan A, Delaloge S, Holmes FA, et al. Neratinib after trastuzumab-based adjuvant therapy in patients with HER2-positive breast cancer (ExteNET): a multicentre, randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet Oncol.* 2016; 17(3):367-77.
3. The NCCN Drugs & Biologics Compendium® © 2021 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed December 6, 2021.

Reference number(s)
1931-A

SPECIALTY GUIDELINE MANAGEMENT

NEULASTA (pegfilgrastim)
FULPHILA (pegfilgrastim-jmdb)
FYLNETRA (pegfilgrastim-pbbk)
NYVEPRIA (pegfilgrastim-apgf)
STIMUFEND (pegfilgrastim-fpgk)
UDENYCA (pegfilgrastim-cbqv)
ZIEXTENZO (pegfilgrastim-bmez)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

Neulasta

1. Patients with Cancer Receiving Myelosuppressive Chemotherapy
   Neulasta is indicated to decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia.
2. Hematopoietic Subsyndrome of Acute Radiation Syndrome
   Neulasta is indicated to increase survival in patients acutely exposed to myelosuppressive doses of radiation (Hematopoietic Subsyndrome of Acute Radiation Syndrome).

Fulphila

Patients with Cancer Receiving Myelosuppressive Chemotherapy
Fulphila is indicated to decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia

Udenyca

Patients with Cancer Receiving Myelosuppressive Chemotherapy
Udenyca is indicated to decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia.

Ziextenzo

Patients with Cancer Receiving Myelosuppressive Chemotherapy
Ziextenzo is indicated to decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia.

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Nyvepria
Patients with Cancer Receiving Myelosuppressive Chemotherapy
Nyvepria is indicated to decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia.

Fylnetra
Patients with Cancer Receiving Myelosuppressive Chemotherapy
Fylnetra is indicated to decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia.

Stimufend
Patients with Cancer Receiving Myelosuppressive Chemotherapy
Stimufend is indicated to decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia.

B. Compendial Use
   1. Stem cell transplantation-related indications
   2. Prophylaxis for chemotherapy-induced febrile neutropenia in patients with solid tumors
   3. Hematopoietic Subsyndrome of Acute Radiation Syndrome
   4. Hairy cell leukemia, neutropenic fever

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Primary Prophylaxis of Febrile Neutropenia

A. Documentation must be provided of the member's diagnosis and chemotherapeutic regimen.
B. If chemotherapeutic regimen has an intermediate risk of febrile neutropenia (10-19% [See Appendix B]), documentation must be provided outlining the patient's risk factors that confirm the member is at high risk for febrile neutropenia.

III. CRITERIA FOR INITIAL APPROVAL

A. Prevention of neutropenia in cancer patients receiving myelosuppressive chemotherapy
Authorization of 6 months may be granted for prevention of febrile neutropenia when all of the following criteria are met (1, 2, 3, and 4):
   1. The requested medication will not be used in combination with other colony stimulating factors within any chemotherapy cycle.
   2. The member will not be receiving chemotherapy and radiation therapy at the same time.
   3. The requested medication will not be administered with weekly chemotherapy regimens.
   4. One of the following criteria is met (i or ii):
      i. The requested medication will be used for primary prophylaxis in members with a solid tumor or non-myeloid malignancies who have received, are currently receiving, or will be receiving myelosuppressive anti-cancer therapy that is expected to result in 20% or higher incidence of

febrile neutropenia (FN) *(See Appendix A)* OR 10 – 19% risk of FN *(See Appendix B)* and who are considered to be at high risk of FN because of bone marrow compromise or co-morbidity, including any of the following (not an all-inclusive list):

a. Active infections, open wounds, or recent surgery
b. Age greater than or equal to 65 years
c. Bone marrow involvement by tumor producing cytopenias
d. Previous chemotherapy or radiation therapy
e. Poor nutritional status
f. Poor performance status
g. Previous episodes of FN
h. Other serious co-morbidities, including renal dysfunction, liver dysfunction, HIV infection, cardiovascular disease
i. Persistent neutropenia

ii. The requested medication will be used for secondary prophylaxis in members with solid tumors or non-myeloid malignancies who experienced a febrile neutropenic complication or a dose-limiting neutropenic event (a nadir or day of treatment count impacting the planned dose of chemotherapy) from a prior cycle of similar chemotherapy, with the same dose and scheduled planned for the current cycle (for which primary prophylaxis was not received).

B. Other indications

Authorization of 6 months may be granted for members with any of the following indications:

1. Stem cell transplantation-related indications
2. Hematopoietic Subsyndrome of Acute Radiation Syndrome
   Treatment for radiation-induced myelosuppression following a radiological/nuclear incident
3. Hairy cell leukemia
   Members with hairy cell leukemia with neutropenic fever following chemotherapy

IV. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

V. APPENDIX

A. APPENDIX A: Selected Chemotherapy Regimens with an Incidence of Febrile Neutropenia of 20% or Higher*†

1. Acute Lymphoblastic Leukemia:
   Select ALL regimens as directed by treatment protocol (see NCCN guidelines ALL)
2. Bladder Cancer:
   i. Dose dense MVAC (methotrexate, vinblastine, doxorubicin, cisplatin)
   ii. CBDCa/Pac (carboplatin, paclitaxel)
3. Bone Cancer
   i. VAI (vincristine, doxorubicin or dactinomycin, ifosfamide)
   ii. VDC-IE (vincristine, doxorubicin or dactinomycin, and cyclophosphamide alternating with ifosfamide and etoposide)
   iii. Cisplatin/doxorubicin
   iv. VDC (cyclophosphamide, vincristine, doxorubicin or dactinomycin)
   v. VIDE (vincristine, ifosfamide, doxorubicin or dactinomycin, etoposide)

4. Breast Cancer:
   i. Docetaxel + trastuzumab
   ii. Dose-dense AC (doxorubicin, cyclophosphamide) + paclitaxel (or dose dense paclitaxel)
   iii. TAC (docetaxel, doxorubicin, cyclophosphamide)
   iv. AT (doxorubicin, docetaxel)
   v. Doc (docetaxel)
   vi. TC (docetaxel, cyclophosphamide)
   vii. TCH (docetaxel, carboplatin, trastuzumab)
5. Colorectal Cancer:
   FOLFOXIRI (fluorouracil, leucovorin, oxaliplatin, irinotecan)
6. Esophageal and Gastric Cancers:
   Docetaxel/cisplatin/fluorouracil
7. Head and Neck Squamous Cell Carcinoma
   TPF (docetaxel, cisplatin, 5-fluorouracil)
8. Hodgkin Lymphoma:
   i. Brentuximab vedotin + AVD (doxorubicin, vinblastine, dacarbazine)
   ii. Escalated BEACOPP (bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, prednisone)
9. Kidney Cancer:
   Doxorubicin/gemcitabine
10. Non-Hodgkin's Lymphoma:
    i. CHP (cyclophosphamide, doxorubicin, prednisone) + brentuximab vedotin
    ii. Dose-adjusted EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin)
    iii. ICE (ifosfamide, carboplatin, etoposide)
    iv. Dose-dense CHOP-14 (cyclophosphamide, doxorubicin, vincristine, prednisone) ± rituximab
    v. MINE (mesna, ifosfamide, mitoxantrone, etoposide)
    vi. DHAP (dexamethasone, cisplatin, cytarabine)
    vii. ESHAP (etoposide, methylprednisolone, cisplatin, cytarabine (Ara-C))
    viii. HyperCVAD ± rituximab (cyclophosphamide, vincristine, doxorubicin, dexamethasone ± rituximab)
    ix. VAPEC-B (vincristine, doxorubicin, prednisolone, etoposide, cyclophosphamide, bleomycin)
11. Melanoma:
    Dacarbazine-based combination with IL-2, interferon alpha (dacarbazine, cisplatin, vinblastine, IL-2, interferon alfa)
12. Multiple Myeloma:
    i. VTD-PACE (dexamethasone/thalidomide/cisplatin/doxorubicin/cyclophosphamide/etoposide + bortezomib)
    ii. DT-PACE (dexamethasone/thalidomide/cisplatin/doxorubicin/cyclophosphamide/etoposide)
13. Ovarian Cancer:
    i. Topotecan
    ii. Docetaxel
14. Pancreatic Cancer:
    FOLFIRINOX (fluorouracil, leucovorin, irinotecan, oxaliplatin)
15. Soft Tissue Sarcoma:
    i. MAID (mesna, doxorubicin, ifosfamide, dacarbazine)
    ii. Doxorubicin
    iii. Ifosfamide/doxorubicin
16. Small Cell Lung Cancer:
    i. Top (topotecan)
    ii. CAV (cyclophosphamide, doxorubicin, vincristine)
17. Testicular Cancer:

i. VeIP (vinblastine, ifosfamide, cisplatin)
ii. VIP (etoposide, ifosfamide, cisplatin)
iii. TIP (paclitaxel, ifosfamide, cisplatin)

18. Gestational Trophoblastic Neoplasia:
    i. EMA/EP (etoposide, methotrexate, dactinomycin/etoposide, cisplatin)
    ii. EP/EMA (etoposide, cisplatin/etoposide, methotrexate, dactinomycin)
    iii. TP/TE (paclitaxel, cisplatin/paclitaxel, etoposide)
    iv. BEP (bleomycin, etoposide, cisplatin)
    v. VIP (etoposide, ifosfamide, cisplatin)
    vi. ICE (ifosfamide, carboplatin, etoposide)
19. Wilms Tumor:
    i. Regimen M (vincristine, dactinomycin, doxorubicin, cyclophosphamide, etoposide)
    ii. Regimen I (vincristine, doxorubicin, cyclophosphamide, etoposide)

*Applies to chemotherapy regimens with or without monoclonal antibodies (e.g., trastuzumab, rituximab)
† This list is not comprehensive; there are other agents/regimens that have an intermediate/high risk for development of febrile neutropenia.

B. APPENDIX B: Selected Chemotherapy Regimens with an Incidence of Febrile Neutropenia of 10% to 19%*†

1. Occult Primary – Adenocarcinoma:
   Gemcitabine/docetaxel
2. Breast Cancer:
   i. Docetaxel
   ii. CMF classic (cyclophosphamide, methotrexate, fluorouracil)
   iii. CA (doxorubicin, cyclophosphamide) (60 mg/m2) (hospitalized)
   iv. AC (doxorubicin, cyclophosphamide) + sequential docetaxel (taxane portion only)
   v. AC + sequential docetaxel + trastuzumab
   vi. A (doxorubicin) (75 mg/m2)
   vii. AC (doxorubicin, cyclophosphamide)
   viii. CapDoc (capecitabine, docetaxel)
   ix. Paclitaxel every 21 days
3. Cervical Cancer:
   i. Irinotecan
   ii. Cisplatin/topotecan
   iii. Paclitaxel/cisplatin
   iv. Topotecan
4. Colorectal Cancer:
   i. FL (fluorouracil, leucovorin)
   ii. CPT-11 (irinotecan) (350 mg/m2 q 3 wk)
   iii. FOLFOX (fluorouracil, leucovorin, oxaliplatin)
5. Esophageal and Gastric Cancers:
   i. Irinotecan/cisplatin
   ii. Epirubicin/cisplatin/5-fluorouracil
   iii. Epirubicin/cisplatin/capecitabine
6. Non-Hodgkin's Lymphomas:
   i. EPOCH-IT chemotherapy
   ii. GDP (gemcitabine, dexamethasone, cisplatin/carboplatin)
   iii. GDP (gemcitabine, dexamethasone, cisplatin/carboplatin) + rituximab
   iv. FMR (fludarabine, mitoxantrone, rituximab)

v. CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) including regimens with pegylated liposomal doxorubicin
vi. CHOP + rituximab (cyclophosphamide, doxorubicin, vincristine, prednisone, rituximab) including regimens with pegylated liposomal doxorubicin
vii. Bendamustine

7. Non-Small Cell Lung Cancer:
   i. Cisplatin/paclitaxel
   ii. Cisplatin/vinorelbine
   iii. Cisplatin/docetaxel
   iv. Cisplatin/etoposide
   v. Carboplatin/paclitaxel
   vi. Docetaxel
8. Ovarian Cancer:
   Carboplatin/docetaxel
9. Prostate Cancer:
   Cabazitaxel
10. Small Cell Lung Cancer:
    Etoposide/carboplatin
11. Testicular Cancer:
    i. BEP (bleomycin, etoposide, cisplatin)
    ii. Etoposide/cisplatin
12. Uterine Sarcoma:
    Docetaxel

*Applies to chemotherapy regimens with or without monoclonal antibodies (e.g., trastuzumab, rituximab)
† This list is not comprehensive; there are other agents/regimens that have an intermediate/high risk for development of febrile neutropenia.

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Reference number(s)
1930-A

SPECIALTY GUIDELINE MANAGEMENT

NEUPOGEN (filgrastim)
GRANIX (tbo-filgrastim)
NIVESTYM (filgrastim-aafi)
RELEUKO (filgrastim-ayow)
ZARXIO (filgrastim-sndz)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

Neupogen

1. Patients with Cancer Receiving Myelosuppressive Chemotherapy
   Neupogen is indicated to decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a significant incidence of severe neutropenia with fever.

2. Patients With Acute Myeloid Leukemia Receiving Induction or Consolidation Chemotherapy
   Neupogen is indicated for reducing the time to neutrophil recovery and the duration of fever, following induction or consolidation chemotherapy treatment of patients with acute myeloid leukemia (AML).

3. Patients with Cancer Undergoing Bone Marrow Transplantation
   Neupogen is indicated to reduce the duration of neutropenia and neutropenia-related clinical sequelae, (e.g., febrile neutropenia) in patients with non-myeloid malignancies undergoing myeloablative chemotherapy followed by marrow transplantation.

4. Patients Undergoing Autologous Peripheral Blood Progenitor Cell Collection and Therapy
   Neupogen is indicated for the mobilization of autologous hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis.

5. Patients With Severe Chronic Neutropenia
   Neupogen is indicated for chronic administration to reduce the incidence and duration of sequelae of neutropenia (e.g., fever, infections, oropharyngeal ulcers) in symptomatic patients with congenital neutropenia, cyclic neutropenia, or idiopathic neutropenia.

6. Patients Acutely Exposed to Myelosuppressive Doses of Radiation (Hematopoietic Syndrome of Acute Radiation Syndrome)
   Neupogen is indicated to increase survival in patients acutely exposed to myelosuppressive doses of radiation (Hematopoietic Syndrome of Acute Radiation Syndrome).

Nivestym

1. Patients with Cancer Receiving Myelosuppressive Chemotherapy
   Nivestym is indicated to decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a significant incidence of severe neutropenia with fever.

2. Patients With Acute Myeloid Leukemia Receiving Induction or Consolidation Chemotherapy
   Nivestym is indicated for reducing the time to neutrophil recovery and the duration of fever, following induction or consolidation chemotherapy treatment of patients with acute myeloid leukemia (AML).

3. Patients with Cancer Undergoing Bone Marrow Transplantation (BMT)
   Nivestym is indicated to reduce the duration of neutropenia and neutropenia-related clinical sequelae, (e.g., febrile neutropenia) in patients with non-myeloid malignancies undergoing myeloablative chemotherapy followed by bone marrow transplantation.

4. Patients Undergoing Autologous Peripheral Blood Progenitor Cell Collection and Therapy
   Nivestym is indicated for the mobilization of autologous hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis.

5. Patients With Severe Chronic Neutropenia
   Nivestym is indicated for chronic administration to reduce the incidence and duration of sequelae of neutropenia (e.g., fever, infections, oropharyngeal ulcers) in symptomatic patients with congenital neutropenia, cyclic neutropenia, or idiopathic neutropenia.

Granix
Granix is indicated to reduce the duration of severe neutropenia in adult and pediatric patients 1 month and older with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia.

Zarxio
1. Patients with Cancer Receiving Myelosuppressive Chemotherapy
   Zarxio is indicated to decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a significant incidence of severe neutropenia with fever.

2. Patients With Acute Myeloid Leukemia Receiving Induction or Consolidation Chemotherapy
   Zarxio is indicated for reducing the time to neutrophil recovery and the duration of fever, following induction or consolidation chemotherapy treatment of patients with acute myeloid leukemia (AML).

3. Patients with Cancer Undergoing Bone Marrow Transplantation
   Zarxio is indicated to reduce the duration of neutropenia and neutropenia-related clinical sequelae, (e.g., febrile neutropenia) in patients with non-myeloid malignancies undergoing myeloablative chemotherapy followed by bone marrow transplantation.

4. Patients Undergoing Autologous Peripheral Blood Progenitor Cell Collection and Therapy
   Zarxio is indicated for the mobilization of autologous hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis.

5. Patients With Severe Chronic Neutropenia
   Zarxio is indicated for chronic administration to reduce the incidence and duration of sequelae of neutropenia (e.g., fever, infections, oropharyngeal ulcers) in symptomatic patients with congenital neutropenia, cyclic neutropenia, or idiopathic neutropenia.

Releuko

1. Patients with Cancer Receiving Myelosuppressive Chemotherapy
   Releuko is indicated to decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a significant incidence of severe neutropenia with fever.

2. Patients With Acute Myeloid Leukemia Receiving Induction or Consolidation Chemotherapy
   Releuko is indicated for reducing the time to neutrophil recovery and the duration of fever, following induction or consolidation chemotherapy treatment of patients with acute myeloid leukemia (AML).

3. Patients with Cancer Undergoing Bone Marrow Transplantation
   Releuko is indicated to reduce the duration of neutropenia and neutropenia-related clinical sequelae, (e.g., febrile neutropenia) in patients with non-myeloid malignancies undergoing myeloablative chemotherapy followed by bone marrow transplantation.

4. Patients With Severe Chronic Neutropenia
   Releuko is indicated for chronic administration to reduce the incidence and duration of sequelae of neutropenia (e.g., fever, infections, oropharyngeal ulcers) in symptomatic patients with congenital neutropenia, cyclic neutropenia, or idiopathic neutropenia.

B. Compendial Uses
   1. Treatment of chemotherapy-induced febrile neutropenia
   2. Prophylaxis for chemotherapy-induced febrile neutropenia in patients with solid tumors
   3. Treatment of anemia and neutropenia in patients with myelodysplastic syndromes (MDS)
   4. Stem cell transplantation-related indications
   5. Agranulocytosis (non-chemotherapy drug induced)
   6. Aplastic anemia
   7. Neutropenia related to HIV/AIDS
   8. Neutropenia related to renal transplantation
   9. Acute myeloid leukemia
   10. Severe chronic neutropenia (congenital, cyclic, or idiopathic)
   11. Hematopoietic Syndrome of Acute Radiation Syndrome
   12. Supportive care for neutropenic patients with CAR T-cell-related toxicities
   13. Hairy Cell Leukemia, neutropenic fever
   14. Chronic Myeloid Leukemia, treatment of persistent neutropenia due to tyrosine kinase inhibitor therapy
   15. Glycogen Storage Disease (GSD) Type 1

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Primary Prophylaxis of Febrile Neutropenia

A. Documentation must be provided of the member's diagnosis and chemotherapeutic regimen.
B. If chemotherapeutic regimen is an intermediate risk of febrile neutropenia (10-19% [See Appendix B]), documentation must be provided outlining the patient's risk factors that confirm the member is at high risk for febrile neutropenia.

III. CRITERIA FOR INITIAL APPROVAL

A. Neutropenia in cancer patients receiving myelosuppressive chemotherapy

Authorization of 6 months may be granted for prevention or treatment of febrile neutropenia when all of the following criteria are met (1, 2, and 3):

1. The requested medication will not be used in combination with other colony stimulating factors within any chemotherapy cycle.
2. The member will not be receiving chemotherapy and radiation therapy at the same time.
3. One of the following criteria is met (i, ii, or iii):
   i. The requested medication will be used for primary prophylaxis in members with solid tumors or non-myeloid malignancies who have received, are currently receiving, or will be receiving myelosuppressive anti-cancer therapy that is expected to result in 20% or higher incidence of FN (febrile neutropenia) (FN) *(See Appendix A)* OR 10 – 19% risk of FN *(See Appendix B)* and who are considered to be at high risk of FN because of bone marrow compromise or co-morbidity, including any of the following (not an all-inclusive list):
      a. Active infections, open wounds, or recent surgery
      b. Age greater than or equal to 65 years
      c. Bone marrow involvement by tumor producing cytopenias
      d. Previous chemotherapy or radiation therapy
      e. Poor nutritional status
      f. Poor performance status
      g. Previous episodes of FN
      h. Other serious co-morbidities, including renal dysfunction, liver dysfunction, HIV infection, cardiovascular disease
      i. Persistent neutropenia
   ii. The requested medication will be used for secondary prophylaxis in members with solid tumors or non-myeloid malignancies who experienced a febrile neutropenic complication or a dose-limiting neutropenic event (a nadir or day of treatment count impacting the planned dose of chemotherapy) from a prior cycle of similar chemotherapy, with the same dose and schedule planned for the current cycle (for which primary prophylaxis was not received)
   iii. The requested medication will be used for treatment of high risk FN in members who have any of the following prognostic factors that are predictive of clinical deterioration:
      a. Age greater than 65 years
      b. Being hospitalized at the time of the development of fever
      c. Sepsis syndrome
      d. Invasive fungal infection
      e. Pneumonia or other clinically documented infection
      f. Prolonged (neutropenia expected to last greater than 10 days) or profound (absolute neutrophil count less than 1 x 10^9/L) neutropenia
      g. Prior episodes of febrile neutropenia

B. Other indications

Authorization of 6 months may be granted for members with any of the following indications:

1. Myelodysplastic syndrome (anemia or neutropenia)
2. Stem cell transplantation-related indications
3. Agranulocytosis (non-chemotherapy drug induced)
4. Aplastic anemia
5. Neutropenia related to HIV/AIDS
6. Neutropenia related to renal transplantation
7. Acute myeloid leukemia
8. Severe chronic neutropenia (congenital, cyclic, or idiopathic)
9. Hematopoietic Syndrome of Acute Radiation Syndrome
   Treatment for radiation-induced myelosuppression following a radiological/nuclear incident
10. CAR T-cell-related toxicities

Supportive care for neutropenic patients with CAR T-cell-related toxicities

11. Hairy Cell Leukemia
    Members with hairy cell leukemia with neutropenic fever following chemotherapy
12. Chronic Myeloid Leukemia
    Members with chronic myeloid leukemia (CML) for treatment of persistent neutropenia due to tyrosine kinase inhibitor therapy
13. Glycogen Storage Disease (GSD) Type 1
    Individuals with GSD Type 1 for treatment of low neutrophil counts

IV. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

V. APPENDIX

A. APPENDIX A: Selected Chemotherapy Regimens with an Incidence of Febrile Neutropenia of 20% or Higher*†
   1. Acute Lymphoblastic Leukemia:
      Select ALL regimens as directed by treatment protocol (see NCCN guidelines ALL)
   2. Bladder Cancer:
      i. Dose dense MVAC (methotrexate, vinblastine, doxorubicin, cisplatin)
      ii. CBDCa/Pac (carboplatin, paclitaxel)
   3. Bone Cancer
      i. VAI (vincristine, doxorubicin or dactinomycin, ifosfamide)
      ii. VDC-IE (vincristine, doxorubicin or dactinomycin, and cyclophosphamide alternating with ifosfamide and etoposide)
      iii. Cisplatin/doxorubicin
      iv. VDC (cyclophosphamide, vincristine, doxorubicin or dactinomycin)
      v. VIDE (vincristine, ifosfamide, doxorubicin or dactinomycin, etoposide)
   4. Breast Cancer:
      i. Docetaxel + trastuzumab
      ii. Dose-dense AC (doxorubicin, cyclophosphamide) + paclitaxel (or dose dense paclitaxel)
      iii. TAC (docetaxel, doxorubicin, cyclophosphamide)
      iv. AT (doxorubicin, docetaxel)
      v. Doc (docetaxel)
      vi. TC (docetaxel, cyclophosphamide)
      vii. TCH (docetaxel, carboplatin, trastuzumab)
   5. Colorectal Cancer:
      FOLFOXIRI (fluorouracil, leucovorin, oxaliplatin, irinotecan)
   6. Esophageal and Gastric Cancers:
      Docetaxel/cisplatin/fluorouracil
   7. Head and Neck Squamous Cell Carcinoma
      TPF (docetaxel, cisplatin, 5-fluorouracil)
   8. Hodgkin Lymphoma:
      i. Brentuximab vedotin + AVD (doxorubicin, vinblastine, dacarbazine)
      ii. Escalated BEACOPP (bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, prednisone)
   9. Kidney Cancer:
      Doxorubicin/gemcitabine

10. Non-Hodgkin's Lymphoma:
    i. CHP (cyclophosphamide, doxorubicin, prednisone) + brentuximab vedotin
    ii. Dose-adjusted EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin)
    iii. ICE (ifosfamide, carboplatin, etoposide)
    iv. Dose-dense CHOP-14 (cyclophosphamide, doxorubicin, vincristine, prednisone) ± rituximab
    v. MINE (mesna, ifosfamide, mitoxantrone, etoposide)
    vi. DHAP (dexamethasone, cisplatin, cytarabine)
    vii. ESHAP (etoposide, methylprednisolone, cisplatin, cytarabine (Ara-C))
    viii. HyperCVAD ± rituximab (cyclophosphamide, vincristine, doxorubicin, dexamethasone ± rituximab)
    ix. VAPEC-B (vincristine, doxorubicin, prednisolone, etoposide, cyclophosphamide, bleomycin)
11. Melanoma:
    Dacarbazine-based combination with IL-2, interferon alpha (dacarbazine, cisplatin, vinblastine, IL-2, interferon alfa)
12. Multiple Myeloma:
    i. VTD-PACE (dexamethasone/thalidomide/cisplatin/doxorubicin/cyclophosphamide/etoposide + bortezomib)
    ii. DT-PACE (dexamethasone/thalidomide/cisplatin/doxorubicin/cyclophosphamide/etoposide)
13. Ovarian Cancer:
    i. Topotecan
    ii. Docetaxel
14. Pancreatic Cancer:
    FOLFIRINOX (fluorouracil, leucovorin, irinotecan, oxaliplatin)
15. Soft Tissue Sarcoma:
    i. MAID (mesna, doxorubicin, ifosfamide, dacarbazine)
    ii. Doxorubicin
    iii. Ifosfamide/doxorubicin
16. Small Cell Lung Cancer:
    i. Top (topotecan)
    ii. CAV (cyclophosphamide, doxorubicin, vincristine)
17. Testicular Cancer:
    i. VeIP (vinblastine, ifosfamide, cisplatin)
    ii. VIP (etoposide, ifosfamide, cisplatin)
    iii. TIP (paclitaxel, ifosfamide, cisplatin)
18. Gestational Trophoblastic Neoplasia:
    i. EMA/EP (etoposide, methotrexate, dactinomycin/etoposide, cisplatin)
    ii. EP/EMA (etoposide, cisplatin/etoposide, methotrexate, dactinomycin)
    iii. TP/TE (paclitaxel, cisplatin/paclitaxel, etoposide)
    iv. BEP (bleomycin, etoposide, cisplatin)
    v. VIP (etoposide, ifosfamide, cisplatin)
    vi. ICE (ifosfamide, carboplatin, etoposide)
19. Wilms Tumor:
    i. Regimen M (vincristine, dactinomycin, doxorubicin, cyclophosphamide, etoposide)
    ii. Regimen I (vincristine, doxorubicin, cyclophosphamide, etoposide)

*Applies to chemotherapy regimens with or without monoclonal antibodies (e.g., trastuzumab, rituximab)
† This list is not comprehensive; there are other agents/regimens that have an intermediate/high risk for development of febrile neutropenia.

B. APPENDIX B: Selected Chemotherapy Regimens with an Incidence of Febrile Neutropenia of 10% to 19%*†

1. Occult Primary – Adenocarcinoma:
   Gemcitabine/docetaxel
2. Breast Cancer:
   i. Docetaxel
   ii. CMF classic (cyclophosphamide, methotrexate, fluorouracil)
   iii. CA (doxorubicin, cyclophosphamide) (60 mg/m2) (hospitalized)
   iv. AC (doxorubicin, cyclophosphamide) + sequential docetaxel (taxane portion only)
   v. AC + sequential docetaxel + trastuzumab
   vi. A (doxorubicin) (75 mg/m2)
   vii. AC (doxorubicin, cyclophosphamide)
   viii. CapDoc (capecitabine, docetaxel)
   ix. Paclitaxel every 21 days
3. Cervical Cancer:
   i. Irinotecan
   ii. Cisplatin/topotecan
   iii. Paclitaxel/cisplatin
   iv. Topotecan
4. Colorectal Cancer:
   i. FL (fluorouracil, leucovorin)
   ii. CPT-11 (irinotecan) (350 mg/m2 q 3 wk)
   iii. FOLFOX (fluorouracil, leucovorin, oxaliplatin)
5. Esophageal and Gastric Cancers:
   i. Irinotecan/cisplatin
   ii. Epirubicin/cisplatin/5-fluorouracil
   iii. Epirubicin/cisplatin/capecitabine
6. Non-Hodgkin's Lymphomas:
   i. EPOCH-IT chemotherapy
   ii. GDP (gemcitabine, dexamethasone, cisplatin/carboplatin)
   iii. GDP (gemcitabine, dexamethasone, cisplatin/carboplatin) + rituximab
   iv. FMR (fludarabine, mitoxantrone, rituximab)
   v. CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) including regimens with pegylated liposomal doxorubicin
   vi. CHOP + rituximab (cyclophosphamide, doxorubicin, vincristine, prednisone, rituximab) including regimens with pegylated liposomal doxorubicin
   vii. Bendamustine
7. Non-Small Cell Lung Cancer:
   i. Cisplatin/paclitaxel
   ii. Cisplatin/vinorelbine
   iii. Cisplatin/docetaxel
   iv. Cisplatin/etoposide
   v. Carboplatin/paclitaxel
   vi. Docetaxel
8. Ovarian Cancer:
   Carboplatin/docetaxel
9. Prostate Cancer:
   Cabazitaxel
10. Small Cell Lung Cancer:
    Etoposide/carboplatin
11. Testicular Cancer:
    i. BEP (bleomycin, etoposide, cisplatin)
    ii. Etoposide/cisplatin
12. Uterine Sarcoma:

Docetaxel

*Applies to chemotherapy regimens with or without monoclonal antibodies (e.g., trastuzumab, rituximab)
† This list is not comprehensive; there are other agents/regimens that have an intermediate/high risk for development of febrile neutropenia.

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Reference number
2027-A

SPECIALTY GUIDELINE MANAGEMENT

NEXAVAR (sorafenib)
sorafenib (generic)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
1. Hepatocellular carcinoma
   Nexavar is indicated for the treatment of patients with unresectable hepatocellular carcinoma (HCC).
2. Renal cell carcinoma
   Nexavar is indicated for the treatment of patients with advanced renal cell carcinoma (RCC).
3. Differentiated thyroid carcinoma
   Nexavar is indicated for the treatment of patients with locally recurrent or metastatic, progressive, differentiated thyroid carcinoma (DTC) that is refractory to radioactive iodine treatment.

B. Compendial Uses
1. Hepatocellular carcinoma (Child-Pugh Class A or B7)
   a. Inoperable by performance status, comorbidity or with minimal or uncertain extrahepatic disease
   b. Metastatic disease or extensive liver tumor burden
2. Acute myeloid leukemia with FLT3-ITD mutation
   a. In combination with azacitidine or decitabine in patients age ≥ 60 years as low-intensity treatment induction or post-induction therapy
   b. In combination with azacitidine or decitabine for relapsed or refractory disease
   c. As maintenance therapy after hematopoietic stem cell transplant (HSCT)
3. Soft tissue sarcoma subtypes
   a. Angiosarcoma
   b. Desmoid tumors (aggressive fibromatosis)
   c. Solitary fibrous tumor
   d. Leiomyosarcoma
4. Gastrointestinal stromal tumors (GIST)
5. Thyroid carcinoma (medullary carcinoma, papillary carcinoma, Hürthle cell carcinoma, or follicular carcinoma)
6. Relapsed/refractory or metastatic bone cancer, as second-line therapy as a single agent for the following subtypes:
   a. Osteosarcoma
   b. Dedifferentiated chondrosarcoma
   c. High-grade undifferentiated pleomorphic sarcoma (UPS)
7. Recurrent chordoma
8. Epithelial ovarian cancer, fallopian tube cancer, and primary peritoneal cancer
9. Lymphoid, myeloid or mixed lineage neoplasms with eosinophilia and FLT3 rearrangement in chronic phase or blast phase

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: FLT3-ITD mutation or FLT3 rearrangement testing results (where applicable)

III. CRITERIA FOR INITIAL APPROVAL

A. Hepatocellular Carcinoma

Authorization of 12 months may be granted for treatment of hepatocellular carcinoma as a single agent.

B. Acute Myeloid Leukemia (AML)

Authorization of 12 months may be granted for treatment of acute myeloid leukemia with FLT3-ITD mutation when either of the following criteria are met:

1. The requested drug will be used in combination with azacitidine or decitabine for either:
   i. Low-intensity treatment induction or post-induction therapy for members 60 years or older
   ii. Relapsed/refractory disease
2. The requested drug will be used as maintenance therapy after HSCT

C. Soft Tissue Sarcoma

Authorization of 12 months may be granted for treatment for the following types of soft tissue sarcoma:

1. Leiomyosarcoma
2. Angiosarcoma, solitary fibrous tumor, or desmoid tumor/aggressive fibromatosis, as single agent therapy.

D. Gastrointestinal Stromal Tumor (GIST)

Authorization of 12 months may be granted for treatment of GIST when either of the following criteria are met:

1. The requested medication will be used as a single agent for unresectable, recurrent/progressive, or metastatic disease and the member has failed at least four FDA-approved therapies (e.g., imatinib, sunitinib, regorafenib, ripretinib)
2. The requested medication will be used for palliation of symptoms if previously tolerated and effective

E. Renal Cell Carcinoma

Authorization of 12 months may be granted for treatment of advanced renal cell carcinoma.

F. Papillary, Hürthle cell, or Follicular Thyroid Carcinoma

Authorization of 12 months may be granted for treatment of progressive and/or symptomatic papillary, Hürthle cell, or follicular thyroid carcinoma not amenable to radioactive iodine (RAI) therapy.

G. Medullary Thyroid Carcinoma

Authorization of 12 months may be granted for treatment of recurrent or metastatic medullary thyroid carcinoma when either of the following criteria are met:

1. Member has an intolerance or contraindication to FDA approved systemic therapy options (e.g., vandetanib [Caprelsa], cabozantinib [Cometriq]); OR
2. Member has disease progression while on FDA approved systemic therapy options (e.g., vandetanib [Caprelsa], cabozantinib [Cometriq]).

H. Bone Cancer
Authorization of 12 months may be granted for treatment as second-line therapy for relapsed/refractory or metastatic disease as a single agent for the following types of bone cancer:
1. Osteosarcoma
2. Dedifferentiated chondrosarcoma
3. High-grade undifferentiated pleomorphic sarcoma (UPS)

I. Chordoma
Authorization of 12 months may be granted for treatment of recurrent chordoma as a single agent.

J. Epithelial Ovarian Cancer/Fallopian Tube Cancer/Primary Peritoneal Cancer
Authorization of 12 months may be granted for treatment of epithelial ovarian, fallopian tube, or primary peritoneal cancer if the disease is platinum-resistant and the requested drug is given in combination with topotecan for persistent disease or recurrence.

K. Myeloid/Lymphoid Neoplasms with Eosinophilia
Authorization of 12 months may be granted for treatment of myeloid and/or lymphoid neoplasms with eosinophilia and FLT3 rearrangement in the chronic phase or blast phase.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication in Section III when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

V. REFERENCES

1. Nexavar [package insert]. Whippany, NJ: Bayer HealthCare Pharmaceuticals Inc.; July 2020.
2. Sorafenib [package insert]. Morgantown, WV: Mylan Pharmaceuticals Inc.; November 2021.
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STEP THERAPY CRITERIA

BRAND NAME*
(generic)

NEXLETOL
(bempedoic acid)

NEXLIZET
(bempedoic acid/ezetimibe)

Status: CVS Caremark Criteria
Type: Initial Step Therapy; Post Step Therapy Prior Authorization

POLICY

FDA-APPROVED INDICATIONS

Nexletol
Nexletol is indicated as an adjunct to diet and maximally tolerated statin therapy for the treatment of adults with heterozygous familial hypercholesterolemia or established atherosclerotic cardiovascular disease who require additional lowering of LDL-C.

Limitations of Use
The effect of Nexletol on cardiovascular morbidity and mortality has not been determined.

Nexlizet
Nexlizet is indicated as an adjunct to diet and maximally tolerated statin therapy for the treatment of adults with heterozygous familial hypercholesterolemia or established atherosclerotic cardiovascular disease who require additional lowering of LDL-C.

Limitations of Use
The effect of Nexlizet on cardiovascular morbidity and mortality has not been determined.

INITIAL STEP THERAPY*

**Include Rx and OTC products unless otherwise stated.*

If the patient has filled a prescription for at least a 30 day supply of a generic or brand statin within the past 120 days under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit. If the patient does not meet the initial step therapy criteria, then the claim will reject with a message indicating that a prior authorization (PA) is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for the treatment of an adult patient with heterozygous familial hypercholesterolemia or established atherosclerotic cardiovascular disease
  AND
- The requested drug is being prescribed as an adjunct to maximally tolerated statin therapy
  AND
- The patient requires additional lowering of low-density lipoprotein cholesterol (LDL-C)

REFERENCES

1. Nexletol [package insert]. Ann Arbor, MI: Esperion Therapeutics, Inc; September 2021.
2. Nexlizet [package insert]. Ann Arbor, MI: Esperion Therapeutics, Inc; September 2021.
3. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2021; Accessed October 18, 2021.
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Reference number(s)
6060-A

SPECIALTY GUIDELINE MANAGEMENT

NGENLA (somatrogon-ghla)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Ngenla is indicated for the treatment of pediatric patients aged 3 years and older who have growth failure due to an inadequate secretion of endogenous growth hormone.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review for both initial and continuation of therapy requests (where applicable):

A. Medical records supporting the diagnosis of neonatal growth hormone (GH) deficiency
B. Pretreatment growth hormone provocative test result(s) (laboratory report or medical record documentation)
C. Growth chart
D. Pretreatment IGF-1 level (laboratory report or medical record documentation)*
E. The following information must be provided for all continuation of therapy requests:
    1. Total duration of treatment (approximate duration is acceptable)
    2. Date of last dose administered
    3. Approving health plan/pharmacy benefit manager
    4. Date of prior authorization/approval
    5. Prior authorization approval letter

* IGF-1 levels vary based on the laboratory performing the analysis. Laboratory-specific values must be provided to determine whether the value is within the normal range.

III. CRITERIA FOR INITIAL APPROVAL

Pediatric growth hormone (GH) deficiency
Authorization of 12 months may be granted to members with pediatric GH deficiency 3 years of age and older when EITHER criteria A. or B. below is met:

A. Member was diagnosed with GH deficiency as a neonate. Medical records must be available to support the diagnosis of neonatal GH deficiency (e.g., hypoglycemia with random GH level, evidence of multiple pituitary hormone deficiency, chart notes, or magnetic resonance imaging [MRI] results).
B. Member meets ALL of the following:
    1. Member has EITHER:

   i. Two pretreatment pharmacologic provocative GH tests with both results demonstrating a peak GH level < 10 ng/mL, OR
   ii. A documented pituitary or CNS disorder (refer to Appendix) and a pretreatment IGF-1 level > 2 standard deviations (SD) below the mean
2. Member meets one of the following:
   i. Pretreatment height is > 2 SD below the mean and 1-year height velocity is > 1 SD below the mean, OR
   ii. Pretreatment 1-year height velocity is > 2 SD below the mean
3. Epiphyses are open

IV. CONTINUATION OF THERAPY

Pediatric GH deficiency
Authorization of 12 months may be granted for continuation of therapy when ALL of the following criteria are met:
A. Epiphyses are open (confirmed by X-ray or X-ray is not available)
B. Member's growth rate is > 2 cm/year unless there is a documented clinical reason for lack of efficacy (e.g., on treatment less than 1 year, nearing final adult height/late stages of puberty)

V. APPENDIX

Examples of Hypothalamic/Pituitary/CNS Disorders

1. Congenital genetic abnormalities
   a. Transcription factor defects (PIT-1, PROP-1, LHX3/4, HESX-1, PITX-2)
   b. Growth hormone releasing hormone (GHRH) receptor gene defects
   c. GH secretagogue receptor gene defects
   d. GH gene defects
   e. GH receptor/post receptor defects
2. Congenital structural abnormalities
   a. Optic nerve hypoplasia/septo-optic dysplasia
   b. Agenesis of corpus callosum
   c. Empty sella syndrome
   d. Ectopic posterior pituitary
   e. Pituitary aplasia/hypoplasia
   f. Pituitary stalk defect
   g. Holoprosencephaly
   h. Encephalocele
   i. Hydrocephalus
   j. Anencephaly or prosencephaly
   k. Arachnoid cyst
   l. Other mid-line facial defects (e.g., single central incisor, cleft lip/palate)
   m. Vascular malformations
3. Acquired structural abnormalities (or causes of hypothalamic/pituitary damage)
   a. CNS tumors/neoplasms (e.g., craniopharyngioma, glioma/astrocytoma, pituitary adenoma, germinoma)
   b. Cysts (Rathke cleft cyst or arachnoid cleft cyst)
   c. Surgery
   d. Radiation
   e. Chemotherapy
   f. CNS infections
   g. CNS infarction (e.g., Sheehan's syndrome)

h. Inflammatory processes (e.g., autoimmune hypophysitis)
i. Infiltrative processes (e.g., sarcoidosis, histiocytosis, hemochromatosis)
j. Head trauma/traumatic brain injury
k. Aneurysmal subarachnoid hemorrhage
l. Perinatal or postnatal trauma
m. Surgery of the pituitary or hypothalamus

VI. REFERENCES

1. Ngenla [package insert]. New York, NY: Pfizer; June 2023.
2. Gharib H, Cook DM, Saenger PH, et al. American Association of Clinical Endocrinologists Growth Hormone Task Force. Medical guidelines for clinical practice for growth hormone use in adults and children 2003 Update. *Endocr Pract*. 2003;9(1):64-76.
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Reference number(s)
2372-A

SPECIALTY GUIDELINE MANAGEMENT

NINLARO (ixazomib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication
Ninlaro is indicated in combination with lenalidomide and dexamethasone for the treatment of patients with multiple myeloma who have received at least one prior therapy.

Limitations of Use: Ninlaro is not recommended for use in the maintenance setting or in newly diagnosed multiple myeloma in combination with lenalidomide and dexamethasone outside of controlled clinical trials.

B. Compendial Uses
1. Multiple Myeloma
2. Systemic light chain amyloidosis
3. Waldenstrom Macroglobulinemia/Lymphoplasmacytic Lymphoma

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Multiple Myeloma
Authorization of 12 months may be granted for treatment of multiple myeloma when any of the following criteria is met:
1. The requested medication is prescribed in combination with lenalidomide and dexamethasone for non-transplant candidates for primary therapy or for patients with relapsed or progressive disease
2. The requested medication is prescribed in combination with pomalidomide and dexamethasone for patients who have received at least two prior therapies including an immunomodulatory agent and a proteasome inhibitor
3. The requested medication is prescribed in combination with cyclophosphamide and dexamethasone for patients who have received at least one prior therapy or are a transplant candidate

B. Systemic Light Chain Amyloidosis
Authorization of 12 months may be granted for treatment of relapsed or refractory systemic light chain amyloidosis.

C. Waldenstrom Macroglobulinemia/Lymphoplasmacytic Lymphoma
Authorization of 12 months may be granted for treatment of Waldenstrom macroglobulinemia/lymphoplasmacytic lymphoma when the requested medication is prescribed in combination with rituximab and dexamethasone.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

IV. REFERENCES

1. Ninlaro [package insert]. Lexington, MA: Takeda Pharmaceuticals America, Inc.; May 2022.
2. The NCCN Drugs & Biologics Compendium © 2022 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed October 4, 2022.

Reference number(s)
2120-A

SPECIALTY GUIDELINE MANAGEMENT

NITYR (nitisinone)
ORFADIN (nitisinone)
nitisinone

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Orfadin is indicated for the treatment of adult and pediatric patients with hereditary tyrosinemia type 1 (HT-1) in combination with dietary restriction of tyrosine and phenylalanine.

Nityr is indicated for the treatment of adult and pediatric patients with hereditary tyrosinemia type 1 (HT-1) in combination with dietary restriction of tyrosine and phenylalanine.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: biochemical testing, enzyme assay, or genetic testing results supporting diagnosis.

III. CRITERIA FOR INITIAL APPROVAL

Authorization of 12 months may be granted for treatment of hereditary tyrosinemia type 1 (HT-1) when the diagnosis is confirmed by biochemical testing (e.g., detection of succinylacetone in urine) or DNA testing and the requested medication is being used as an adjunct to dietary restriction of tyrosine and phenylalanine.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for hereditary tyrosinemia type 1 (HT-1) who are experiencing beneficial clinical response from therapy.

V. REFERENCE

1. Orfadin [package insert]. Ardmore, PA: Sobi, Inc; May 2019.
2. Nityr [package insert]. Cambridge, United Kingdom: Cycle Pharmaceuticals Ltd.; June 2021.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME*
(generic)

NOXAFIL (all dosage forms)
(posaconazole)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization ***Ref # 3094-A***

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Treatment of Invasive Aspergillosis

Noxafil injection and **Noxafil delayed-release tablets** are indicated for the treatment of invasive aspergillosis in adults and pediatric patients 13 years of age and older.

Prophylaxis of Invasive Aspergillus and Candida Infections

Noxafil is indicated for the prophylaxis of invasive *Aspergillus* and *Candida* infections in patients who are at high risk of developing these infections due to being severely immunocompromised, such as hematopoietic stem cell transplant (HSCT) recipients with graft-versus-host disease (GVHD) or those with hematologic malignancies with prolonged neutropenia from chemotherapy as follows:

- **Noxafil Injection:** adults and pediatric patients 2 years of age and older
- **Noxafil delayed-release tablets:** adults and pediatric patients 2 years of age and older who weigh greater than 40 kg
- **Noxafil oral suspension:** adults and pediatric patients 13 years of age and older
- **Noxafil PowderMix for delayed-release oral suspension:** pediatric patients 2 years of age and older who weigh 40 kg or less

Treatment of Oropharyngeal Candidiasis Including Oropharyngeal Candidiasis Refractory to Itraconazole and/or Fluconazole

Noxafil oral suspension is indicated for the treatment of oropharyngeal candidiasis, including oropharyngeal candidiasis refractory to itraconazole and/or fluconazole in adults and pediatric patients 13 years of age and older.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for the prevention of invasive Aspergillus and Candida infections in a patient who is at a high risk of developing these infections due to being severely immunocompromised

OR

- Noxafil injection or Noxafil delayed-release tablets are being prescribed for the treatment of invasive aspergillosis

OR

- Noxafil oral suspension (immediate-release) is being prescribed for the treatment of moderate to severe oropharyngeal candidiasis

  AND

  - The patient has experienced an inadequate treatment response, intolerance or has a contraindication to fluconazole AND itraconazole oral solution

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Noxafil is indicated for the prophylaxis of invasive

Aspergillus and Candida infections in patients who are at high risk of developing these infections due to being severely immunocompromised, such as hematopoietic stem cell transplant (HSCT) recipients with graft-versus-host disease (GVHD) or those with hematologic malignancies with prolonged neutropenia from chemotherapy as follows: Noxafil injection in adults and pediatric patients 2 years of age and older, Noxafil delayed-release tablets in adults and pediatric patients 2 years of age and older who weigh greater than 40 kg, Noxafil oral suspension in adults and pediatric patients 13 years of age and older, and Noxafil PowderMix for delayed-release oral suspension in pediatric patients 2 years of age and older who weigh 40 kg or less. Noxafil injection and Noxafil delayed-release tablets are also indicated for the treatment of invasive aspergillosis in adults and pediatric patients 13 years of age and older. Additionally, Noxafil oral suspension is indicated for the treatment of oropharyngeal candidiasis, including oropharyngeal candidiasis refractory to itraconazole and/or fluconazole in adults and pediatric patients 13 years of age and older.[1]

Noxafil oral suspension is not substitutable with Noxafil delayed-release tablets or Noxafil PowderMix for delayed-release oral suspension due to the differences in the dosing of each formulation.[1]

For the prophylaxis of invasive Aspergillus and Candida infections, the duration of therapy is based on recovery from neutropenia or immunosuppression. Liver tests should be evaluated at the start of and during the course of posaconazole therapy. Patients who develop abnormal liver tests during posaconazole therapy should be monitored for the development of more severe hepatic injury. Patient management should include laboratory evaluation of hepatic function (particularly liver tests and bilirubin). Discontinuation of posaconazole must be considered if clinical signs and symptoms consistent with liver disease develop that may be attributable to posaconazole.[1] Therefore, approvals for prophylaxis of invasive Aspergillus and Candida infections will be for 6 months to allow for monitoring and for reevaluation of the underlying condition.

For the treatment of invasive aspergillosis, a loading dose of Noxafil injection or Noxafil delayed-release tablets should be administered on the first day. Starting on the second day, a maintenance dose of Noxafil injection or Noxafil delayed-release tablets should be administered once daily for a total recommended treatment duration of 6 to 12 weeks. Switching between the intravenous and delayed-release tablets is acceptable; a loading dose is not required when switching between formulations.[1] Therefore, approvals for this indication will be for 3 months to allow for treatment of invasive aspergillosis at the maximum recommended duration of therapy.

The Infectious Diseases Society of America (IDSA) recommends clotrimazole, miconazole or nystatin for mild oropharyngeal candidiasis. For mild disease, clotrimazole troches or miconazole buccal tablets are recommended. Alternatives for mild disease include nystatin suspension. For moderate to severe oropharyngeal candidiasis, oral fluconazole is recommended. For fluconazole-refractory disease, itraconazole solution or posaconazole suspension are recommended. Fluconazole-refractory infections should be treated initially with itraconazole solution; between 64% and 80% of patients will respond to this therapy. Posaconazole suspension is efficacious in approximately 75% of patients with refractory oropharyngeal candidiasis.[4] Therefore, Noxafil oral suspension (immediate-release) will be approved for the treatment of moderate to severe oropharyngeal candidiasis when the patient has experienced an inadequate treatment response, intolerance or has a contraindication to fluconazole and itraconazole oral solution.

For the treatment of oropharyngeal candidiasis (OPC) refractory to fluconazole and/or itraconazole, the duration of therapy is based on the severity of the patient's underlying disease and clinical response. Forty-five subjects with refractory OPC were treated with posaconazole oral suspension 400 mg BID for 3 days, followed by 400 mg QD for 25 days with an option for further treatment during a 3-month maintenance period. Following a dosing amendment, a further 44 subjects were treated with posaconazole 400 mg BID for 28 days. The efficacy of posaconazole was assessed by the clinical success (cure or improvement) rate after 4 weeks of treatment.[1] The Infectious Diseases Society of America (IDSA) recommends for fluconazole-refractory disease, itraconazole solution, 200mg once daily or posaconazole suspension, 400mg twice daily for 3 days then 400mg daily, for up to 28 days.[4] Therefore, approvals for Noxafil oral suspension (immediate-release) for the treatment of moderate to severe oropharyngeal candidiasis will be for 1 month.

REFERENCES

1. Noxafil [package insert]. Whitehouse Station, NJ: Merck & Co., Inc.; January 2022.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, Ohio: UpToDate, Inc.; 2021; Accessed January 24, 2022.

3. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed January 18, 2022.
4. Pappas P, Kauffman C, Andes D, et al. Clinical Practice Guidelines for the Management of Candidiasis: 2016 Update by the Infectious Diseases Society of America. *Clinical Infectious Diseases*. 2016;62:1-50.

Written by:	UM Development (ME)
Date Written:	05/2019
Revised:	(ME) 02/2020; (NZ) 02/2021 (updated DOA and updated t/f to specify itraconazole oral solution), 06/2021 (updated to include newly FDA-approved dosage form Noxafil PowderMix for delayed-release oral suspension); (CJH) 06/2021 (updated q-set to include new indication for treatment of aspergillosis for Noxafil injection and Noxafil delayed-release tabs), (DFW) 02/2022 (no clinical changes)
Reviewed:	Medical Affairs (AN) 06/2019, (CHART) 02/27/2020, 02/25/2021, 06/17/2021, 07/15/2021, 02/24/2022 External Review: 06/2019, 06/2020, 06/2021, 08/2021 (FYI), 06/2022

CRITERIA FOR APPROVAL

1	Is the requested drug being prescribed for the prevention of invasive Aspergillus and Candida infections in a patient who is at a high risk of developing these infections due to being severely immunocompromised? [If yes, then no further questions.]	Yes	No
2	Which drug is being requested? [Note: Please check the drug being requested.] [] Noxafil Injection (if checked, go to 3) [] Noxafil delayed-release tablets (if checked, go to 3) [] Noxafil oral suspension (immediate-release) (if checked, go to 4) [] Noxafil PowderMix for delayed-release oral suspension (if checked, deny)		
3	Is the requested drug being prescribed for the treatment of invasive aspergillosis? [No further questions.]	Yes	No
4	Is the requested drug being prescribed for the treatment of moderate to severe oropharyngeal candidiasis? [If no, then no further questions.]	Yes	No
5	Has the patient experienced an inadequate treatment response, intolerance or does the patient have a contraindication to fluconazole AND itraconazole oral solution?	Yes	No

Mapping Instructions			
	Yes	**No**	**DENIAL REASONS – DO NOT USE FOR MEDICARE PART D**
1.	Approve, 6 months	Go to 2	
2.	1=3, 2=3, 3=4, 4=Deny		You do not meet the requirements of your plan. Your plan covers this drug when you are at high risk of specific types of fungal infections. Your request has been denied based on the information we have. [Short Description: No approvable diagnosis-Noxafil PowderMix]
3.	Approve, 3 months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you meet any of these conditions: - You are at high risk of specific types of fungal infections - You are using it to treat a specific type of fungal infection

			Your request has been denied based on the information we have. [Short Description: No approvable diagnosis-Noxafil Injection or Noxafil Tablets]
4.	Go to 5	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you meet any of these conditions: - You are at high risk of specific types of fungal infections - You are using it to treat a moderate to severe fungal infection of the mouth and throat Your request has been denied based on the information we have. [Short Description: No approvable diagnosis- Noxafil Oral Suspension]
5.	Approve, 1 month	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you tried fluconazole and itraconazole oral solution and they did not work for you, or you cannot use them. Your request has been denied based on the information we have. [Short Description: No inadequate response, intolerance or contraindication to fluconazole and itraconazole oral solution]

Reference number(s)
3147-A

SPECIALTY GUIDELINE MANAGEMENT

NUBEQA (darolutamide)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. Nubeqa is indicated for the treatment of adult patients with non-metastatic castration-resistant prostate cancer (nmCRPC).
   2. Nubeqa is indicated for the treatment of adult patients with metastatic hormone-sensitive prostate cancer (mHSPC) in combination with docetaxel.

B. Compendial Use
   Prostate Cancer

All other indications are considered experimental/investigational and not medically necessary.

II. EXCLUSIONS

Coverage will not be provided if the requested medication is used in combination with a second-generation oral anti-androgen (e.g., apalutamide [Erleada]) or an oral androgen metabolism inhibitor (e.g., abiraterone acetate [Zytiga]).

III. CRITERIA FOR INITIAL APPROVAL

Prostate Cancer
Authorization of 12 months may be granted when either of the following criteria are met:
1. The member has non-metastatic castration-resistant prostate cancer and the member has had a bilateral orchiectomy or will be using the requested medication in combination with a GnRH agonist or degarelix.
2. The member has metastatic hormone-sensitive prostate cancer and meets both of the following criteria:
   i. The requested drug will be used in combination with docetaxel
   ii. The member has had a bilateral orchiectomy or will be using the requested medication in combination with a GnRH agonist or degarelix.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

V. REFERENCES

1. Nubeqa [package insert]. Whippany, NJ: Bayer Healthcare Pharmaceuticals Inc.; August 2022.
2. The NCCN Drugs & Biologics Compendium™ © 2023 National Comprehensive Cancer Network, Inc. https://www.nccn.org Accessed August 6, 2023.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME
(generic)

NUEDEXTA
(dextromethorphan hydrobromide/quinidine sulfate)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

POLICY

FDA-APPROVED INDICATIONS
Nuedexta is indicated for the treatment of pseudobulbar affect (PBA).
PBA occurs secondary to a variety of otherwise unrelated neurologic conditions, and is characterized by involuntary, sudden, and frequent episodes of laughing and/or crying. PBA episodes typically occur out of proportion or incongruent to the underlying emotional state. PBA is a specific condition, distinct from other types of emotional lability that may occur in patients with neurological disease or injury.

COVERAGE CRITERIA
The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has a diagnosis of pseudobulbar affect (PBA)

REFERENCES

1. Nuedexta [package insert]. Aliso Viejo, CA: Avanir Pharmaceuticals, Inc.; June 2019.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2022; Accessed February 18, 2022.
3. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed February 18, 2022.

Reference number(s)
2319-A

SPECIALTY GUIDELINE MANAGEMENT

NUPLAZID (pimavanserin)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Nuplazid is indicated for the treatment of hallucinations and delusions associated with Parkinson's disease psychosis.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Parkinson's disease
Authorization of 6 months may be granted for initial treatment of hallucinations and delusions associated with Parkinson's disease psychosis when the member has mild or no cognitive impairment as determined by physician's clinical diagnosis and/or cognitive impairment screening tests (e.g. Mini-Mental Status Examination [MMSE], Montreal Cognitive Assessment [MOCA]).

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment of hallucinations and delusions associated with Parkinson's disease psychosis when the member has experienced improvement in psychotic symptoms (hallucinations and/or delusions) since starting therapy.

IV. REFERENCES

1. Nuplazid [package insert]. San Diego, CA: Acadia Pharmaceuticals, Inc.; November 2020.
2. Cummings J, Isaacson S, Mills R, et al. Pimavanserin for patients with Parkinson's disease psychosis: a randomized, placebo-controlled phase 3 trial. *Lancet.* 2014; 383:533-540.
3. Hoops S, Nazem S, et al. Validity of the MoCA and MMSE in the detection of MCI and dementia in Parkinson disease. *Neurology*. 2009; 73 (21): 1738-1745.

PRIOR AUTHORIZATION CRITERIA

DRUG CLASS	**NARCOLEPSY AGENTS**
BRAND NAME (generic)	**NUVIGIL (armodafinil)**

Status: CVS Caremark Criteria
Type: Initial Prior Authorization with Quantity Limit

POLICY

FDA-APPROVED INDICATIONS
Nuvigil is indicated to improve wakefulness in adult patients with excessive sleepiness associated with obstructive sleep apnea (OSA), narcolepsy, or shift work disorder (SWD).

Limitations of Use
In OSA, Nuvigil is indicated to treat excessive sleepiness and not as treatment for the underlying obstruction. If continuous positive airway pressure (CPAP) is the treatment of choice for a patient, a maximal effort to treat with CPAP for an adequate period of time should be made prior to initiating Nuvigil for excessive sleepiness.

COVERAGE CRITERIA
The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has a diagnosis of narcolepsy
  AND
  - The request is for continuation of therapy
    AND
  - The patient had a positive response to treatment

  OR
  - The requested drug is being prescribed by, or in consultation with, a sleep specialist
    AND
  - The diagnosis is confirmed by sleep lab evaluation

OR

- The patient has a diagnosis of shift work disorder (SWD)
  AND
  - The request is for continuation of therapy
    AND
  - The patient had a positive response to treatment
    AND
  - The patient is still a shift-worker

  OR
  - The requested drug is being prescribed by, or in consultation with, a sleep specialist
    AND
  - A sleep log and actigraphy monitoring have been completed for at least 14 days and shows a disrupted sleep and wake pattern
    AND
  - Symptoms have been present for 3 or more months

OR

- The patient has a diagnosis of obstructive sleep apnea (OSA)
  AND
  - The request is for continuation of therapy
    AND
  - The patient had a positive response to treatment
    AND
  - The patient is compliant with using continuous positive airway pressure (CPAP) or bilevel positive airway pressure (BIPAP)

  OR
  - The requested drug is being prescribed by, or in consultation with, a sleep specialist
    AND
  - The diagnosis has been confirmed by polysomnography
    AND
  - The patient has been receiving treatment for the underlying airway obstruction (continuous positive airway pressure [CPAP] or bilevel positive airway pressure [BIPAP]) for at least one month
    AND
  - Treatment with continuous positive airway pressure (CPAP) or bilevel positive airway pressure (BIPAP) will continue

Quantity Limits Apply.

QUANTITY LIMIT

Drug	**1 Month Limit***	**3 Month Limit***
Nuvigil (armodafinil) 50 mg	60 tablets / 25 days	180 tablets / 75 days
Nuvigil (armodafinil) 150 mg, 200 mg, 250 mg	30 tablets / 25 days	90 tablets / 75 days

**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*

REFERENCES

1. Nuvigil [package insert]. North Wales, Pennsylvania: Cephalon, Inc; November 2018.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2022; Accessed January 26, 2022.
3. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed January 26, 2022.
4. American Academy of Sleep Medicine. *International Classification of Sleep Disorders: Diagnostic and Coding Manual*. 3rd edition. Westchester, IL: American Academy of Sleep Medicine; 2014.
5. Morgenthaler TJ, Kapur VK, Brown T, et al. Practice parameters for the treatment of narcolepsy and other hypersomnias of central origin. *Sleep.* 2007;30(12):1705-1711.
6. Maski K, Trotti LM, Kotagal S, et al. Treatment of central disorders of hypersomnolence: an American Academy of Sleep Medicine clinical practice guideline. *J Clin Sleep Med.* 2021;17(9):1881-1893.
7. Maski K, Trotti LM, Kotagal S, et al. Treatment of central disorders of hypersomnolence: an American Academy of Sleep Medicine systematic review, meta-analysis, and GRADE assessment. *J Clin Sleep Med* 2021;17(9):1895-1945.
8. Czeisler CA, Walsh JK, Wesnes KA, Arora S, Roth T. Armodafinil for Treatment of Excessive Sleepiness Associated with Shift Work Disorder: A Randomized Controlled Study. *Mayo Clin Proc*. 2009; 84(11):958-972.
9. Epstein LJ, Kristo D, Strollo PJ et al. Clinical Guidelines for the Evaluation, Management and Long-term Care of Obstructive Sleep Apnea in Adults. *J Clin Sleep Med* 2009:5(3):263-276.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME
(generic)

NOXAFIL (all dosage forms)
(posaconazole)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

POLICY

FDA-APPROVED INDICATIONS

Treatment of Invasive Aspergillosis

Noxafil injection and **Noxafil delayed-release tablets** are indicated for the treatment of invasive aspergillosis in adults and pediatric patients 13 years of age and older.

Prophylaxis of Invasive Aspergillus and Candida Infections

Noxafil is indicated for the prophylaxis of invasive *Aspergillus* and *Candida* infections in patients who are at high risk of developing these infections due to being severely immunocompromised, such as hematopoietic stem cell transplant (HSCT) recipients with graft-versus-host disease (GVHD) or those with hematologic malignancies with prolonged neutropenia from chemotherapy as follows:

- **Noxafil Injection:** adults and pediatric patients 2 years of age and older
- **Noxafil delayed-release tablets:** adults and pediatric patients 2 years of age and older who weigh greater than 40 kg
- **Noxafil oral suspension:** adults and pediatric patients 13 years of age and older
- **Noxafil PowderMix for delayed-release oral suspension:** pediatric patients 2 years of age and older who weigh 40 kg or less

Treatment of Oropharyngeal Candidiasis Including Oropharyngeal Candidiasis Refractory to Itraconazole and/or Fluconazole

Noxafil oral suspension is indicated for the treatment of oropharyngeal candidiasis, including oropharyngeal candidiasis refractory to itraconazole and/or fluconazole in adults and pediatric patients 13 years of age and older.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for the prevention of invasive Aspergillus and Candida infections in a patient who is at a high risk of developing these infections due to being severely immunocompromised

OR

- Noxafil injection or Noxafil delayed-release tablets are being prescribed for the treatment of invasive aspergillosis

OR

- Noxafil oral suspension (immediate-release) is being prescribed for the treatment of moderate to severe oropharyngeal candidiasis

  AND

  - The patient has experienced an inadequate treatment response, intolerance or has a contraindication to fluconazole AND itraconazole oral solution

REFERENCES

1. Noxafil [package insert]. Rahway, NJ: Merck Sharp & Dohme LLC; September 2022.

2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, Ohio: UpToDate, Inc.; 2023; Accessed January 19, 2023.
3. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed January 19, 2023.
4. Pappas P, Kauffman C, Andes D, et al. Clinical Practice Guidelines for the Management of Candidiasis: 2016 Update by the Infectious Diseases Society of America. *Clinical Infectious Diseases*. 2016;62:1-50**.**

Reference number(s)
2029-A

SPECIALTY GUIDELINE MANAGEMENT

OCALIVA (obeticholic acid)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Ocaliva is indicated for the treatment of adult patients with primary biliary cholangitis (PBC):
- without cirrhosis or
- with compensated cirrhosis who do not have evidence of portal hypertension,

either in combination with ursodeoxycholic acid (UDCA) with an inadequate response to UDCA, or as monotherapy in patients unable to tolerate UDCA.

This indication is approved under accelerated approval based on a reduction in alkaline phosphatase (ALP). An improvement in survival or disease-related symptoms has not been established. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
A. For initial requests: Pretreatment serum alkaline phosphatase (ALP) level
B. For continuation of therapy: Current serum alkaline phosphatase (ALP) and/or current total bilirubin level

III. EXCLUSIONS

Coverage will not be provided for members with any of the following exclusions:
A. Member has decompensated cirrhosis (e.g., Child-Pugh Class B or C) or a prior decompensation event
B. Member has compensated cirrhosis with evidence of portal hypertension (e.g., ascites, gastroesophageal varices, persistent thrombocytopenia).

IV. CRITERIA FOR INITIAL APPROVAL

Primary biliary cholangitis (PBC) (previously known as primary biliary cirrhosis)
Authorization of 6 months may be granted for treatment of PBC in members 18 years of age or older when all of the following criteria are met:
A. Diagnosis of PBC is confirmed by at least two of the following three criteria:
    1. Biochemical evidence of cholestasis with elevation of alkaline phosphatase (ALP) level for at least 6 months duration

2. Presence of antimitochondrial antibodies (AMA) (titer >1:40 by immunofluorescence or immunoenzymatic reactivity) or PBC-specific antinuclear antibodies (ANA) (e.g., anti-gp210, anti-sp100)
3. Histologic evidence of PBC on liver biopsy (e.g., non-suppurative inflammation and destruction of interlobular and septal bile ducts)

B. Member has an elevated serum ALP level prior to initiation of therapy with the requested drug
C. Member meets at least one of the following requirements:
1. Inadequate response to at least 12 months of prior therapy with ursodeoxycholic acid (UDCA)/ursodiol and the member will continue concomitant therapy with UDCA/ursodiol, or
2. Intolerance to UDCA/ursodiol

V. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for members who have achieved or maintained a clinical benefit from Ocaliva therapy (i.e., at least a 15% reduction in ALP level, ALP level less than 1.67-times upper limit of normal [ULN], or total bilirubin less than or equal to ULN).

VI. REFERENCES

1. Ocaliva [package insert]. Morristown, NJ: Intercept Pharmaceuticals, Inc.; May 2022.
2. Lindor KD, Gershwin E, Poupon R, et al. Primary biliary cirrhosis. *Hepatology.* 2009;50:291-308.
3. European Association for the Study of the Liver. EASL clinical practice guidelines: Management of cholestatic liver diseases. *J Hepatol.* 2017;67:145-172.

Reference number
1734-A

SPECIALTY GUIDELINE MANAGEMENT

SANDOSTATIN (octreotide acetate injection)
BYNFEZIA PEN (octreotide acetate injection)
MYCAPSSA (octreotide delayed-release capsule)
SANDOSTATIN LAR DEPOT (octreotide acetate for injectable suspension)
octreotide acetate injection

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. octreotide acetate/Sandostatin/Bynfezia Pen:
      a. Indicated to reduce blood levels of growth hormone (GH) and insulin growth factor-1 (IGF-1; somatomedin C) in acromegaly patients who have had inadequate response to or cannot be treated with surgical resection, pituitary irradiation, and bromocriptine mesylate at maximally tolerated doses.
      b. Indicated for the symptomatic treatment of patients with metastatic carcinoid tumors where it suppresses or inhibits the severe diarrhea and flushing episodes associated with the disease.
      c. Indicated for the treatment of the profuse watery diarrhea associated with vasoactive intestinal peptide (VIP)-secreting tumors.

   2. Sandostatin LAR: Sandostatin LAR Depot is indicated in patients who have responded to and tolerated Sandostatin subcutaneous injection for:
      a. Long-term maintenance therapy in acromegalic patients who have had an inadequate response to surgery and/or radiotherapy, or for whom surgery and/or radiotherapy is not an option.
      b. Long-term treatment of the severe diarrhea and flushing episodes associated with metastatic carcinoid tumors.
      c. Long-term treatment of the profuse watery diarrhea associated with vasoactive intestinal peptide (VIP)-secreting tumors.

   3. Mycapssa is indicated for long-term maintenance treatment in acromegaly patients who have responded to and tolerated treatment with octreotide or lanreotide.

B. Compendial Uses *(applies to injectable products)*
   1. Neuroendocrine tumors (NETs):
      a. Tumors of the gastrointestinal (GI) tract, lung, and thymus (carcinoid tumors)
      b. Tumors of the pancreas (islet cell tumors)
      c. Well-differentiated grade 3 NETs with favorable biology
   2. Pheochromocytoma and paraganglioma
   3. Thymomas and thymic carcinomas
   4. Congenital hyperinsulinism (CHI)/persistent hyperinsulinemic hypoglycemia of infancy (PHHI)(octreotide and Sandostatin only)
   5. Acquired immune deficiency syndrome (AIDS)-associated diarrhea

Reference number
1734-A

SPECIALTY GUIDELINE MANAGEMENT

SANDOSTATIN (octreotide acetate injection)
BYNFEZIA PEN (octreotide acetate injection)
MYCAPSSA (octreotide delayed-release capsule)
SANDOSTATIN LAR DEPOT (octreotide acetate for injectable suspension)
octreotide acetate injection

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. octreotide acetate/Sandostatin/Bynfezia Pen:
      a. Indicated to reduce blood levels of growth hormone (GH) and insulin growth factor-1 (IGF-1; somatomedin C) in acromegaly patients who have had inadequate response to or cannot be treated with surgical resection, pituitary irradiation, and bromocriptine mesylate at maximally tolerated doses.
      b. Indicated for the symptomatic treatment of patients with metastatic carcinoid tumors where it suppresses or inhibits the severe diarrhea and flushing episodes associated with the disease.
      c. Indicated for the treatment of the profuse watery diarrhea associated with vasoactive intestinal peptide (VIP)-secreting tumors.

   2. Sandostatin LAR: Sandostatin LAR Depot is indicated in patients who have responded to and tolerated Sandostatin subcutaneous injection for:
      a. Long-term maintenance therapy in acromegalic patients who have had an inadequate response to surgery and/or radiotherapy, or for whom surgery and/or radiotherapy is not an option.
      b. Long-term treatment of the severe diarrhea and flushing episodes associated with metastatic carcinoid tumors.
      c. Long-term treatment of the profuse watery diarrhea associated with vasoactive intestinal peptide (VIP)-secreting tumors.

   3. Mycapssa is indicated for long-term maintenance treatment in acromegaly patients who have responded to and tolerated treatment with octreotide or lanreotide.

B. Compendial Uses *(applies to injectable products)*
   1. Neuroendocrine tumors (NETs):
      a. Tumors of the gastrointestinal (GI) tract, lung, and thymus (carcinoid tumors)
      b. Tumors of the pancreas (islet cell tumors)
      c. Well-differentiated grade 3 NETs with favorable biology
      d. Gastroenteropancreatic NETs
   2. Pheochromocytoma and paraganglioma
   3. Thymomas and thymic carcinomas
   4. Congenital hyperinsulinism (CHI)/persistent hyperinsulinemic hypoglycemia of infancy (PHHI)(octreotide and Sandostatin only)

5. Acquired immune deficiency syndrome (AIDS)-associated diarrhea
6. Inoperable bowel obstruction
7. Cancer-related diarrhea
8. Enterocutaneous fistula
9. Gastroesophageal varices
10. Pancreatic fistulas
11. Pituitary adenoma
12. Short bowel syndrome
13. Zollinger-Ellison syndrome

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

A. For acromegaly:
   1. For initial approval: Laboratory report indicating high pretreatment insulin-like growth factor-1 (IGF-1) level and chart notes indicating an inadequate or partial response to surgery or radiotherapy or a clinical reason for not having surgery or radiotherapy.
   2. For continuation: Laboratory report indicating normal current IGF-1 levels or chart notes indicating that the member's IGF-1 level has decreased or normalized since initiation of therapy.

B. Cancer-related diarrhea: Chart notes indicating grade 3 or 4 diarrhea.

III. CRITERIA FOR INITIAL APPROVAL

A. Acromegaly

Authorization of 12 months may be granted for the treatment of acromegaly when all of the following criteria are met:

1. Member has a high pretreatment IGF-1 level for age and/or gender based on the laboratory reference range.
2. Member had an inadequate or partial response to surgery or radiotherapy OR there is a clinical reason why the member has not had surgery or radiotherapy.
3. For Mycapssa requests, member has previously responded to and tolerated treatment with octreotide or lanreotide.

B. Neuroendocrine tumors (NETs) (injectable products only)

1. Tumors of the gastrointestinal (GI) tract (carcinoid tumor)
   Authorization of 12 months may be granted for treatment of NETs of the GI tract.
2. Tumors of the thymus (carcinoid tumor)
   Authorization of 12 months may be granted for treatment of NETs of the thymus.
3. Tumors of the lung (carcinoid tumor)
   Authorization of 12 months may be granted for treatment of NETs of the lung.
4. Tumors of the pancreas (islet cell tumors)
   Authorization of 12 months may be granted for treatment of NETs of the pancreas, including gastrinomas, glucagonomas, and insulinomas.
5. Well-differentiated grade 3 NETs with favorable biology
   Authorization of 12 months may be granted for treatment of well-differentiated grade 3 NETs with favorable biology (e.g., relatively low Ki-67 [less than 55%], somatostatin receptor [SSR] positive imaging).
6. Gastroenteropancreatic neuroendocrine tumors (GEP-NETs)

Authorization of 12 months may be granted for treatment of GEP-NETs.

C. Carcinoid syndrome (injectable products only)
Authorization of 12 months may be granted for treatment of carcinoid syndrome.

D. Vasoactive intestinal peptide tumors (VIPomas) (injectable products only)
Authorization of 12 months may be granted for management of symptoms related to hormone hypersecretion of VIPomas.

E. Pheochromocytoma and paraganglioma (injectable products only)
Authorization of 12 months may be granted for treatment of pheochromocytoma and paraganglioma.

F. Thymomas and thymic carcinomas (injectable products only)
Authorization of 12 months may be granted for treatment of thymomas and thymic carcinomas.

G. Congenital hyperinsulinism (CHI)/persistent hyperinsulinemic hypoglycemia of infancy (octreotide and Sandostatin only)
Authorization of 6 months may be granted for treatment of CHI and persistent hyperinsulinemic hypoglycemia in an infant.

H. AIDS-associated diarrhea (injectable products only)
Authorization of 12 months may be granted for treatment of AIDS-associated severe secretory diarrhea when anti-microbial (e.g., ciprofloxacin or metronidazole) or anti-motility agents (e.g., loperamide or diphenoxylate and atropine) have become ineffective.

I. Inoperable bowel obstruction in cancer (injectable products only)
Authorization of 12 months may be granted for management of GI symptoms (e.g., nausea, pain, vomiting) of inoperable bowel obstruction in members with cancer.

J. Cancer-related diarrhea (injectable products only)
Authorization of 12 months may be granted for treatment of cancer-related diarrhea when the member has grade 3 or greater diarrhea according to National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE).

K. Enterocutaneous fistula (injectable products only)
Authorization of 12 months may be granted for management of volume depletion from enterocutaneous fistula.

L. Gastroesophageal varices (injectable products only)
Authorization of 6 months may be granted for treatment of acute bleeding of gastroesophageal varices associated with cirrhosis.

M. Pancreatic fistulas (injectable products only)
Authorization of 6 months may be granted for prevention and treatment of pancreatic fistulas following pancreatic surgery.

N. Pituitary adenoma (injectable products only)
Authorization of 12 months may be granted for treatment of pituitary adenoma.

O. Short bowel syndrome (injectable products only)
Authorization of 12 months may be grated for treatment of short bowel syndrome when the daily intravenous fluid requirement is greater than 3 liters.

P. Zollinger-Ellison syndrome (injectable products only)
Authorization of 12 months may be grated for treatment of Zollinger-Ellison syndrome.

IV. CONTINUATION OF THERAPY

A. Acromegaly
Authorization of 12 months may be granted for continuation of therapy for acromegaly when the member's IGF-1 level has decreased or normalized since initiation of therapy.

B. NETs, Carcinoid syndrome, VIPomas, pheochromocytoma/paraganglioma, thymomas/thymic carcinomas, AIDS-associated diarrhea, bowel obstruction, cancer-related diarrhea, and Zollinger-Ellison syndrome (injectable products only)
Authorization of 12 months may be granted for continued treatment in members requesting reauthorization when the member is experiencing clinical benefit as evidenced by improvement or stabilization in clinical signs and symptoms since initiation of therapy.

C. All other indications
All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

V. REFERENCES

1. Octreotide acetate [package insert]. Morgantown, WV: Mylan Institutional LLC; June 2021.
2. Sandostatin [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; October 2022.
3. Sandostatin LAR Depot [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; March 2021.
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5. Katznelson L, Laws ER, Melmed S, et al. Acromegaly: an endocrine society clinical practice guideline. *J Clin Endocrinol Metab*. 2014;99:3933-3951.
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Reference number
1786-A

SPECIALTY GUIDELINE MANAGEMENT

ODOMZO (sonidegib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication
Odomzo is indicated for the treatment of adult patients with locally advanced basal cell carcinoma (BCC) that has recurred following surgery or radiation therapy, or those who are not candidates for surgery or radiation therapy.

B. Compendial Use
Basal cell carcinoma

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Basal Cell Carcinoma
Authorization of 12 months may be granted for treatment of locally advanced or diffuse (e.g., Gorlin syndrome) basal cell carcinoma.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

IV. REFERENCES

1. Odomzo [package insert]. Cranberry, NJ: Sun Pharmaceutical Industries, Inc.; May 2019.
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Reference number(s)
1882-A

SPECIALTY GUIDELINE MANAGEMENT

OFEV (nintedanib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

A. Idiopathic Pulmonary Fibrosis
   Ofev is indicated for the treatment of idiopathic pulmonary fibrosis (IPF).
B. Chronic Fibrosing Interstitial Lung Diseases with a Progressive Phenotype
   Ofev is indicated for the treatment of chronic fibrosing interstitial lung diseases (ILDs) with a progressive phenotype.
C. Systemic Sclerosis-Associated Interstitial Lung Disease
   Ofev is indicated to slow the rate of decline in pulmonary function in patients with systemic sclerosis-associated interstitial lung disease (SSc-ILD).

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review (where applicable):

A. Result of a chest high-resolution computed tomography (HRCT) study.
B. If a lung biopsy is conducted, submit the associated pathology report.

III. CRITERIA FOR INITIAL APPROVAL

A. Idiopathic Pulmonary Fibrosis (IPF)

Authorization of 12 months may be granted for treatment of idiopathic pulmonary fibrosis when the member has undergone a diagnostic work-up which includes the following:[2]

1. Other known causes of interstitial lung disease (e.g., domestic and occupational environmental exposures, connective tissue disease, drug toxicity) have been excluded AND
2. The member has completed a high-resolution computed tomography (HRCT) study of the chest or a lung biopsy which reveals a result consistent with the usual interstitial pneumonia (UIP) pattern, OR has completed an HRCT study of the chest which reveals a result other than the UIP pattern (e.g., probable UIP, indeterminate for UIP) and the diagnosis is supported by a lung biopsy. If a lung biopsy has not been previously conducted, the diagnosis is supported by a multidisciplinary discussion between a radiologist and pulmonologist who are experienced in IPF.

B. Chronic Fibrosing Interstitial Lung Diseases with a Progressive Phenotype

Authorization of 12 months may be granted for treatment of chronic fibrosing interstitial lung diseases with a progressive phenotype when the member meets both of the following criteria:

1. The member has completed a high-resolution computed tomography (HRCT) study of the chest that shows fibrosis affecting at least 10 percent of the lungs.
2. The member has progressive disease (e.g., forced vital capacity [FVC] decline greater than or equal to 10% of the predicted value, worsening respiratory symptoms, increased extent of fibrosis on HRCT).

C. Systemic Sclerosis-Associated Interstitial Lung Disease

Authorization of 12 months may be granted for treatment of systemic sclerosis-associated interstitial lung disease when the member has completed a high-resolution computed tomography (HRCT) study of the chest that shows fibrosis affecting at least 10 percent of the lungs.

IV. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy for an indication listed in Section III may be granted an authorization of 12 months when the member is currently receiving treatment with Ofev, excluding when Ofev is obtained as samples or via manufacturer's patient assistance programs.

V. OTHER

Note: If the member is a current smoker, they should be counseled on the harmful effects of smoking on pulmonary conditions and available smoking cessation options.

VI. REFERENCES

1. Ofev [package insert]. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc. October 2020.
2. Raghu G, Remy-Jardin M, Myers JL, et al. Diagnosis of Idiopathic Pulmonary Fibrosis. An Official ATS/ERS/JRS/ALAT Clinical Practice Guideline. *Am J Respir Crit Care Med*. 2018 Sep 1;198(5):e44-e68.
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6. Flaherty KR, Wells AU, Cottin V, et al. Nintedanib in progressive fibrosing interstitial lung diseases. *N Engl J Med*. 2019;381:1718-27.

Reference number
2597-A

SPECIALTY GUIDELINE MANAGEMENT

OLUMIANT (baricitinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

A. Olumiant is indicated for the treatment of adult patients with moderately to severely active rheumatoid arthritis who have had an inadequate response to one or more tumor necrosis factor (TNF) blockers.
B. Olumiant is indicated for the treatment of coronavirus disease 2019 (COVID-19) in hospitalized adults requiring supplemental oxygen, non-invasive or invasive mechanical ventilation, or extracorporeal membrane oxygenation (ECMO).
C. Olumiant is indicated for the treatment of adult patients with severe alopecia areata.

Note: The criteria outlined in this policy is only applicable to coverage in the outpatient setting. Hospitalized members receiving Olumiant for the treatment of COVID-19 will be managed according to the member's inpatient benefit.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

A. Rheumatoid arthritis (RA)
    1. Initial requests: Chart notes, medical record documentation, or claims history supporting previous medications tried, including response to therapy (if applicable).
    2. Continuation requests: Chart notes or medical record documentation supporting positive clinical response.

B. Alopecia areata: Chart notes or medical record documentation of Severity of Alopecia Tool (SALT) score.

III. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with one of the following:

A. Rheumatoid arthritis: rheumatologist
B. Alopecia areata: dermatologist

IV. CRITERIA FOR INITIAL APPROVAL

A. Rheumatoid arthritis (RA)

1. Authorization of 12 months may be granted for adult members for treatment of moderately to severely active rheumatoid arthritis (RA) when the member has experienced an inadequate response or intolerance to at least one tumor necrosis factor (TNF) inhibitor.

2. Authorization of 12 months may be granted for adult members who have previously received a biologic (other than a TNF inhibitor) or targeted synthetic drug (e.g., Rinvoq, Xeljanz) indicated for moderately to severely active rheumatoid arthritis.

B. Alopecia areata

Authorization of 12 months may be granted for adult members for treatment of severe alopecia areata when all of the following criteria are met:

1. Member has at least 50% scalp hair loss as measured by the Severity of Alopecia Tool (SALT).
2. Other forms of alopecia have been ruled out (e.g., androgenetic alopecia, trichotillomania, telogen effluvium, chemotherapy-induced hair loss, tinea capitis).

V. CONTINUATION OF THERAPY

A. Rheumatoid arthritis (RA)

Authorization of 12 months may be granted for all adult members (including new members) who are using the requested medication for moderately to severely active RA and who achieve or maintain a positive clinical response as evidenced by disease activity improvement of at least 20% from baseline in tender joint count, swollen joint count, pain, or disability.

B. Alopecia areata

Authorization of 12 months may be granted for all adult members (including new members) who are using the requested medication for severe alopecia areata and who achieve or maintain a positive clinical response as evidenced by a SALT score of 20 or less and an improvement in signs and symptoms of the condition from baseline (e.g., increased scalp hair coverage).

VI. OTHER

For all indications: Member has had a documented negative TB test (which can include a tuberculosis skin test [PPD], an interferon-release assay [IGRA], or a chest x-ray)* within 6 months of initiating therapy for persons who are naïve to biologic drugs or targeted synthetic drugs associated with an increased risk of TB.

* If the screening testing for TB is positive, there must be further testing to confirm there is no active disease. Do not administer the requested medication to members with active TB infection. If there is latent disease, TB treatment must be started before initiation of the requested medication.

For all indications: Member cannot use the requested medication concomitantly with any other biologic drug, targeted synthetic drug, or potent immunosuppressants such as azathioprine or cyclosporine.

VII. DOSAGE AND ADMINISTRATION

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

VIII. REFERENCES

1. Olumiant [package insert]. Indianapolis, IN: Lilly USA, LLC; June 2022.
2. Testing for TB Infection. Centers for Disease Control and Prevention. Retrieved on June 15, 2022 from: https://www.cdc.gov/tb/topic/basics/risk.htm.
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5. King B, Ohyama M, Kwon O, et al. Two phase 3 trials of baricitinib for alopecia areata. *NEJM*. 2022;386(18):1687-1699.
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PRIOR AUTHORIZATION CRITERIA

DRUG CLASS	**OMEGA-3 FATTY ACIDS**
BRAND NAME (generic)	**LOVAZA (omega-3-acid ethyl esters)** **VASCEPA (icosapent ethyl)**

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

POLICY

FDA-APPROVED INDICATIONS

Lovaza

Lovaza (omega-3-acid ethyl esters) is indicated as an adjunct to diet to reduce triglyceride (TG) levels in adult patients with severe (≥500 mg/dL) hypertriglyceridemia.

Usage Considerations: Patients should be placed on an appropriate lipid-lowering diet before receiving Lovaza and should continue this diet during treatment with Lovaza.

Laboratory studies should be done to ascertain that the lipid levels are consistently abnormal before instituting Lovaza therapy. Every attempt should be made to control serum lipids with appropriate diet, exercise, weight loss in obese patients, and control of any medical problems such as diabetes mellitus and hypothyroidism that are contributing to the lipid abnormalities. Medications known to exacerbate hypertriglyceridemia (such as beta blockers, thiazides, estrogens) should be discontinued or changed if possible prior to consideration of triglyceride-lowering drug therapy.

Limitations of Use

The effect of Lovaza on the risk for pancreatitis has not been determined.

The effect of Lovaza on cardiovascular mortality and morbidity has not been determined.

Vascepa

Vascepa (icosapent ethyl) is indicated:

- As an adjunct to maximally tolerated statin therapy to reduce the risk of myocardial infarction, stroke, coronary revascularization, and unstable angina requiring hospitalization in adult patients with elevated triglyceride (TG) levels (≥ 150 mg/dL) and
  - o established cardiovascular disease or
  - o diabetes mellitus and 2 or more additional risk factors for cardiovascular disease.

- As an adjunct to diet to reduce TG levels in adult patients with severe (≥ 500 mg/dL) hypertriglyceridemia.

Limitations of Use:

The effect of Vascepa on the risk for pancreatitis in patients with severe hypertriglyceridemia has not been determined.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The patient will be on an appropriate lipid-lowering diet and exercise regimen during treatment

AND

- The patient has, or did have prior to the start of treatment with a triglyceride lowering drug, a triglyceride level greater than or equal to 500 milligrams/deciliter

OR

- Vascepa is being prescribed to reduce the risk of myocardial infarction, stroke, coronary revascularization, or unstable angina requiring hospitalization in an adult patient with elevated triglyceride (TG) levels (greater than or equal to 150 milligrams/deciliter) **AND**
    - Vascepa is being prescribed as an adjunct to maximally tolerated statin therapy
      AND
    - The patient has established cardiovascular disease
      OR
    - The patient has diabetes mellitus and two or more additional risk factors for cardiovascular disease

REFERENCES

1. Lovaza [package insert]. Research Triangle Park, NC: GlaxoSmithKline; September 2020.
2. Vascepa [package insert]. Bridgewater, NJ: Amarin Pharma Inc.; September 2021.
3. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, Ohio: UpToDate, Inc.; 2021; Accessed November 2021.
4. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com/. Accessed November 2021.
5. Grundy SM, Stone NJ, Bailey AL, et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol. *Circulation.* 2019;139:e1082-1143.
6. Miller, M., Stone, N.J., Ballantyne, C., et al. Triglycerides and Cardiovascular Disease: A Scientific Statement from the American Heart Association. *Circulation*. 2011;123:2293-2333.
7. Berglund L, Brunzell JD, Goldberg AC, et al. Evaluation and Treatment of Hypertriglyceridemia: An Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab*. 2012;97:2969–2989.

PRIOR AUTHORIZATION CRITERIA

DRUG CLASS	**ANTICONVULSANTS**
BRAND NAME* **(generic)**	**ONFI** **(clobazam)**
	SYMPAZAN **(clobazam)**
Status: CVS Caremark Criteria	***Ref # 871-A***
Type: Initial Prior Authorization	***Ref # 718-A***

** Drugs that are listed in the target drug box include both brand and generic and all dosages forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Onfi

Onfi (clobazam) is indicated for the adjunctive treatment of seizures associated with Lennox-Gastaut Syndrome (LGS) in patients 2 years of age or older.

Sympazan

Sympazan (clobazam) is indicated for adjunctive treatment of seizures associated with Lennox-Gastaut Syndrome (LGS) in patients 2 years of age or older.

Compendial Uses

Seizures associated with Dravet Syndrome[3-5]

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for adjunctive treatment of seizures associated with Lennox-Gastaut Syndrome **AND**
  - The patient is 2 years of age or older

OR

- The requested drug is being prescribed for the treatment of seizures associated with Dravet Syndrome

OR

- The request is for continuation of therapy **AND**
  - The patient meets one of the following:
    - The requested drug is being prescribed for adjunctive treatment of seizures associated with Lennox-Gastaut Syndrome **AND**
      - The patient is 2 years of age or older

    OR

    - The requested drug is being prescribed for the treatment of seizures associated with Dravet Syndrome

  AND

  - The patient has achieved and maintained positive clinical response as evidenced by reduction in frequency or duration of seizures compared with seizure activity prior to initiation of the requested drug

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Onfi and Sympazan are indicated for adjunctive treatment of seizures associated with Lennox-Gastaut Syndrome (LGS) in patients 2 years of age or older.[1-4]

Use of clobazam for the treatment of seizures associated with Dravet syndrome is supported by compendia. Dravet Syndrome (also known as severe myoclonic epilepsy of infancy) is a rare and severe type of epilepsy characterized by early onset of multiple seizure types, frequent episodes of status epilepticus, and developmental delay with cognitive and psychomotor impairment. Patients typically present within the first year of life. Seizures in patients with Dravet syndrome are generally refractory to current anticonvulsant drug options, and anticonvulsants that inhibit the sodium channel (e.g., carbamazepine, oxcarbazepine, lamotrigine, phenytoin), phenobarbital, or vigabatrin may exacerbate the condition. Clobazam and valproic acid are the optimal first-line medications in Dravet syndrome. Treatment should be initiated with one of these agents and the other added if control remains suboptimal.[3-5]

REFERENCES

1. Onfi [package insert]. Deerfield, IL: Lundbeck Inc.; February 2021.
2. Sympazan [package insert]. Warren, NJ: Aquestive Therapeutics.; March 2021.
3. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2021; Accessed March 17, 2022.
4. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed March 17, 2022.
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Written by:	UM Development (JK)
Date Written:	11/2011
Revised:	(CT) 05/2012 (created MDC-1 document); (PL) 10/2012 (extended duration); (MS) 05/2013; (GS/CF) 05/2014; (CF) 05/2015; (MS) 05/2016 (no clinical changes); (JG) 05/2017 (no clinical changes), 05/2018 (no clinical changes); (ME) 11/2018 (add Sympazan); (CF) 05/2019 (no clinical changes, combined 718-A + 871-A, removed MDC from 718-A), (RP) 05/2020 (no clinical changes), (MAK) 05/2021 (no clinical changes), (DFW) 05/2022 (added Dravet Syndrome as compendia supported indication), 08/2022 (added COT requirements)
Reviewed:	Medical Affairs: (KP) 11/2011; (MG) 05/2012; (DC) 05/2013; (LMS) 05/2014; (DNC) 05/2015; (AM) 11/2018; (GAD) 05/2019; (CHART) 05/28/2020, 05/27/2021, 05/26/2022, 08/25/2022 External Review: 12/2011, 06/2012, 10/2013, 10/2014, 10/2015, 10/2016, 07/2017, 10/2018, 12/2018 (FYI), 10/2019, 10/2020, 08/2021, 08/2022, 12/2022

CRITERIA FOR APPROVAL

1	Is the requested drug being prescribed for adjunctive treatment of seizures associated with Lennox-Gastaut syndrome? [If yes, go to 2. If no, go to 3.]	Yes	No
2	Is the patient 2 years of age or older? [If yes, go to 4. If no, then no further questions.]	Yes	No
3	Is the requested drug being prescribed for the treatment of seizures associated with Dravet Syndrome? [If yes, go to 4. If no, then no further questions.]	Yes	No
4	Is this request for continuation of therapy? [If yes, go to 5. If no, then no further questions.]	Yes	No
5	Has the patient achieved and maintained positive clinical response as evidenced by reduction in frequency or duration of seizures compared with seizure activity prior to	Yes	No

initiation of the requested drug?
[No further questions]

Mapping Instructions			
	Yes	**No**	**DENIAL REASONS**
1.	Go to 2	Go to 3	
2.	Go to 4	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you are two years of age or older. Your request has been denied based on the information we have. [Short Description: No approvable age, LGS]
3.	Go to 4	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you meet any of the conditions: - You are 2 years of age or older, have seizures associated with Lennox Gastaut Syndrome and are taking this drug along with another seizure drug - You have seizures associated with Dravet Syndrome Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]
4.	Go to 5	Approve, 36 Months	
5.	Approve, 36 Months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have less seizures or shorter seizures compared to before you started this drug. Your request has been denied based on the information we have. [Short Description: No response to treatment]

Reference number(s)
4194-A

SPECIALTY GUIDELINE MANAGEMENT

ONUREG (azacitidine)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Onureg is indicated for continued treatment of adult patients with acute myeloid leukemia who achieved first complete remission (CR) or complete remission with incomplete blood count recovery (CRi) following intensive induction chemotherapy and are not able to complete intensive curative therapy.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Acute Myeloid Leukemia (AML)
Authorization of 12 months may be granted for treatment of AML when all of the following criteria are met:
1. The requested medication will be used as a single agent.
2. The member has achieved first complete remission (CR) or complete remission with incomplete blood count recovery (CRi) following intensive induction chemotherapy.
3. The member is not able to complete intensive curative therapy.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

IV. REFERENCES

1. Onureg [package insert]. Summit, NJ: Celgene Corporation; May 2021.

QUANTITY LIMIT PRIOR AUTHORIZATION CRITERIA

DRUG CLASS	**OPIOID CONTAINING COUGH AND COLD PRODUCTS (RX AND OTC)**
BRAND NAME* (generic)	
	CAPCOF (codeine/phenylephrine/chlorpheniramine syrup)
	CODITUSSIN AC (codeine/guaifenesin syrup)
	CODITUSSIN DAC (codeine/guaifenesin/pseudoephedrine syrup)
	HISTEX AC (codeine/phenylephrine/triprolidine syrup)
	(hydrocodone/homatropine tablet)
	HYDROMET (hydrocodone/homatropine solution)
	MAR-COF BP (codeine/pseudoephedrine/brompheniramine syrup)
	MAR-COF CG (codeine/guaifenesin syrup)
	MAXI-TUSS AC (codeine/guaifenesin liquid)
	MAXI-TUSS CD (codeine/phenylephrine/chlorpheniramine liquid)
	M-CLEAR WC (codeine/guaifenesin liquid)
	M-END PE (codeine/phenylephrine/brompheniramine liquid)
	NINJACOF-XG (codeine/guaifenesin liquid)
	POLY-TUSSIN AC (codeine/phenylephrine/brompheniramine liquid)

(promethazine/codeine)

(promethazine/codeine/phenylephrine)

PRO-RED AC
(codeine/dexchlorpheniramine/phenylephrine syrup)

RYDEX
(codeine/pseudoephedrine/brompheniramine liquid)

TUSNEL C
(codeine/guaifenesin/pseudoephedrine liquid)

TUSSICAPS
(hydrocodone/chlorpheniramine extended-release capsule)

TUSSIONEX PENNKINETIC
(hydrocodone/chlorpheniramine extended-release suspension)

TUXARIN ER
(codeine/chlorpheniramine extended-release tablet)

TUZISTRA XR
(codeine/chlorpheniramine extended-release suspension)

VIRTUSSIN DAC
(codeine/guaifenesin/pseudoephedrine liquid)

Z-TUSS AC
(codeine/chlorpheniramine liquid)

Status: CVS Caremark Criteria
Type: Quantity Limit; Post Limit Prior Authorization ***Ref # 4428-HJ***

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Hydrocodone and homatropine solution, tablets

Hydrocodone and homatropine is indicated for the symptomatic relief of cough in patients 18 years of age and older.

Limitations of Use:

- Not indicated for pediatric patients under 18 years of age.
- Contraindicated in pediatric patients less than 6 years of age.
- Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, reserve hydrocodone and homatropine for use in adult patients for whom the benefits of cough suppression are expected to outweigh the risks, and in whom an adequate assessment of the etiology of the cough has been made.

Promethazine with codeine oral solution

Promethazine with codeine oral solution is indicated for the temporary relief of coughs and upper respiratory symptoms associated with allergy or the common cold in patients 18 years of age and older.

Limitations of Use:
- Not indicated for pediatric patients under 18 years of age.
- Contraindicated in pediatric patients under 12 years of age.
- Contraindicated in pediatric patients 12 to 18 years of age after tonsillectomy or adenoidectomy.
- Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, reserve promethazine with codeine oral solution for use in adult patients for whom the benefits of cough suppression are expected to outweigh the risks, and in whom an adequate assessment of the etiology of the cough has been made.

Promethazine, codeine, phenylephrine oral solution
Promethazine, codeine, phenylephrine Oral Solution is indicated for the temporary relief of coughs and upper respiratory symptoms, including nasal congestion, associated with allergy or the common cold in patients 18 years of age and older.

Limitations of Use:
- Not indicated for pediatric patients under 18 years of age.
- Contraindicated in pediatric patients under 12 years of age.
- Contraindicated in pediatric patients 12 to 18 years of age after tonsillectomy or adenoidectomy.
- Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, reserve promethazine, codeine, phenylephrine oral solution for use in adult patients for whom the benefits of cough suppression are expected to outweigh the risks, and in whom an adequate assessment of the etiology of the cough has been made.

TussiCaps, Tussionex
TussiCaps (hydrocodone polistirex and chlorpheniramine polistirex) extended-release capsules and Tussionex (hydrocodone polistirex and chlorpheniramine polistirex) extended release suspension are indicated for relief of cough and upper respiratory symptoms associated with allergy or a cold in adults and children 6 years of age and older.

Tuxarin ER
Tuxarin ER is indicated for the relief of cough and symptoms associated with upper respiratory allergies or a common cold in adults 18 years of age and older.

Limitations of Use:
- Not indicated for pediatric patients under 18 years of age.

Tuzistra XR
Tuzistra XR is indicated for the temporary relief of cough and upper respiratory symptoms associated with allergy or the common cold in patients 18 years of age and older.

Limitations of Use:
- Not indicated for pediatric patients under 18 years of age.
- Contraindicated in pediatric patients under 12 years of age.
- Contraindicated in pediatric patients 12 to 18 years of age after tonsillectomy or adenoidectomy.
- Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, reserve Tuzistra XR for use in adult patients for whom the benefits of cough suppression are expected to outweigh the risks, and in whom an adequate assessment of the etiology of the cough has been made.

OVER-THE-COUNTER PRODUCT USES

CapCof
Temporarily relieves these symptoms due to common cold, hay fever (allergic rhinitis), or other upper respiratory allergies:
- Runny nose
- Sneezing

- Itching of the nose or throat
- Itchy, watery eyes
- Cough due to minor throat and bronchial irritation
- Nasal congestion
- Reduces swelling of nasal passages

Coditussin AC
Temporarily relieves these symptoms due to common cold, hay fever (allergic rhinitis), or other upper respiratory allergies:
- cough due to minor throat and bronchial irritation
- helps loosen phlegm (mucus) and thin bronchial secretions to drain bronchial tubes and make coughs more productive

Coditussin DAC
Temporarily relieves these symptoms due to common cold, hay fever (allergic rhinitis), or other upper respiratory allergies:
- cough due to minor throat and bronchial irritation
- helps loosen phlegm (mucus) and thin bronchial secretions to drain bronchial tubes and make coughs more productive
- reduces swelling of nasal passages

Histex AC
Temporarily relieves these symptoms due to common cold, hay fever (allergic rhinitis), or other upper respiratory allergies:
- Runny nose
- Sneezing
- Itching of the nose or throat
- Itchy, watery eyes
- Cough due to minor throat and bronchial irritation
- Nasal congestion
- Reduces swelling of nasal passages

Mar-cof BP
Temporarily relieves these symptoms due to cold, hay fever or other respiratory allergies:
- runny nose, sneezing, itching of the nose or throat, and itchy watery eyes
- cough due to minor throat and bronchial irritation
- nasal congestion

Mar-cof CG
Temporarily relieves:
- cough due to minor throat and bronchial irritations as may occur with a cold or inhaled irritants
- your cough to help you sleep
- helps loosen phlegm (mucus) and thin bronchial secretions to rid the bronchial passageways of bothersome mucus and makes cough more productive

Maxi-Tuss AC
Temporarily relieves:
- cough due to minor throat and bronchial irritations as may occur with a cold or inhaled irritants
- your cough to help you sleep
- helps loosen phlegm (mucus) and thin bronchial secretions to rid the bronchial passageways of bothersome mucus and makes cough more productive

Maxi-Tuss CD
Temporarily relieves these symptoms due to the common cold, hay fever (allergic rhinitis) or other upper respiratory allergies:
- cough due to minor throat and bronchial irritation
- runny nose
- sneezing

- itching of the nose or throat
- itchy, watery eyes
- nasal congestion
- reduces swelling of nasal passages
- calms the cough control center and relieves coughing

M-Clear WC
Temporarily relieves these symptoms due to the common cold:
- cough due to minor throat and bronchial irritation
- helps loosen phlegm (mucus) and thin bronchial secretions to drain bronchial tubes and make coughs more productive

M-END PE
Temporarily relieves these symptoms due to the common cold, hay fever (allergic rhinitis) or other upper respiratory allergies:
- cough due to minor throat and bronchial irritation
- nasal congestion
- itching of nose or throat
- runny nose
- itchy, watery eyes
- sneezing
- reduces swelling of nasal passages

Ninjacof-XG
Temporarily relieves:
- cough due to minor throat and bronchial irritations
- helps loosen phlegm (mucus) and thin bronchial secretions to drain bronchial tubes and make coughs more productive

Poly-Tussin AC
Temporarily relieves these symptoms due to the common cold, hay fever (allergic rhinitis), or other upper respiratory allergies:
- runny nose
- sneezing
- itching of the nose or throat
- itchy, watery eyes
- cough due to minor throat and bronchial irritation
- nasal congestion
- reduces swelling of the nasal passages

Pro-Red AC
Temporarily relieves these symptoms due to the common cold, hay fever (allergic rhinitis) or other upper respiratory allergies:
- cough due to minor throat and bronchial irritation
- nasal congestion
- reduces swelling of nasal passages
- runny nose
- sneezing
- itching of nose or throat
- itchy, watery eyes

Rydex
Temporarily relieves these symptoms due to the common cold, hay fever or other upper respiratory allergies (allergic rhinitis):

- cough due to minor throat and bronchial irritation
- nasal congestion
- reduces swelling of the nasal passages
- runny nose
- sneezing
- itching of the nose or throat
- itchy, watery eyes

Tusnel C
Uses:
- helps loosen phlegm (mucus) and thin bronchial secretions to make coughs more productive
- temporarily relieves: nasal congestion due to the common cold, hay fever or other upper respiratory allergies and nasal congestion associated with sinusitis, cough due to minor bronchial irritation as may occur with the common cold
- temporarily restores freer breathing through the nose
- calms the cough control center and relieves coughing

Virtussin DAC
Uses:
- temporarily relieves cough due to minor throat and bronchial irritation as may occur with a cold
- temporarily relieves nasal congestion due to the common cold
- temporarily restores freer breathing through the nose
- helps loosen phlegm (mucus) and thin bronchial secretions to make coughs more productive
- calms the cough control center and relieves coughing

Z-Tuss AC
Temporarily relieves these symptoms due to common cold, hay fever (allergic rhinitis), or other upper respiratory allergies:
- runny nose
- sneezing
- itching of the nose or throat
- itchy, watery eyes
- cough due to minor throat and bronchial irritation

QUANTITY LIMIT**

LIMIT CRITERIA
This limit is coded for daily dose.

Drug	Daily Limit
CapCof (codeine/phenylephrine/chlorpheniramine [10 mg-5 mg-2 mg/5 mL] syrup)	60 mL/day
Coditussin AC (codeine/guaifenesin [10 mg-200 mg/5 mL] syrup)	60 mL/day
Coditussin DAC (codeine/guaifenesin/pseudoephedrine [10 mg-200 mg-30 mg/5 mL] syrup)	40 mL/day
Histex AC (codeine/phenylephrine/triprolidine [10 mg-10 mg-2.5 mg/5 mL] syrup)	20 mL/day
(hydrocodone and homatropine [5 mg-1.5 mg/5 mL] solution)	30 mL/day
(hydrocodone and homatropine [5 mg-1.5 mg] tablets)	6 tablets/day

Mar-cof BP (codeine/pseudoephedrine/brompheniramine [7.5 mg-30 mg-2 mg/5 mL] syrup)	60 mL/day
Mar-cof CG (codeine/guaifenesin [7.5 mg-225 mg/5 mL] syrup)	45 mL/day
Maxi-Tuss AC (codeine/guaifenesin [10 mg-100 mg/5 mL] liquid)	60 mL/day
Maxi-Tuss CD (codeine/phenylephrine/chlorpheniramine [10 mg-10 mg-4 mg/5 mL] liquid)	30 mL/day
M-Clear WC (codeine/guaifenesin [6.3 mg-100 mg/5 mL] liquid)	90 mL/day
M-END PE (codeine/phenylephrine/brompheniramine [6.33 mg-3.33 mg-1.33 mg/5 mL] liquid)	90 mL/day
Ninjacof-XG (codeine/guaifenesin [8 mg-200 mg/5 mL] liquid)	60 mL/day
Poly-Tussin AC (codeine/phenylephrine/brompheniramine [10 mg-10 mg-4 mg/5 mL] liquid)	30 mL/day
(promethazine with codeine [6.25 mg-10 mg/5 mL] oral solution)	30 mL/day
(promethazine, codeine, phenylephrine [6.25 mg-10 mg-5 mg/5 mL] oral solution)	30 mL/day
Pro-RED AC (codeine/dexchlorpheniramine/phenylephrine [9 mg-1 mg-5 mg/5 mL] syrup)	60 mL/day
Rydex (codeine/pseudoephedrine/brompheniramine [6.33 mg-10 mg-1.33 mg/5 mL] liquid)	90 mL/day
Tusnel C (codeine/guaifenesin/pseudoephedrine liquid [10 mg-100 mg-30 mg/5 mL])	40 mL/day
TussiCaps (hydrocodone/chlorpheniramine extended-release [10 mg-8 mg] capsule)	2 capsules/day
Tussionex (hydrocodone/chlorpheniramine extended-release [10 mg-8 mg/5 mL] suspension)	10 mL/day
Tuxarin ER (codeine/chlorpheniramine extended-release [54.3 mg-8 mg] tablet)	2 capsules/day
Tuzistra XR (codeine/chlorpheniramine [14.7 mg-2.8 mg/5 mL] extended-release suspension)	20 mL/day
Virtussin DAC (codeine/guaifenesin/pseudoephedrine [10 mg-100 mg-30 mg/5 mL] liquid)	40 mL/day
Z-Tuss AC (codeine/chlorpheniramine [9 mg-2 mg/5 mL] liquid)	60 mL/day

***If the patient is requesting more than the initial quantity limit, then the claim will reject with a message indicating that the daily dose has been exceeded. No PA allowed to exceed daily dose limit.*

DURATION LIMIT*

Drug	Duration Limit (per month)
ALL TARGET DRUGS	7-day supply

**If the patient is requesting more than a 7-day supply within the past month, then the claim will reject with a message indicating that the patient can receive a 7-day supply or submit a prior authorization (PA): "MAX 7 DS per 30 days. PA req call 800-XXX-XXXX." [Note: Benefits coding to populate correct PA phone number.]*

The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has a persistent cough requiring treatment beyond 7 days

AND

- The patient has been reevaluated for the cause of the cough to address any underlying pathology, such as foreign body or lower respiratory tract disease

AND

- The need for continued use of the requested drug has been assessed considering the relative incidence of adverse reactions, and the development of addiction, abuse, or misuse

Quantity Limits apply.

RATIONALE

CapCof

The recommended dosage for adults and children 12 years of age and older is two teaspoonfuls (10 mL) every 4 hours, not to exceed 6 doses in 24 hours. The recommended dosage for children 6 to under 12 years of age is one teaspoonful (5 mL) every 4 hours, not to exceed 6 doses in 24 hours.

Coditussin AC

The recommended dosage for adults and children 12 years of age and older is two teaspoonfuls (10 mL) every 4 to 6 hours, not to exceed 6 doses in 24 hours. The recommended dosage for children 6 to under 12 years of age is one teaspoonful (5 mL) every 4 to 6 hours, not to exceed 6 doses in 24 hours.

Coditussin DAC

The recommended dosage for adults and children 12 years of age and older is two teaspoonfuls (10 mL) every 4 to 6 hours, not to exceed 4 doses in 24 hours. The recommended dosage for children 6 to under 12 years of age is one teaspoonful (5 mL) every 4 to 6 hours, not to exceed 8 doses in 24 hours.

Histex AC

The recommended dosage for adults and children 12 years of age and older is 1 teaspoonful (5 mL) every 4 hours, not to exceed 4 teaspoonfuls (20 mL) in 24 hours. The recommended dosage for children 6 to under 12 years of age is one-half teaspoonful (2.5 mL) every 4 hours, not to exceed 2 teaspoonfuls (10 mL) in 24 hours.

Hydrocodone and homatropine solution, tablets

Hydrocodone and homatropine is indicated for the symptomatic relief of cough in patients 18 years of age and older. The recommended dosage is one tablet or 5 mL of the oral solution every 4 to 6 hours as needed; not to exceed 6 tables or 30 mL in 24 hours.

Mar-cof BP

The recommended dosage for adults and children 12 years of age and older is two teaspoonfuls (10 mL) every 4 to 6 hours, not to exceed 6 doses in 24 hours. The recommended dosage for children 6 to under 12 years of age is one teaspoonful (5 mL) every 4 to 6 hours, not to exceed 6 doses in 24 hours.

Mar-cof CG

The recommended dosage for adults and children 12 years of age and older is one and one-half teaspoonfuls (7.5 mL) every 4 to 6 hours, not to exceed 6 doses in 24 hours. The recommended dosage for children 6 to under 12 years of age is three-quarters teaspoonful (3.75mL) every 4 to 6 hours, not to exceed 6 doses in 24 hours.

Maxi-Tuss AC

The recommended dosage for adults and children 12 years of age and older is two teaspoonfuls (10 mL) every 4 hours, not to exceed 6 doses in 24 hours. The recommended dosage for children 6 to under 12 years of age is one teaspoonful (5 mL) every 4 hours, not to exceed 6 doses in 24 hours.

Maxi-Tuss CD
The recommended dosage for adults and children 12 years of age and older is one teaspoonful (5 mL) every 4 hours, not to exceed 6 doses in 24 hours. The recommended dosage for children 6 to under 12 years of age is one-half teaspoonful (2.5 mL) every 4 hours, not to exceed 6 doses in 24 hours.

M-Clear WC
The recommended dosage for adults and children 12 years of age and older is three teaspoonfuls (15 mL) every 4 to 6 hours, not to exceed 6 doses in 24 hours. The recommended dosage for children 6 to under 12 years of age is one and one-half teaspoonfuls (7.5 mL) every 4 to 6 hours, not to exceed 6 doses in 24 hours.

M-END PE
The recommended dosage for adults and children 12 years of age and older is three teaspoonfuls (15 mL) every 4 to 6 hours, not to exceed 6 doses in 24 hours. The recommended dosage for children 6 to under 12 years of age is one and one-half teaspoonfuls (7.5 mL) every 4 to 6 hours, not to exceed 6 doses in 24 hours.

Ninjacof-XG
The recommended dosage for adults and children 12 years of age and older is two teaspoonfuls (10 mL) every 4 hours, not to exceed 6 doses in 24 hours. The recommended dosage for children 6 to under 12 years of age is one teaspoonful (5 mL) every 4 hours, not to exceed 6 doses in 24 hours.

Poly-Tussin Ac
The recommended dosage for adults and children 12 years of age and older is 1 teaspoonful (5 mL) every 4 to 6 hours, not to exceed 6 doses in 24 hours. The recommended dosage for children 6 to under 12 years of age is one-half teaspoonful (2.5 mL) every 4 to 6 hours, not to exceed 6 doses in 24 hours.

Promethazine with codeine oral solution
Promethazine with codeine oral solution is indicated for the temporary relief of coughs and upper respiratory symptoms associated with allergy or the common cold in patients 18 years of age and older. The recommended dosage is 5 mL every 4 to 6 hours as needed, not to exceed 6 doses (30 mL) in 24 hours.

Promethazine, codeine, phenylephrine oral solution
Promethazine, codeine, phenylephrine Oral Solution is indicated for the temporary relief of coughs and upper respiratory symptoms, including nasal congestion, associated with allergy or the common cold in patients 18 years of age and older. The recommended dosage is 5 mL every 4 to 6 hours as needed, not to exceed 6 doses (30 mL) in 24 hours.

Pro-RED AC
The recommended dosage for adults and children 12 years of age and older is two teaspoonfuls (10 mL) every 4 hours, not to exceed 6 doses in 24 hours. The recommended dosage for children 6 to under 12 years of age is one teaspoonful (5 mL) every 4 hours, not to exceed 6 doses in 24 hours.

Rydex
The recommended dosage for adults and children 12 years of age and older is three teaspoonfuls (15 mL) every 4 to 6 hours, not to exceed 6 doses in 24 hours. The recommended dosage for children 6 to under 12 years of age is one and one-half teaspoonfuls (7.5 mL) every 4 to 6 hours, not to exceed 6 doses in 24 hours.

Tusnel C
The recommended dosage for adults and children 12 years of age and older is two teaspoonfuls (10 mL) every 6 hours, not to exceed 4 doses in 24 hours. The recommended dosage for children 6 to under 12 years of age is one teaspoonful (5 mL) every 6 hours, not to exceed 4 doses in 24 hours.

TussiCaps, Tussionex
TussiCaps (hydrocodone polistirex and chlorpheniramine polistirex) extended-release capsules and Tussionex (hydrocodone polistirex and chlorpheniramine polistirex) extended release suspension are indicated for relief of cough and upper respiratory symptoms associated with allergy or a cold in adults and children 6 years of age and older. The recommended dosage for adults and children 12 years of age and older is one full-strength extended-release capsule (10

mg/8 mg) every 12 hours, not to exceed 2 capsules in 24 hours, and 5 mL of the extended-release suspension every 12 hours, not to exceed 10 mL in 24 hours. The recommended dosage for children 6 to 11 years of age is one half-strength extended-release capsule (5 mg/4 mg) every 12 hours, not to exceed 2 capsules in 24 hours, and 2.5 mL of the extended-release suspension every 12 hours, not to exceed 5 mL in 24 hours.

Tuxarin ER
Tuxarin ER is indicated for the relief of cough and symptoms associated with upper respiratory allergies or a common cold in adults 18 years of age and older. Tuxarin ER should be administered orally at a dosage of one tablet every 12 hours, not to exceed 2 tablets in 24 hours.

Tuzistra XR
Tuzistra XR is indicated for the temporary relief of cough and upper respiratory symptoms associated with allergy or the common cold in patients 18 years of age and older. The recommended dosage for adults 18 years of age and older is 10 mL every 12 hours as needed, not to exceed 2 doses (20 mL) in 24 hours.

Virtussin DAC
The recommended dosage for adults and children 12 years of age and older is two teaspoonfuls (10 mL) every 4 hours, not to exceed 4 doses in 24 hours. The recommended dosage for children 6 to under 12 years of age is one teaspoonful (5 mL) every 4 hours, not to exceed 4 doses in 24 hours.

Z-Tuss AC
The recommended dosage for adults and children 12 years of age and older is two teaspoonfuls (10 mL) every 4 to 6 hours, not to exceed 6 doses in 24 hours. The recommended dosage for children 6 to under 12 years of age is one teaspoonful (5 mL) every 4 to 6 hours, not to exceed 6 doses in 24 hours.

The initial limits for the requested drugs are set at the FDA maximum approved daily doses; therefore, post limit quantities for these drugs are set to the same quantity as the initial quantity limit.

If a patient requires a refill, reevaluate patients with unresponsive cough in 5 days or sooner for possible underlying pathology, such as foreign body or lower respiratory tract disease. If a patient requires a refill, reevaluate the cause of the cough and assess the need for continued treatment with the requested drug, the relative incidence of adverse reactions, and the development of addiction, abuse, or misuse.[5,6,15,16,23] Therefore, for extended treatment beyond 7-days of therapy in a one-month time frame, the patient will need to be reevaluated for the cause of the cough, and the need for continued use of the requested drug will need to be assessed considering the relative incidence of adverse reactions, and the development of addiction, abuse, or misuse.

Due to the acute nature of the conditions the target drugs are indicated to treat, there will be a duration limit of 7 days per month. Patients who meet the prior authorization criteria will be approved for 1 month of the requested drug at the daily dose limit.

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Reviewed:	Medical Affairs: (CHART) 01/28/2021, 03/11/2021, 02/03/2022 External Review: 04/2021, 04/2022

CRITERIA FOR APPROVAL

1	Does the patient have a persistent cough requiring treatment beyond 7 days? [If no, then no further questions.]	Yes	No
2	Has the patient been reevaluated for the cause of the cough to address any underlying pathology, such as foreign body or lower respiratory tract disease? [If no, then no further questions.]	Yes	No
3	Has the need for continued use of the requested drug been assessed considering the relative incidence of adverse reactions and the development of addiction, abuse, or misuse?	Yes	No

Mapping Instructions			
	Yes	**No**	**DENIAL REASONS – DO NOT USE FOR MEDICARE PART D**
1.	Go to 2	Deny	You do not meet the requirements of your plan. Your plan covers additional quantities of this drug when you have a persistent cough requiring treatment beyond 7 days. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: No persistent cough.]
2.	Go to 3	Deny	You do not meet the requirements of your plan. Your plan covers additional quantities of this drug when you have been reevaluated for the cause of your cough. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Not reevaluated for cause of cough.]

3.	Approve, 1 month, See Quantity Limit Chart	Deny	You do not meet the requirements of your plan. Your plan covers additional quantities of this drug when you have been evaluated for the need of continued use. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: No balance of continued use vs harms.]

QUANTITY LIMIT CRITERIA

BRAND NAME
(generic)

METHADOSE 10 MG/ML**
(methadone oral concentrate)

METHADOSE 40 MG DISPERSIBLE TABLET**
(methadone dispersible tablets)

Status: CVS Caremark Criteria
Type: Quantity Limit

***Please note that these methadone products are indicated for detoxification/opioid use disorder ONLY. Methadone products indicated for BOTH detoxification/opioid use disorder AND pain are targeted on the Opioids ER criteria.*

POLICY

FDA-APPROVED INDICATIONS

Methadone Concentrate

Methadone hydrochloride oral concentrate contains methadone, an opioid agonist indicated for the:

- Detoxification treatment of opioid addiction (heroin or other morphine-like drugs).
- Maintenance treatment of opioid addiction (heroin or other morphine-like drugs), in conjunction with appropriate social and medical services.

Methadone Dispersible

Methadone hydrochloride tablets for oral suspension contain methadone, an opioid agonist indicated for the:

- Detoxification treatment of opioid addiction (heroin or other morphine-like drugs).
- Maintenance treatment of opioid addiction (heroin or other morphine-like drugs), in conjunction with appropriate social and medical services.

Limitations of Use

Methadone products used for the treatment of opioid addiction in detoxification or maintenance programs are subject to the conditions for distribution and use required under 42 CFR 8.12.

Conditions For Distribution And Use Of Methadone Products For The Treatment Of Opioid Addiction

Code of Federal Regulations, Title 42, Sec 8: Methadone products when used for the treatment of opioid addiction in detoxification or maintenance programs, shall be dispensed only by opioid treatment programs (and agencies, practitioners or institutions by formal agreement with the program sponsor) certified by the Substance Abuse and Mental Health Services Administration and approved by the designated state authority. Certified treatment programs shall dispense and use methadone in oral form only and according to the treatment requirements stipulated in the Federal Opioid Treatment Standards (42 CFR 8.12). See below for important regulatory exceptions to the general requirement for certification to provide opioid agonist treatment.

Failure to abide by the requirements in these regulations may result in criminal prosecution, seizure of the drug supply, revocation of the program approval, and injunction precluding operation of the program.

Regulatory Exceptions To The General Requirement For Certification To Provide Opioid Agonist Treatment:

- During inpatient care, when the patient was admitted for any condition other than concurrent opioid addiction [pursuant to 21 CFR 1306.07(c)], to facilitate the treatment of the primary admitting diagnosis.
- During an emergency period of no longer than 3 days while definitive care for the addiction is being sought in an appropriately licensed facility [pursuant to 21 CFR 1306.07(b)].

INITIAL LIMIT QUANTITY

Limits should accumulate across all drugs and strengths up to highest quantity listed depending on the order the claims are processed.

Drug	1 Month Limit*	3 Month Limit
Methadose 10 mg/mL (methadone oral concentrate)	30 mL/25 days**	Does Not Apply**
Methadose 40 mg (methadone dispersible tablet)	9 tablets/25 days**	Does Not Apply**

**The duration of 25 days is used for a 30-day fill period to allow time for refill processing.*
***The limits for methadone concentrate and dispersible tablets are set to accommodate a 3-day supply.*

REFERENCES

1. Methadone Concentrate [package insert]. Berkeley Heights, NJ: Hikma Pharmaceuticals USA Inc; September 2021.
2. Methadone Dispersible [package insert]. Webster Groves, MO: SpecGX LLC; May 2022.
3. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2022; Accessed October 7, 2022.
4. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed October 7, 2022.
5. U.S. Department of Justice Drug Enforcement Administration. Title 21 Code of Federal Regulations: Part 1306.04 Purpose of Issue of Prescription. https://www.govinfo.gov/content/pkg/CFR-2001-title21-vol9/xml/CFR-2001-title21-vol9-part1306.xml. Accessed October 26, 2022.
6. U.S. Department of Health & Human Services. Substance Abuse and Mental Health Services Administration. Methadone. https://www.samhsa.gov/medication-assisted-treatment/medications-counseling-related-conditions. Accessed October 26, 2022.

STEP THERAPY WITH QUANTITY LIMIT AND POST LIMIT PRIOR AUTHORIZATION CRITERIA

DRUG CLASS	**EXTENDED-RELEASE OPIOID ANALGESICS**
BRAND NAME (generic)	
	ARYMO ER (morphine sulfate extended-release tablets)
	AVINZA (morphine extended-release capsules)
	BELBUCA (buprenorphine buccal film)
	BUTRANS (buprenorphine transdermal system)
	CONZIP (tramadol hydrochloride extended-release)
	DOLOPHINE 5 MG, 10 MG (methadone hydrochloride tablets)
	DURAGESIC (fentanyl transdermal system)
	EMBEDA (morphine sulfate and naltrexone hydrochloride extended-release caps)
	EXALGO (hydromorphone hydrochloride extended-release tablets)
	HYSINGLA ER (hydrocodone bitartrate extended-release tablets)
	KADIAN (morphine extended-release capsules)

METHADONE 5 MG, 10 MG
(methadone hydrochloride tablets)

METHADONE 200 MG/20 ML INJ
(methadone hydrochloride injection)

METHADONE INTENSOL 10 MG/ML
(methadone oral concentrate)

METHADONE 5 MG/5 ML & 10 MG/5 ML ORAL SOLN
(methadone hydrochloride oral solution)

MORPHABOND ER
(morphine extended-release tablets)

MS CONTIN
(morphine extended-release tablets)

NUCYNTA ER
(tapentadol extended-release tablets)

OPANA ER
(oxymorphone hydrochloride extended-release tablets)

OXYCONTIN
(oxycodone hydrochloride extended-release tablets)

(oxymorphone hydrochloride extended-release tablets)

TARGINIQ ER
(oxycodone HCl/naloxone HCl extended-release tablets)

(tramadol hydrochloride extended-release)

TROXYCA ER
(oxycodone hydrochloride/naltrexone extended-release capsules)

ULTRAM ER
(tramadol hydrochloride extended-release tablets)

VANTRELA ER
(hydrocodone bitartrate extended-release tablets)

XTAMPZA ER
(oxycodone extended-release capsules)

ZOHYDRO ER
(hydrocodone bitartrate extended-release capsules)

Status: Client Requested Criteria

Type: Initial Step Therapy; Initial Limit; Post Limit PA ***Ref # C17531-M***

INITIAL STEP THERAPY
If the patient has filled a prescription for at least a 1-day supply of a drug indicating the patient is being treated for cancer or sickle cell disease within the past 365 days under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit.

If a claim is submitted with an ICD 10 diagnosis code indicating cancer, sickle cell disease, or palliative care under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit.

If the patient has an ICD 10 diagnosis code indicating cancer, sickle cell disease, or palliative care in their member health profile in the past 365 days, then the requested drug will be paid under that prescription benefit.

If a claim is submitted using a hospice patient residence code under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit.

For patients with no prescription claims of a cancer drug or a sickle cell disease drug in the past 365 days, no ICD 10 diagnosis code indicating cancer, sickle cell disease, or palliative care submitted with their prescription claim, no ICD 10 diagnosis code indicating cancer, sickle cell disease, or palliative care in the member health profile in the past 365 days, or no hospice patient residence code submitted with their prescription claim:
If the patient has filled a prescription for at least a 7-day supply of an immediate-release (IR) opioid agent indicated for the management of pain within prescription claim history in the past 90 days under a prescription benefit administered by CVS Caremark, then the initial daily dose limit criteria will apply (see Column A in the Opioid Analgesics ER Quantity Limits Chart below).

If the patient has filled a prescription for at least a 30-day supply of an extended-release (ER) opioid agent indicated for the management of pain within prescription claim history in the past 90 days under a prescription benefit administered by CVS Caremark, then the initial daily dose limit criteria will apply (see Column A in the Opioid Analgesics ER Quantity Limits Chart below).

If the patient does not have at least a 7-day supply of an immediate-release opioid agent indicated for the management of pain OR at least a 30-day supply of an extended-release opioid agent indicated for the management of pain within prescription claim history in the past 90 days (i.e., the patient has not used an IR opioid prior to the ER opioid OR the patient is not already stable on an ER opioid), then the claim will reject with a message indicating that a prior authorization (PA) is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

Opioid Analgesics ER Quantity Limits Chart			
Coverage is provided without prior authorization for a 30-day or 90-day supply of an extended-release opioid for a daily dose that corresponds to ≤ 90 MME/day (when Step Therapy criteria met). Coverage for a daily dose that corresponds to ≤ 200 MME/day (unless minimum FDA-labeled strength/dose/frequency exceeds 200 MME/day) for a 30-day or 90-day supply is provided through prior authorization when coverage conditions are met. **Accumulation does not apply if limit is coded for daily dose.**			
		COLUMN A	**COLUMN B**
Drug/Strength	**Labeled Dosing**	**Daily Dose Initial Limit ≤ 90 MME/day**	**Daily Dose Post Limit ≤ 200 MME/day***
Arymo ER 15 mg	q8-12h	3 tabs/day (45 MME/day)	4 tabs/day (60 MME/day)
Arymo ER 30 mg	q8-12h	3 tabs/day (90 MME/day)	4 tabs/day (120 MME/day)
Arymo ER 60 mg	q8-12h	0**	3 tabs/day (180 MME/day)
Avinza 30 mg	q24h, MAX 1600 mg/day	1 cap/day (30 MME/day)	2 caps/day (60 MME/day)
Avinza 45 mg	q24h, MAX 1600 mg/day	1 cap/day (45 MME/day)	2 caps/day (90 MME/day)
Avinza 60 mg	q24h, MAX 1600 mg/day	1 cap/day (60 MME/day)	2 caps/day (120 MME/day)
Avinza 75 mg	q24h, MAX 1600 mg/day	1 cap/day (75 MME/day)	2 caps/day (150 MME/day)
Avinza 90 mg	q24h, MAX 1600 mg/day	1 cap/day (90 MME/day)	2 caps/day (180 MME/day)
Avinza 120 mg	q24h, MAX 1600 mg/day	0**	1 cap/day (120 MME/day)
Belbuca 75 mcg	q12h, MAX 900 mcg/12 hrs	2 films/day (4.5 MME/day)	3 films/day (6.75 MME/day)
Belbuca 150 mcg	q12h, MAX 900 mcg/12 hrs	2 films/day (9 MME/day)	3 films/day (13.5 MME/day)
Belbuca 300 mcg	q12h, MAX 900 mcg/12 hrs	2 films/day (18 MME/day)	3 films/day (27 MME/day)
Belbuca 450 mcg	q12h, MAX 900 mcg/12 hrs	2 films/day (27 MME/day)	3 films/day (40.5 MME/day)
Belbuca 600 mcg	q12h, MAX 900 mcg/12 hrs	0**	2 films/day (36 MME/day)
Belbuca 750 mcg	q12h, MAX 900 mcg/12 hrs	0**	2 films/day (45 MME/day)
Belbuca 900 mcg	q12h, MAX 900 mcg/12 hrs	0**	2 films/day (54 MME/day)
Butrans 5 mcg/hr	q7d, MAX 20 mcg/hr	0.143 patch/day	0.286 patch/day

		(i.e., 1 patch per week) (9 MME/day)	(i.e., 2 patches per week) (18 MME/day)
Butrans 7.5 mcg/hr	q7d, MAX 20 mcg/hr	0.143 patch/day (i.e., 1 patch per week) (13.5 MME/day)	0.286 patch/day (i.e., 2 patches per week) (27 MME/day)
Butrans 10 mcg/hr	q7d, MAX 20 mcg/hr	0.143 patch/day (i.e., 1 patch per week) (18 MME/day)	0.286 patch/day (i.e., 2 patches per week) (36 MME/day)
Butrans 15 mcg/hr	q7d, MAX 20 mcg/hr	0**	0.143 patch/day (i.e., 1 patch per week) (27 MME/day)
Butrans 20 mcg/hr	q7d, MAX 20 mcg/hr	0**	0.143 patch/day (i.e., 1 patch per week) (36 MME/day)
Conzip 100 mg	qd, MAX 300 mg/day	1 cap/day (10 MME/day)	2 caps/day (20 MME/day)
Conzip 200 mg	qd, MAX 300 mg/day	0**	1 cap/day (20 MME/day)
Conzip 300 mg	qd, MAX 300 mg/day	0**	1 cap/day (30 MME/day)
Dolophine 5 mg	q8-12h	3 tabs/day (60 MME/day)	4 tabs/day (80 MME/day)
Dolophine 10 mg	q8-12h	2 tabs/day (80 MME/day)	3 tabs/day (120 MME/day)
Duragesic 12 mcg/hr	q72h	0.333 patch/day (i.e., 1 patch per 3 days) (28.8 MME/day)	0.666 patch/day (i.e., 2 patches per 3 days) (57.6 MME/day)
Duragesic 25 mcg/hr	q72h	0.333 patch/day (i.e., 1 patch per 3 days) (60 MME/day)	0.666 patch/day (i.e., 2 patches per 3 days) (120 MME/day)
Duragesic 37.5 mcg/hr	q72h	0.333 patch/day (i.e., 1 patch per 3 days) (90 MME/day)	0.666 patch/day (i.e., 2 patches per 3 days) (180 MME/day)
Duragesic 50 mcg/hr	q72h	0**	0.333 patch/day (i.e., 1 patch per 3 days) (120 MME/day)
Duragesic 62.5 mcg/hr	q72h	0**	0.333 patch/day (i.e., 1 patch per 3 days) (150 MME/day)
Duragesic 75 mcg/hr	q72h	0**	0.333 patch/day (i.e., 1 patch per 3 days) (180 MME/day)
Duragesic 87.5 mcg/hr	q72h	0**	0.333 patch/day (i.e., 1 patch per 3 days) (210 MME/day)
Duragesic 100 mcg/hr	q72h	0**	0.333 patch/day (i.e., 1 patch per 3 days) (240 MME/day)
Embeda 20 mg/0.8 mg	q12-24h	2 caps/day (40 MME/day)	3 caps/day (60 MME/day)
Embeda 30 mg/1.2 mg	q12-24h	2 cap/day (60 MME/day)	3 caps/day (90 MME/day)
Embeda 50 mg/2 mg	q12-24h	1 cap/day (50 MME/day)	2 caps/day (100 MME/day)

Embeda 60 mg/2.4 mg	q12-24h	1 cap/day (60 MME/day)	2 caps/day (120 MME/day)
Embeda 80 mg/3.2 mg	q12-24h	1 cap/day (80 MME/day)	2 caps/day (160 MME/day)
Embeda 100 mg/4 mg	q12-24h	0**	2 caps/day (200 MME/day)
Exalgo 8 mg	qd	1 tab/day (32 MME/day)	2 tabs/day (64 MME/day)
Exalgo 12 mg	qd	1 tab/day (48 MME/day)	2 tabs/day (96 MME/day)
Exalgo 16 mg	qd	1 tab/day (64 MME/day)	2 tabs/day (128 MME/day)
Exalgo 32 mg	qd	0**	1 tab/day (128 MME/day)
Hysingla ER 20 mg	q24h	1 tab/day (20 MME/day)	2 tabs/day (40 MME/day)
Hysingla ER 30 mg	q24h	1 tab/day (30 MME/day)	2 tabs/day (60 MME/day)
Hysingla ER 40 mg	q24h	1 tab/day (40 MME/day)	2 tabs/day (80 MME/day)
Hysingla ER 60 mg	q24h	1 tab/day (60 MME/day)	2 tabs/day (120 MME/day)
Hysingla ER 80 mg	q24h	1 tab/day (80 MME/day)	2 tabs/day (160 MME/day)
Hysingla ER 100 mg	q24h	0**	2 tabs/day (200 MME/day)
Hysingla ER 120 mg	q24h	0**	1 tab/day (120 MME/day)
Kadian 10 mg	q12-24h	2 caps/day (20 MME/day)	3 caps/day (30 MME/day)
Kadian 20 mg	q12-24h	2 caps/day (40 MME/day)	3 caps/day (60 MME/day)
Kadian 30 mg	q12-24h	2 caps/day (60 MME/day)	3 caps/day (90 MME/day)
Kadian 40 mg	q12-24h	2 caps/day (80 MME/day)	3 caps/day (120 MME/day)
Kadian 50 mg	q12-24h	1 cap/day (50 MME/day)	2 caps/day (100 MME/day)
Kadian 60 mg	q12-24h	1 cap/day (60 MME/day)	2 caps/day (120 MME/day)
Kadian 70 mg	q12-24h	1 cap/day (70 MME/day)	2 caps/day (140 MME/day)
Kadian 80 mg	q12-24h	1 cap/day (80 MME/day)	2 caps/day (160 MME/day)
Kadian 100 mg	q12-24h	0**	2 caps/day (200 MME/day)
Kadian 130 mg	q12-24h	0**	1 cap/day (130 MME/day)
Kadian 150 mg	q12-24h	0**	1 cap/day (150 MME/day)
Kadian 200 mg	q12-24h	0**	1 cap/day (200 MME/day)
Methadone 5 mg	q8-12h	3 tabs/day (60 MME/day)	4 tabs/day (80 MME/day)
Methadone 10 mg	q8-12h	2 tabs/day	3 tabs/day

		(80 MME/day)	(120 MME/day)
Methadone 200 mg/20 mL injection	q8-12h	0.666 mL/day (i.e., one 20 mL multidose vial per month) (26.7 MME/day)	1.333 mL/day (i.e., two 20 mL multidose vials per month) (53.3 MME/day)
Methadone 10 mg/mL Intensol soln	q8-12h	2 mL/day (80 MME/day)	3 mL/day (120 MME/day)
Methadone 5 mg/5 mL Oral soln	q8-12h	15 mL/day (60 MME/day)	20 mL/day (80 MME/day)
Methadone 10 mg/5 mL Oral soln	q8-12h	10 mL/day (80 MME/day)	15 mL/day (120 MME/day)
MorphaBond ER 15 mg	q8-12h	3 tabs/day (45 MME/day)	4 tabs/day (60 MME/day)
MorphaBond ER 30 mg	q8-12h	3 tabs/day (90 MME/day)	4 tabs/day (120 MME/day)
MorphaBond ER 60 mg	q8-12h	0**	3 tabs/day (180 MME/day)
MorphaBond ER 100 mg	q8-12h	0**	2 tabs/day (200 MME/day)
MS Contin 15 mg	q8-12h	3 tabs/day (45 MME/day)	4 tabs/day (60 MME/day)
MS Contin 30 mg	q8-12h	3 tabs/day (90 MME/day)	4 tabs/day (120 MME/day)
MS Contin 60 mg	q8-12h	0**	3 tabs/day (180 MME/day)
MS Contin 100 mg	q8-12h	0**	2 tabs/day (200 MME/day)
MS Contin 200 mg	q8-12h	0**	2 tabs/day (400 MME/day)
Nucynta ER 50 mg	q12h, MAX 500 mg/day	2 tabs/day (40 MME/day)	3 tabs/day (60 MME/day)
Nucynta ER 100 mg	q12h, MAX 500 mg/day	2 tabs/day (80 MME/day)	3 tabs/day (120 MME/day)
Nucynta ER 150 mg	q12h, MAX 500 mg/day	0**	3 tabs/day (180 MME/day)
Nucynta ER 200 mg	q12h, MAX 500 mg/day	0**	2 tabs/day (160 MME/day)
Nucynta ER 250 mg	q12h, MAX 500 mg/day	0**	2 tabs/day (200 MME/day)
Opana ER 5 mg	q12h	2 tabs/day (30 MME/day)	3 tabs/day (45 MME/day)
Opana ER 7.5 mg	q12h	2 tabs/day (45 MME/day)	3 tabs/day (67.5 MME/day)
Opana ER 10 mg	q12h	2 tabs/day (60 MME/day)	3 tabs/day (90 MME/day)
Opana ER 15 mg	q12h	2 tabs/day (90 MME/day)	3 tabs/day (135 MME/day)
Opana ER 20 mg	q12h	0**	3 tabs/day (180 MME/day)
Opana ER 30 mg	q12h	0**	2 tabs/day (180 MME/day)
Opana ER 40 mg	q12h	0**	2 tabs/day (240 MME/day)

OxyContin 10 mg	q12h	2 tabs/day (30 MME/day)	3 tabs/day (45 MME/day)
OxyContin 15 mg	q12h	2 tabs/day (45 MME/day)	3 tabs/day (67.5 MME/day)
OxyContin 20 mg	q12h	2 tabs/day (60 MME/day)	3 tabs/day (90 MME/day)
OxyContin 30 mg	q12h	2 tabs/day (90 MME/day)	3 tabs/day (135 MME/day)
OxyContin 40 mg	q12h	0**	3 tabs/day (180 MME/day)
OxyContin 60 mg	q12h	0**	2 tabs/day (180 MME/day)
OxyContin 80 mg	q12h	0**	2 tabs/day (240 MME/day)
Targiniq ER 10 mg/5 mg	q12h, MAX 80 mg/40 mg (40 mg/20 mg q12h)	2 tabs/day (30 MME/day)	3 tabs/day (45 MME/day)
Targiniq ER 20 mg/10 mg	q12h, MAX 80 mg/40 mg (40 mg/20 mg q12h)	2 tabs/day (60 MME/day)	3 tabs/day (90 MME/day)
Targiniq ER 40 mg/20 mg	q12h, MAX 80 mg/40 mg (40 mg/20 mg q12h)	0**	2 tabs/day (120 MME/day)
Tramadol ER 100 mg	qd, MAX 300 mg/day	1 tab/day (10 MME/day)	2 tabs/day (20 MME/day)
Tramadol ER 150 mg	qd, MAX 300 mg/day	1 cap/day (15 MME/day)	2 caps/day (30 MME/day)
Tramadol ER 200 mg	qd, MAX 300 mg/day	0**	1 tab/day (20 MME/day)
Tramadol ER 300 mg	qd, MAX 300 mg/day	0**	1 tab/day (30 MME/day)
Troxyca ER 10 mg/1.2 mg	q12h	2 caps/day (30 MME/day)	3 caps/day (45 MME/day)
Troxyca ER 20 mg/2.4 mg	q12h	2 caps/day (60 MME/day)	3 caps/day (90 MME/day)
Troxyca ER 30 mg/3.6 mg	q12h	2 caps/day (90 MME/day)	3 caps/day (135 MME/day)
Troxyca ER 40 mg/4.8 mg	q12h	0**	3 caps/day (180 MME/day)
Troxyca ER 60 mg/7.2 mg	q12h	0**	2 caps/day (180 MME/day)
Troxyca ER 80 mg/9.6 mg	q12h	0**	2 caps/day (240 MME/day)
Ultram ER 100 mg	qd, MAX 300 mg/day	1 tab/day (10 MME/day)	2 tabs/day (20 MME/day)
Ultram ER 200 mg	qd, MAX 300 mg/day	0**	1 tab/day (20 MME/day)
Ultram ER 300 mg	qd, MAX 300 mg/day	0**	1 tab/day (30 MME/day)
Vantrela ER 15 mg	q12h, MAX 90 mg q12h (180 mg/day)	2 tabs/day (30 MME/day)	3 tabs/day (45 MME/day)
Vantrela ER 30 mg	q12h, MAX 90 mg q12h (180 mg/day)	2 tabs/day (60 MME/day)	3 tabs/day (90 MME/day)
Vantrela ER 45 mg	q12h, MAX 90 mg q12h (180 mg/day)	2 tabs/day (90 MME/day)	3 tabs/day (135 MME/day)

Vantrela ER 60 mg	q12h, MAX 90 mg q12h (180 mg/day)	0**	2 tabs/day (120 MME/day)
Vantrela ER 90 mg	q12h, MAX 90 mg q12h (180 mg/day)	0**	2 tabs/day (180 MME/day)
Xtampza ER 9 mg	q12h, MAX 288 mg/day	2 caps/day (30 MME/day)	3 caps/day (45 MME/day)
Xtampza ER 13.5 mg	q12h, MAX 288 mg/day	2 caps/day (45 MME/day)	3 caps/day (67.5 MME/day)
Xtampza ER 18 mg	q12h, MAX 288 mg/day	2 caps/day (60 MME/day)	3 caps/day (90 MME/day)
Xtampza ER 27 mg	q12h, MAX 288 mg/day	2 caps/day (90 MME/day)	3 caps/day (135 MME/day)
Xtampza ER 36 mg	q12h, MAX 288 mg/day	0**	3 caps/day (180 MME/day)
Zohydro ER 10 mg	q12h	2 caps/day (20 MME/day)	3 caps/day (30 MME/day)
Zohydro ER 15 mg	q12h	2 caps/day (30 MME/day)	3 caps/day (45 MME/day)
Zohydro ER 20 mg	q12h	2 caps/day (40 MME/day)	3 caps/day (60 MME/day)
Zohydro ER 30 mg	q12h	2 caps/day (60 MME/day)	3 caps/day (90 MME/day)
Zohydro ER 40 mg	q12h	2 caps/day (80 MME/day)	3 caps/day (120 MME/day)
Zohydro ER 50 mg	q12h	0**	2 caps/day (100 MME/day)

QUANTITY LIMIT CRITERIA

DRUG CLASS	**ACETAMINOPHEN/ASPIRIN/IBUPROFEN CONTAINING OPIOID ANALGESICS (BRAND AND GENERIC)***
(generic name)	
	(acetaminophen and benzhydrocodone)
	(acetaminophen and codeine)
	(acetaminophen and hydrocodone)
	(acetaminophen and oxycodone)
	(acetaminophen and tramadol)
	(acetaminophen, caffeine, and dihydrocodeine)
	(aspirin and oxycodone)
	(celecoxib and tramadol)
	(ibuprofen and hydrocodone)

Status: CVS Caremark Criteria
Type: Quantity Limit* ***Ref # 1365-H***

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*
***1365-H may be used as a stand-alone criteria OR in combination with Opioids IR Combo Products – Acute Pain Duration Limit 1358-E. The Opioids IR Combo Products – Acute Pain Duration Limit 1358-E will be coded separately.*

FDA-APPROVED INDICATIONS

Apadaz (benzhydrocodone/acetaminophen)
Apadaz (benzhydrocodone and acetaminophen) is indicated for the short-term (no more than 14 days) management of acute pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate.
Limitations of Use
Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, reserve Apadaz for use in patients for whom alternative treatment options [e.g., non-opioid analgesics]:

- Have not been tolerated, or are not expected to be tolerated,
- Have not provided adequate analgesia, or are not expected to provide adequate analgesia.

Codeine/Acetaminophen
Acetaminophen and codeine phosphate oral solution and tablets are indicated for the management of mild to moderate pain, where treatment with an opioid is appropriate and for which alternative treatments are inadequate.
Limitations of Use

Because of the risks of addiction, abuse, and misuse, with opioids, even at recommended doses, reserve acetaminophen and codeine phosphate oral solution and tablets for use in patients for whom alternative treatment options [e.g., non-opioid analgesics]:

- Have not provided adequate analgesia, or are not expected to provide adequate analgesia,
- Have not been tolerated, or are not expected to be tolerated.

Hydrocodone/Acetaminophen

Hydrocodone bitartrate and acetaminophen Tablets are indicated for the management of pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate.

Limitations of Use

Because of the risks of addiction, abuse, and misuse, with opioids, even at recommended doses, reserve hydrocodone bitartrate and acetaminophen Tablets for use in patients for whom alternative treatment options (e.g., non-opioid analgesics):

- Have not been tolerated, or are not expected to be tolerated,
- Have not provided adequate analgesia, or are not expected to provide adequate analgesia.

Hydrocodone/Ibuprofen

Hydrocodone bitartrate and ibuprofen tablets are indicated for the short-term management of acute pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate.

Limitations of Use

Carefully consider the potential benefits and risks of hydrocodone bitartrate and ibuprofen tablets and other treatment options before deciding to use hydrocodone bitartrate and ibuprofen tablets. Use the lowest effective dosage for the shortest duration consistent with individual treatment goals. Do not use hydrocodone bitartrate and ibuprofen tablets for the treatment of conditions such as osteoarthritis or rheumatoid arthritis.

Because of the risks of addiction, abuse, and misuse, with opioids, even at recommended doses, reserve hydrocodone bitartrate and ibuprofen tablets for use in patients for whom alternative treatment options (e.g., non-opioid analgesics):

- Have not been tolerated, or are not expected to be tolerated,
- Have not provided adequate analgesia, or are not expected to provide adequate analgesia.

Lortab Elixir (hydrocodone/acetaminophen), Hydrocodone/Acetaminophen Solution

Hydrocodone bitartrate and acetaminophen oral solution is indicated for the management of pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate.

Limitations of Use

Because of the risks of addiction, abuse, and misuse, with opioids, even at recommended doses, reserve Lortab Elixir (hydrocodone bitartrate and acetaminophen) oral solution for use in patients for whom alternative treatment options (e.g., non-opioid analgesics):

- Have not been tolerated, or are not expected to be tolerated
- Have not provided adequate analgesia, or are not expected to provide adequate analgesia.

Nalocet, Percocet, Prolate Tablets (oxycodone/acetaminophen), Oxycodone/Acetaminophen Tablets

Oxycodone and acetaminophen tablets are indicated for the management of pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate.

Limitations of Use

Because of the risks of addiction, abuse, and misuse, with opioids, even at recommended doses, reserve oxycodone and acetaminophen for use in patients for whom alternative treatment options [e.g., non-opioid analgesics]:

- Have not been tolerated, or are not expected to be tolerated,
- Have not provided adequate analgesia, or are not expected to provide adequate analgesia.

Oxycodone/Aspirin

Oxycodone and aspirin tablets are indicated for the management of pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate.

Limitations of Use

Because of the risks of addiction, abuse, and misuse, with opioids, even at recommended doses, reserve oxycodone and aspirin tablets for use in patients for whom alternative treatment options (e.g., non-opioid analgesics):

- Have not been tolerated, or are not expected to be tolerated,
- Have not provided adequate analgesia, or are not expected to provide adequate analgesia

Prolate Solution (oxycodone/acetaminophen), Oxycodone/Acetaminophen Solution

Oxycodone hydrochloride and acetaminophen oral solution is indicated for the management of acute pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate.

Limitations of Use

Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, reserve oxycodone hydrochloride and acetaminophen oral solution for use in patients for whom alternative treatment options [e.g., non-opioid analgesics]:

- Have not been tolerated, or are not expected to be tolerated,
- Have not provided adequate analgesia, or are not expected to provide adequate analgesia

Seglentis (tramadol/celecoxib)

Seglentis (tramadol and celecoxib) is indicated for the management of acute pain in adults that is severe enough to require an opioid analgesic and for which alternative treatments are inadequate.

Limitations of Use

Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, reserve Seglentis (tramadol and celecoxib) for use in patients for whom alternative treatment options [e.g., non-opioid analgesics]:

- Have not been tolerated, or are not expected to be tolerated
- Have not provided adequate analgesia, or are not expected to provide adequate analgesia.

Trezix Capsules (acetaminophen/caffeine/dihydrocodeine), Acetaminophen/Caffeine/Dihydrocodeine Tablets

Acetaminophen, caffeine, dihydrocodeine bitartrate capsules and tablets are indicated for the management of pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate.

Limitations of Use

Because of the risks of addiction, abuse, and misuse, with opioids, even at recommended doses, reserve acetaminophen, caffeine, dihydrocodeine bitartrate capsules and tablets for use in patients for whom alternative treatment options [e.g., non-opioid analgesics]:

- Have not been tolerated, or are not expected to be tolerated
- Have not provided adequate analgesia, or are not expected to provide adequate analgesia

Ultracet (tramadol/acetaminophen)

Ultracet (tramadol and acetaminophen) tablets are indicated for the management of acute pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate.

Limitations of Use

Ultracet (tramadol and acetaminophen) tablets are indicated for short-term use of five days or less.

Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, reserve Ultracet (tramadol and acetaminophen) for use in patients for whom alternative treatment options [e.g., non-opioid analgesics]:

- Have not been tolerated, or are not expected to be tolerated,
- Have not provided adequate analgesia, or are not expected to provide adequate analgesia.

Opioid Analgesics IR Combo Products Quantity Limits Chart
Coverage is provided without prior authorization for a 30-day or 90-day supply of an immediate-release combination product opioid for a monthly quantity that does not exceed the maximum daily dose listed in product labeling. Quantities also do not exceed 90 MME/day (unless maximum FDA-labeled strength/dose/frequency exceeds 90 MME/day), 4 g/day of acetaminophen or aspirin, or 3200 mg/day of ibuprofen. If the patient is requesting more than the initial quantity limit, then the claim will reject with a message indicating that quantity limits are exceeded.

This quantity limit will accumulate drugs in the following 5 groups up to highest quantity listed in each group depending on the order the claims are processed: 1) Acetaminophen-containing solutions, suspensions, elixirs accumulate together, 2) Acetaminophen-containing tablets and capsules accumulate together, 2a) Acetaminophen-containing tablets with the same 1 month and 3 month limit accumulate together, 3) Aspirin-containing tablets and capsules accumulate together, 4) Ibuprofen-containing tablets accumulate together, 5) Celecoxib-containing tablets accumulate together. See Accumulation Group column in chart below for more detail.

Accum-ulation Group	Drug/Strength***	Labeled Dosing	Initial 1 Month Limit* ≤ 90 MME/day** and ≤ 4 g APAP or ASA and ≤ 3200 mg IBU (per 25 days)	Initial 3 Month Limit* ≤ 90 MME/day** and ≤ 4 g APAP or ASA and ≤ 3200 mg IBU (per 75 days)
1	APAP/codeine soln 120-12 mg/5 mL	q4h, MAX 360 mg codeine/day	2700 mL/month 90 mL/day (32.4 MME/day)	8100 mL/3 months 90 mL/day (32.4 MME/day)
2	APAP/codeine tab 300/15 mg	q4h, MAX 360 mg codeine/day	400 tabs/month 13.34 tabs/day (30 MME/day)	1200 tabs/3 months 13.34 tabs/day (30 MME/day)
2	APAP/codeine tab 300/30 mg	q4h, MAX 360 mg codeine/day	360 tabs/month 12 tabs/day (54 MME/day)	1080 tabs/3 months 12 tabs/day (54 MME/day)
2	APAP/codeine tab 300/60 mg	q4h, MAX 360 mg codeine/day	180 tabs/month 6 tabs/day (54 MME/day)	540 tabs/3 months 6 tabs/day (54 MME/day)
2	APAP/caffeine/dihydrocodeine cap 320.5/30/16 mg	q4h, MAX 10 caps/day	300 caps/month 10 caps/day (40 MME/day)	900 caps/3 months 10 caps/day (40 MME/day)
2	APAP/caffeine/dihydrocodeine tab 325/30/16 mg	q4h, MAX 10 tabs/day	300 tabs/month 10 tabs/day (40 MME/day)	900 tabs/3 months 10 tabs/day (40 MME/day)
2	Benzhydrocodone/APAP 4.08 mg/325 mg	q4-6h, MAX 12 tabs/day for 14 days	168 tabs/month 12 tabs/day (60 MME/day)	Does Not Apply****
2	Benzhydrocodone/APAP 6.12 mg/325 mg	q4-6h, MAX 12 tabs/day for 14 days	168 tabs/month 12 tabs/day (90 MME/day)	Does Not Apply****
2	Benzhydrocodone/APAP 8.16 mg/325 mg	q4-6h, MAX 12 tabs/day for 14 days	168 tabs/month 12 tabs/day (120 MME/day)	Does Not Apply****
5	Celecoxib/Tramadol (Seglentis) 56 mg/44 mg	q12h, MAX 4 tabs/day	120 tabs/month 4 tabs/day (35.2 MME/day)	360 tabs/3 months 4 tabs/day (35.2 MME/day)
2	Hydrocodone/APAP tab 5/300 mg	q4-6h, MAX 8 tabs/day	240 tabs/month 8 tabs/day (40 MME/day)	720 tabs/3 months 8 tabs/day (40 MME/day)
2	Hydrocodone/APAP tab 5/325 mg	q4-6h, MAX 8 tabs/day	240 tabs/month 8 tabs/day (40 MME/day)	720 tabs/3 months 8 tabs/day (40 MME/day)
2	Hydrocodone/APAP tab 7.5/300 mg	q4-6h, MAX 6 tabs/day	180 tabs/month 6 tabs/day	540 tabs/3 months 6 tabs/day

			(45 MME/day)	(45 MME/day)
2	Hydrocodone/APAP tab 7.5/325 mg	q4-6h, MAX 6 tabs/day	180 tabs/month 6 tabs/day (45 MME/day)	540 tabs/3 months 6 tabs/day (45 MME/day)
2	Hydrocodone/APAP tab 10/300 mg	q4-6h, MAX 6 tabs/day	180 tabs/month 6 tabs/day (60 MME/day)	540 tabs/3 months 6 tabs/day (60 MME/day)
2	Hydrocodone/APAP tab 10/325 mg	q4-6h, MAX 6 tabs/day	180 tabs/month 6 tabs/day (60 MME/day)	540 tabs/3 months 6 tabs/day (60 MME/day)
1	Hydrocodone/APAP soln 7.5-325 mg/15 mL (5-217 mg/10 mL)	q4-6h, MAX 90 mL/day	2700 mL/month 90 mL/day (45 MME/day)	8100 mL/3 months 90 mL/day (45 MME/day)
1	Hydrocodone/APAP (Lortab Elixir) 10/300 mg/15 mL	q4-6h, MAX 67.5 mL/day	2025 mL/month 67.5 mL/day (45 MME/day)	6075 mL/3 months 67.5 mL/day (45 MME/day)
1	Hydrocodone/APAP soln 10-325 mg/15 mL	q4-6h, MAX 90 mL/day	2700 mL/month 90 mL/day (60 MME/day)	8100 mL/3 months 90 mL/day (60 MME/day)
4	Hydrocodone/ibuprofen tab 5/200 mg	q4-6h, MAX 5 tabs/day for 10 days	50 tabs/month 5 tabs/day (25 MME/day)	Does Not Apply****
4	Hydrocodone/ibuprofen tab 7.5/200 mg	q4-6h, MAX 5 tabs/day for 10 days	50 tabs/month 5 tabs/day (37.5 MME/day)	Does Not Apply****
4	Hydrocodone/ibuprofen tab 10/200 mg	q4-6h, MAX 5 tabs/day for 10 days	50 tabs/month 5 tabs/day (50 MME/day)	Does Not Apply****
1	Oxycodone/APAP soln 5/325 mg/5 mL	q6h, MAX 60 mL/day	1800 mL/month 60 mL/day (90 MME/day)	5400 mL/3 months 60 mL/day (90 MME/day)
1	Oxycodone/APAP soln 10/300 mg/5 mL	q6h, MAX 30 mL/day	900 mL/month 30 mL/day (90 MME/day)	2700 mL/3 months 30 mL/day (90 MME/day)
2	Oxycodone/APAP tab 2.5/300 mg	q6h, MAX 12 tabs/day	360 tabs/month 12 tabs/day (45 MME/day)	1080 tabs/3 months 12 tabs/day (45 MME/day)
2	Oxycodone/APAP tab 2.5/325 mg	q6h, MAX 12 tabs/day	360 tabs/month 12 tabs/day (45 MME/day)	1080 tabs/3 months 12 tabs/day (45 MME/day)
2	Oxycodone/APAP tab 5/300 mg	q6h, MAX 12 tabs/day	360 tabs/month 12 tabs/day (90 MME/day)	1080 tabs/3 months 12 tabs/day (90 MME/day)
2	Oxycodone/APAP tab 5/325 mg	q6h, MAX 12 tabs/day	360 tabs/month 12 tabs/day (90 MME/day)	1080 tabs/3 months 12 tabs/day (90 MME/day)
2	Oxycodone/APAP tab 7.5/300 mg	q6h, MAX 8 tabs/day	240 tabs/month 8 tabs/day (90 MME/day)	720 tabs/3 months 8 tabs/day (90 MME/day)
2	Oxycodone/APAP tab 7.5/325 mg	q6h, MAX 8 tabs/day	240 tabs/month 8 tabs/day (90 MME/day)	720 tabs/3 months 8 tabs/day (90 MME/day)

2	Oxycodone/APAP tab 10/300 mg	q6h, MAX 6 tabs/day	180 tabs/month 6 tabs/day (90 MME/day)	540 tabs/3 months 6 tabs/day (90 MME/day)
2	Oxycodone/APAP tab 10/325 mg	q6h, MAX 6 tabs/day	180 tabs/month 6 tabs/day (90 MME/day)	540 tabs/3 months 6 tabs/day (90 MME/day)
3	Oxycodone/ASA tab 4.8355/325 mg	q6h, MAX 12 tabs/day	360 tabs/month 12 tabs/day (87 MME/day)	1080 tabs/3 months 12 tabs/day (87 MME/day)
2a	Tramadol/APAP 37.5/325 mg	q4-6h, MAX 8 tabs/day for 5 days	40 tabs/month 8 tabs/day (60 MME/day)	Does Not Apply****

RATIONALE

The Centers for Disease Control and Prevention (CDC) Clinical Practice Guideline for Prescribing Opioids for Pain provides recommendations for clinicians who are providing pain care, including those prescribing opioids for outpatients aged ≥ 18 years. The recommendations do not apply to pain related to sickle cell disease or cancer or to patients receiving palliative or end-of-life care.[24] However, opioid immediate-release (IR) combination products include non-opioid components (acetaminophen, aspirin, and ibuprofen) with established maximum Food and Drug Administration (FDA)-labeled daily doses. FDA-labeled dosing allows for up to a maximum 24-hour dose of 4 grams (4000 mg) of acetaminophen, a maximum 24-hour dose of 4 grams (4000 mg) of aspirin, and a maximum 24-hour dose of 3200 mg of ibuprofen.[1-23] Limits will apply to all patients regardless of concomitant conditions (e.g., active cancer treatment, sickle cell disease, palliative care, and end-of-life care) due to the non-opioid components.

The CDC Clinical Practice Guideline for Prescribing Opioids for Pain recommends that when opioids are initiated for opioid-naïve patients, clinicians should prescribe the lowest effective dosage. If opioids are continued, clinicians should use caution when prescribing opioids at any dosage, should carefully evaluate individual benefits and risks when considering increasing dosage, and should avoid increasing dosage above levels likely to yield diminishing returns in benefits relative to risks to patients. Many patients do not experience benefit in pain or function from increasing opioid dosages to ≥ 50 morphine milliequivalents per day (MME/day) but are exposed to progressive increases in risk as dosage increases. Opioid dosages of 50-90 MME/day were associated with a minimally greater improvement in mean pain intensity compared with dosages of < 50 MME/day. Few trials evaluated opioid dosages of ≥ 90 MME/day.[24] The immediate-release opioid combination products initial quantity limits are set for a monthly quantity that does not exceed the maximum daily dose listed in labeling. Monthly quantities also correspond to ≤ 90 MME/day and contain ≤ 4 g/day acetaminophen or aspirin and ≤ 3200 mg/day ibuprofen. If the patient is requesting more than the initial quantity limit, then the claim will reject with a message indicating that quantity limits are exceeded. Quantities above the initial limit are not approved due to the potential for serious adverse effects if the FDA-labeled dosing is exceeded.

For the short-term (no more than 14 days) management of acute pain, the recommended dose of Apadaz (benzhydrocodone/acetaminophen) is 1 to 2 tablets every 4 to 6 hours as needed for pain. Dosage should not exceed 12 tablets in a 24-hour period.[4] Since benzhydrocodone/acetaminophen is only indicated for short-term use, the 1 month and 3 months limits are the same and allow for a quantity sufficient for a 14-day supply (168 tablets).

For the short-term (generally less than 10 days) management of acute pain, the recommended dose of hydrocodone bitartrate/ibuprofen is one tablet every four to six hours, as necessary. Dosages should not exceed five tablets in a 24-hour period.[8] Since hydrocodone bitartrate/ibuprofen is only indicated for short-term use, the 1 month and 3 months limits are the same and allow for a quantity sufficient for a 10-day supply (50 tablets).

For the short-term (five days or less) management of acute pain, the recommended dose of Ultracet (tramadol/acetaminophen) is 2 tablets every 4 to 6 hours as needed for pain relief, up to a maximum of 8 tablets per

day.[20] Since tramadol/acetaminophen is only indicated for short-term use, the 1 month and 3 months limits are the same and allow for a quantity sufficient for a 5-day supply (40 tablets).

For the management of acute pain in adults, the recommended dose of Seglentis (tramadol/celecoxib) is 2 tablets every 12 hours as needed for pain. Dosages should not exceed the recommended dose.[18] Therefore, the quantity limit for tramadol/celecoxib will be set at 4 tablets per day.

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External Review:	12/2004, 09/2005, 12/2006, 02/2008, 12/2008, 10/2009, 12/2010, 12/2011, 12/2012, 10/2013, 10/2014, 10/2015, 06/2016, 04/2017, 04/2018, 08/2018, 04/2019 (FYI), 04/2019, 04/2020, 02/2021 (FYI), 04/2021, 12/2021 (FYI), 04/2022, 04/2023

DURATION LIMIT WITH QUANTITY LIMIT AND POST LIMIT PRIOR AUTHORIZATION CRITERIA

DRUG CLASS **IMMEDIATE-RELEASE OPIOID ANALGESICS (BRAND AND GENERIC)***

Prior authorization applies only to patients ≤ 19 years of age.

generic name, dosage form

(codeine sulfate tablets)

(hydromorphone hydrochloride oral solution, suppositories, tablets)

(levorphanol tartrate tablets)

(meperidine hydrochloride oral solution, tablets)

(morphine sulfate oral soln, oral soln concentrate, suppositories, tablets)

(oxycodone hydrochloride capsules, oral soln, oral soln concentrate, tabs)

(oxymorphone hydrochloride tablets)

(pentazocine/naloxone tablets)

(tapentadol oral solution, tablets)

(tramadol hydrochloride tablets)

Status: Client Requested Criteria
Type: Initial Step; Duration Limit; Initial Limit; Post Limit PA ***Ref # C17539-M***

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

INITIAL STEP THERAPY

If the patient is ≤ 19 years of age and has filled a prescription for at least a 1-day supply of a drug indicating the patient is being treated for cancer or sickle cell disease within the past 365 days under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit.

If a claim is submitted with an ICD 10 diagnosis code indicating cancer, sickle cell disease, or palliative care under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit.

If the patient has an ICD 10 diagnosis code indicating cancer, sickle cell disease, or palliative care in their member health profile in the past 365 days, then the requested drug will be paid under that prescription benefit.

If a claim is submitted using a hospice patient residence code under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit.

For patients ≤ 19 years of age with no prescription claims of a cancer drug or a sickle cell disease drug in the past 365 days, no ICD 10 diagnosis code indicating cancer, sickle cell disease, or palliative care submitted with their prescription claim, no ICD 10 diagnosis code indicating cancer, sickle cell disease, or palliative care in the member health profile in the past 365 days, or no hospice patient residence code submitted with their prescription claim:
If the patient is ≤ 19 years of age and has filled a prescription for at least a 7-day supply of an opioid agent indicated for the management of pain (immediate- or extended-release) within prescription claim history in the past 90 days under a prescription benefit administered by CVS Caremark, then the initial quantity limit criteria will apply (see Column A in the Opioid Analgesics IR Quantity Limits Chart below).

If the patient is ≤ 19 years of age and does not have at least a 7-day supply of an opioid agent indicated for the management of pain (immediate- or extended-release) within prescription claim history in the past 90 days and the incoming prescription drug is being filled for more than a 3-day supply, then the claim will reject with a message indicating that the patient can receive a 3-day supply or submit a prior authorization (PA) for additional quantities. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit. If the incoming prescription drug is being filled for less than a 3-day supply, then the initial quantity limit criteria will apply (see Column A in the Opioid Analgesics IR Quantity Limits Chart below).

LIMIT CRITERIA
Neither acute pain duration limits nor quantity limits apply if the patient is ≤ 19 years of age and has a drug in claims history in the past year that indicates the patient is being treated for cancer or sickle cell disease. In addition, neither acute pain duration limits nor quantity limits will apply if a prescription claim is submitted with an ICD 10 diagnosis code indicating cancer, sickle cell disease, or palliative care, if the patient has an ICD 10 diagnosis code indicating cancer, sickle cell disease, or palliative care in their member health profile in the past 365 days, or if a prescription claim is submitted using a hospice patient residence code.

ACUTE PAIN DURATION LIMIT*:
The acute pain duration limit portion of this program applies to patients ≤ 19 years of age and are identified with potential first fills of immediate-release opioid prescriptions for the treatment of non-cancer, non-sickle cell, and non-palliative care related pain. A first fill is defined as at least a 7-day supply of an opioid agent indicated for the management of pain (immediate- or extended-release) within prescription claim history during the past 90 days.

If the patient is ≤ 19 years of age and does not have at least a 7-day supply of an opioid agent indicated for the management of pain (immediate- or extended-release) within prescription claim history in the past 90 days and the incoming prescription drug is being filled for more than a 3-day supply, then the claim will reject with a message indicating that the patient can receive a 3-day supply or submit a prior authorization (PA) for additional quantities. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit. If the incoming prescription drug is being filled for less than a 3-day supply, then the initial quantity limit criteria will apply (see Column A in the Opioid Analgesics IR Quantity Limits Chart below).

INITIAL QUANTITY LIMIT:

Morphine milligram equivalent (MME) quantity limits for immediate-release opioids provide coverage for an initial amount of a quantity that corresponds to 90 MME or less per day. Coverage is provided for up to the initial quantity limit per Column A in the Opioid Analgesics IR Quantity Limits Chart below. Prior authorization review is required to determine coverage for additional quantities above the initial limit.

**Acute Pain Duration Limit logic will apply first, followed by initial quantity limit logic.*

Opioid Analgesics IR Quantity Limits Chart

Coverage is provided without prior authorization (for patients not identified as potential first fills) for a 30-day or 90-day supply of an immediate-release opioid for a daily dose that corresponds to ≤ 90 MME/day. Coverage for a daily dose that corresponds to ≤ 200 MME/day for a 30-day or 90-day supply is provided through prior authorization when criteria for approval are met.

Accumulation does not apply if limit is coded for daily dose.

		COLUMN A	COLUMN B
Drug/Strength*	**Labeled Dosing**	**Daily Dose Initial Limit ≤ 90 MME/day**	**Daily Dose Post Limit ≤ 200 MME/day**
Codeine sulfate tab 15 mg	15 to 60 mg q4h. Max Daily Dose 360 mg.	6 tabs/day** (13.5 MME/day)	6 tabs/day** (13.5 MME/day)
Codeine sulfate tab 30 mg	15 to 60 mg q4h. Max Daily Dose 360 mg.	6 tabs/day** (27 MME/day)	6 tabs/day** (27 MME/day)
Codeine sulfate tab 60 mg	15 to 60 mg q4h. Max Daily Dose 360 mg.	6 tabs/day** (54 MME/day)	6 tabs/day** (54 MME/day)
Hydromorphone oral soln 5 mg/5 mL (1 mg/mL)	2.5 mg – 10 mg (2.5 mL to 10 mL) q3-6h	20 mL/day (80 MME/day)	50 mL/day (200 MME/day)
Hydromorphone supp 3 mg	1 supp q6-8h	4 supps/day (48 MME/day)	6 supps/day (72 MME/day)
Hydromorphone tab 2 mg	2-4 mg q4-6h	6 tabs/day (48 MME/day)	9 tabs/day (72 MME/day)
Hydromorphone tab 4 mg	2-4 mg q4-6h	5 tabs/day (80 MME/day)	7.5 tabs/day (120 MME/day)
Hydromorphone tab 8 mg	2-4 mg q4-6h	2 tabs/day (64 MME/day)	3 tabs/day (96 MME/day)
Levorphanol tab 1 mg	1-3 mg q6-8h	4 tabs/day (44 MME/day)	6 tabs/day (66 MME/day)
Levorphanol tab 2 mg	1-3 mg q6-8h	4 tabs/day (88 MME/day)	6 tabs/day (132 MME/day)

Levorphanol tab 3 mg	1-3 mg q6-8h	2 tabs/day (66 MME/day)	6 tabs/day (198 MME/day)
Meperidine oral soln 50 mg/5 mL	50-150 mg (5-15 mL) q3-4h	30 mL/day*** (30 MME/day)	30 mL/day*** (30 MME/day)
Meperidine tab 50 mg	50-150 mg q3-4h	6 tabs/day*** (30 MME/day)	6 tabs/day*** (30 MME/day)
Meperidine tab 100 mg	50-150 mg q3-4h	6 tabs/day*** (60 MME/day)	6 tabs/day*** (60 MME/day)
Morphine sulfate (conc) oral soln 20 mg/mL (100 mg/5 mL)	10-20 mg q4h	4.5 mL/day (90 MME/day)	9 mL/day (180 MME/day)
Morphine sulfate oral soln 10 mg/5 mL	10-20 mg q4h	30 mL/day (60 MME/day)	45 mL/day (90 MME/day)
Morphine sulfate oral soln 20 mg/5 mL	10-20 mg q4h	22.5 mL/day (90 MME/day)	45 mL/day (180 MME/day)
Morphine sulfate supp 5 mg	10-20 mg q4h	6 supps/day (30 MME/day)	9 supps/day (45 MME/day)
Morphine sulfate supp 10 mg	10-20 mg q4h	6 supps/day (60 MME/day)	9 supps/day (90 MME/day)
Morphine sulfate supp 20 mg	10-20 mg q4h	4 supps/day (80 MME/day)	9 supps/day (180 MME/day)
Morphine sulfate supp 30 mg	10-20 mg q4h	3 supps/day (90 MME/day)	6 supps/day (180 MME/day)
Morphine sulfate tab 15 mg	15-30 mg q4h	6 tabs/day (90 MME/day)	9 tabs/day (135 MME/day)
Morphine sulfate tab 30 mg	15-30 mg q4h	3 tabs/day (90 MME/day)	6 tabs/day (180 MME/day)
Oxycodone cap 5 mg	5-15 mg q4-6h	6 caps/day (45 MME/day)	9 caps/day (67.5 MME/day)
Oxycodone oral concentrate 100 mg/5 mL (20 mg/mL)	5-15 mg q4-6h	3 mL/day (90 MME/day)	6 mL/day (180 MME/day)
Oxycodone soln 5 mg/5 mL	5-15 mg q4-6h	30 mL/day (45 MME/day)	90 mL/day (135 MME/day)
Oxaydo 5 mg	5-15 mg q4-6h	6 tabs/day (45 MME/day)	9 tabs/day (67.5 MME/day)
Oxaydo 7.5 mg	5-15 mg q4-6h	6 tabs/day (67.5 MME/day)	9 tabs/day (101.25 MME/day)
Oxycodone tab 5 mg	5-15 mg q4-6h	6 tabs/day (45 MME/day)	9 tabs/day (67.5 MME/day)
Oxycodone tab 10 mg	5-15 mg q4-6h	6 tabs/day (90 MME/day)	9 tabs/day (135 MME/day)
Oxycodone tab 15 mg	5-15 mg q4-6h	4 tabs/day (90 MME/day)	6 tabs/day (135 MME/day)
Oxycodone tab 20 mg	5-15 mg q4-6h	3 tabs/day (90 MME/day)	6 tabs/day (180 MME/day)
Oxycodone tab 30 mg	5-15 mg q4-6h	2 tabs/day (90 MME/day)	4 tabs/day (180 MME/day)
Oxymorphone tab 5 mg	10-20 mg q4-6h	6 tabs/day (90 MME/day)	12 tabs/day (180 MME/day)
Oxymorphone tab 10 mg	10-20 mg q4-6h	3 tabs/day (90 MME/day)	6 tabs/day (180 MME/day)
Pentazocine/naloxone 50/0.5 mg	1-2 tabs q3-4h. Total daily dose should not exceed 12 tablets.	4 tabs/day (74 MME/day)	10 tabs/day (185 MME/day)
RoxyBond 5 mg	5-15 mg q4-6h	6 tabs/day	9 tabs/day

		(45 MME/day)	(67.5 MME/day)
RoxyBond 15 mg	5-15 mg q4-6h	4 tabs/day (90 MME/day)	6 tabs/day (135 MME/day)
RoxyBond 30 mg	5-15 mg q4-6h	2 tabs/day (90 MME/day)	4 tabs/day (180 MME/day)
Tapentadol oral soln 20 mg/mL	50 mg (2.5 mL) to 100 mg (5 mL) every 4 to 6 hours. Max daily dose is 700 mg on the first day and 600 mg on subsequent days.	10 mL/day (80 MME/day)	23.33 mL/day (186.7 MME/day)
Tapentadol tab 50 mg	50 mg, 75 mg, or 100 mg every 4 to 6 hours. Max daily dose is 700 mg on the first day and 600 mg on subsequent days.	4 tabs/day (80 MME/day)	8 tabs/day (160 MME/day)
Tapentadol tab 75 mg	50 mg, 75 mg, or 100 mg every 4 to 6 hours. Max daily dose is 700 mg on the first day and 600 mg on subsequent days.	3 tabs/day (90 MME/day)	6 tabs/day (180 MME/day)
Tapentadol tab 100 mg	50 mg, 75 mg, or 100 mg every 4 to 6 hours. Max daily dose is 700 mg on the first day and 600 mg on subsequent days.	2 tabs/day (80 MME/day)	4 tabs/day (160 MME/day)
Tramadol 50 mg	50-100 mg q4-6h, MAX = 400 mg/day	6 tabs/day (30 MME/day)	8 tabs/day (40 MME/day)
Tramadol 100 mg	50-100 mg q4-6h, MAX = 400 mg/day	3 tabs/day (30 MME/day)	4 tabs/day (40 MME/day)

**The limit criteria apply to both brand and generic, if available.*
*** The limit for codeine is set reflective of its questionable role in chronic or moderate to severe pain management as compared to other opioid medications. Therefore, the post limit quantity will be set as the same as the initial quantity limit.*
**** Although meperidine is commonly used for acute pain relief, use of this drug as first-line opiate therapy is discouraged because of central excitatory toxicity of the metabolite (normeperidine). Therefore, the post limit quantity will be set as the same as the initial quantity limit.*

REFERENCES

1. CareFirst Prior Authorization Approval Policy.

Written by: UM Development (CF/DS)
Date Written: 11/2019
Revised:
Reviewed: Medical Affairs: (DNC) 02/2020

DURATION LIMIT CRITERIA

DRUG CLASS **ACETAMINOPHEN/ASPIRIN/IBUPROFEN CONTAINING OPIOID ANALGESICS (BRAND AND GENERIC)**

Prior authorization applies only to patients ≤ 19 years of age.

(generic)*

(acetaminophen and benzhydrocodone)

(acetaminophen and codeine)

(acetaminophen and hydrocodone)

(acetaminophen and oxycodone)

(acetaminophen and tramadol)

(acetaminophen, caffeine, and dihydrocodeine)

(aspirin and oxycodone)

(aspirin, caffeine, and dihydrocodeine)

(ibuprofen and hydrocodone)

(ibuprofen and oxycodone)

Status: Client Requested Criteria**
Type: Initial Step; Duration Limit; Post Limit Criteria ***Ref # C17540-E***

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*
***C17540-E will be used in combination with Opioids IR APAP-ASA-IBU Combo Products Limit CareFirst C17534-H. The Opioids IR APAP-ASA-IBU Combo Products Limit CareFirst C17534-H will be coded separately.*

INITIAL STEP THERAPY

If the patient is ≤ 19 years of age and has filled a prescription for at least a 1-day supply of a drug indicating the patient is being treated for cancer or sickle cell disease within the past 365 days under a prescription benefit administered by CVS Caremark, then the claim will proceed to the subsequent initial quantity limit criteria Opioids IR APAP-ASA-IBU Combo Products Limit CareFirst C17534-H.

If a claim is submitted with an ICD 10 diagnosis code indicating cancer, sickle cell disease, or palliative care under a prescription benefit administered by CVS Caremark, then the claim will proceed to the subsequent initial quantity limit criteria Opioids IR APAP-ASA-IBU Combo Products Limit CareFirst C17534-H.

If the patient has an ICD 10 diagnosis code indicating cancer, sickle cell disease, or palliative care in their member health profile in the past 365 days, then the claim will proceed to the subsequent initial quantity limit criteria Opioids IR APAP-ASA-IBU Combo Products Limit CareFirst C17534-H.

If a claim is submitted using a hospice patient residence code under a prescription benefit administered by CVS Caremark, then the claim will proceed to the subsequent initial quantity limit criteria Opioids IR APAP-ASA-IBU Combo Products Limit CareFirst C17534-H.

For patients ≤ 19 years of age with no prescription claims of a cancer drug or a sickle cell disease drug in the past 365 days, no ICD 10 diagnosis code indicating cancer, sickle cell disease, or palliative care submitted with their prescription claim, no ICD 10 diagnosis code indicating cancer, sickle cell disease, or palliative care in the member health profile in the past 365 days, or no hospice patient residence code submitted with their prescription claim:
If the patient is ≤ 19 years of age and has filled a prescription for at least a 7-day supply of an opioid agent indicated for the management of pain (immediate- or extended-release) within prescription claim history in the past 90 days under a prescription benefit administered by CVS Caremark, then the claim will proceed to the subsequent initial quantity limit criteria Opioids IR APAP-ASA-IBU Combo Products Limit CareFirst C17534-H.

If the patient is ≤ 19 years of age and does not have at least a 7-day supply of an opioid agent indicated for the management of pain (immediate- or extended-release) within prescription claim history in the past 90 days, and the incoming prescription drug is being filled for more than a 3-day supply, then the claim will reject with a message indicating that the patient can receive a 3-day supply or submit a prior authorization (PA). The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit. The subsequent initial quantity limits from the Opioids IR APAP-ASA-IBU Combo Products Limit CareFirst C17534-H would then apply. If the incoming prescription drug is being filled for less than a 3-day supply, then the claim will proceed to the subsequent initial quantity limit criteria Opioids IR APAP-ASA-IBU Combo Products Limit CareFirst C17534-H.

LIMIT CRITERIA (DAY SUPPLY)**
Acute pain duration limits do not apply if the patient is ≤ 19 years of age and has a drug in claims history in the past year that indicates the patient is being treated for cancer or sickle cell disease. In addition, acute pain duration limits will not apply if a prescription claim is submitted with an ICD 10 diagnosis code indicating cancer, sickle cell disease, or palliative care, if the patient has an ICD 10 diagnosis code indicating cancer, sickle cell disease, or palliative care in their member health profile in the past 365 days, or if a prescription claim is submitted using a hospice patient residence code. The subsequent initial quantity limits from the Opioids IR APAP-ASA-IBU Combo Products Limit CareFirst C17534-H would then apply to all patients regardless of concomitant conditions (e.g., active cancer treatment, palliative care, and end-of-life care) due to the non-opioid components.

If the patient is ≤ 19 years of age and has filled a prescription for at least a 7-day supply of an opioid agent indicated for the management of pain (immediate- or extended-release) within prescription claim history in the past 90 days under a prescription benefit administered by CVS Caremark, then the claim will proceed to the subsequent initial quantity limit criteria Opioids IR APAP-ASA-IBU Combo Products Limit CareFirst C17534-H.

If the patient is ≤ 19 years of age and does not have at least a 7-day supply of an opioid agent indicated for the management of pain (immediate- or extended-release) within prescription claim history in the past 90 days, and the incoming prescription drug is being filled for more than a 3-day supply, then the claim will reject with a message indicating that the patient can receive a 3-day supply or submit a prior authorization (PA) for additional days supply. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit. The subsequent initial quantity limits from the Opioids IR APAP-ASA-IBU Combo Products Limit CareFirst C17534-H would then apply. If the incoming prescription drug is being filled for less than a 3-day supply, then the claim will proceed to the subsequent initial quantity limit criteria Opioids IR APAP-ASA-IBU Combo Products Limit CareFirst C17534-H.

REFERENCES

1. CareFirst Prior Authorization Approval Policy.

Written by: UM Development (CF/DS)

Date Written: 11/2019
Revised:
Reviewed: Medical Affairs: (DNC) 02/2020

***C17540-E will be used in combination with Opioids IR APAP-ASA-IBU Combo Products Limit C17534-H. The Opioids IR APAP-ASA-IBU Combo Products Limit C17534-H will be coded separately.*

DURATION LIMIT WITH QUANTITY LIMIT AND POST LIMIT PRIOR AUTHORIZATION CRITERIA

DRUG CLASS **IMMEDIATE-RELEASE OPIOID ANALGESICS (BRAND AND GENERIC)***

generic name, dosage form

(codeine sulfate tablets)

(hydromorphone hydrochloride oral solution, suppositories, tablets)

(levorphanol tartrate tablets)

(meperidine hydrochloride oral solution, tablets)

(morphine sulfate oral soln, oral soln concentrate, suppositories, tablets)

(oxycodone hydrochloride capsules, oral soln, oral soln concentrate, tabs)

(oxymorphone hydrochloride tablets)

(pentazocine/naloxone tablets)

(tapentadol oral solution, tablets)

(tramadol hydrochloride tablets)

Status: Client Requested Criteria
Type: Initial Step; Duration Limit; Initial Limit; Post Limit PA ***Ref # C17533-M***

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

INITIAL STEP THERAPY
If the patient has filled a prescription for at least a 1-day supply of a drug indicating the patient is being treated for cancer or sickle cell disease within the past 365 days under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit.

If a claim is submitted with an ICD 10 diagnosis code indicating cancer, sickle cell disease, or palliative care under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit.

If the patient has an ICD 10 diagnosis code indicating cancer, sickle cell disease, or palliative care in their member health profile in the past 365 days, then the requested drug will be paid under that prescription benefit.

If a claim is submitted using a hospice patient residence code under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit.

For patients with no prescription claims of a cancer drug or a sickle cell disease drug in the past 365 days, no ICD 10 diagnosis code indicating cancer, sickle cell disease, or palliative care submitted with their prescription claim, no ICD 10 diagnosis code indicating cancer, sickle cell disease, or palliative care in the member health profile in the past 365 days, or no hospice patient residence code submitted with their prescription claim:
If the patient has filled a prescription for at least a 7-day supply of an opioid agent indicated for the management of pain (immediate- or extended-release) within prescription claim history in the past 90 days under a prescription benefit administered by CVS Caremark, then the initial quantity limit criteria will apply (see Column A in the Opioid Analgesics IR Quantity Limits Chart below).

If the patient does not have at least a 7-day supply of an opioid agent indicated for the management of pain (immediate- or extended-release) within prescription claim history in the past 90 days (i.e., this is the patient's first fill of an opioid) and the incoming prescription drug is being filled for more than a 7-day supply, then the claim will reject with a message indicating that the patient can receive a 7-day supply or submit a prior authorization (PA) for additional quantities. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit. If the incoming prescription drug is being filled for less than a 7-day supply, then the initial quantity limit criteria will apply (see Column A in the Opioid Analgesics IR Quantity Limits Chart below).

LIMIT CRITERIA*
Neither acute pain duration limits nor quantity limits apply if the patient has a drug in claims history in the past year that indicates the patient is being treated for cancer or sickle cell disease. In addition, neither acute pain duration limits nor quantity limits will apply if a prescription claim is submitted with an ICD 10 diagnosis code indicating cancer, sickle cell disease, or palliative care, if the patient has an ICD 10 diagnosis code indicating cancer, sickle cell disease, or palliative care in their member health profile in the past 365 days, or if a prescription claim is submitted using a hospice patient residence code.

ACUTE PAIN DURATION LIMIT:
The acute pain duration limit portion of this program applies to patients identified with potential first fills of immediate-release opioid prescriptions for the treatment of non-cancer and non-sickle cell related pain. A first fill is defined as at least a 7-day supply of an opioid agent indicated for the management of pain (immediate- or extended-release) within prescription claim history during the past 90 days.

If the patient does not have at least a 7-day supply of an opioid agent indicated for the management of pain (immediate- or extended-release) within prescription claim history in the past 90 days (i.e., this is the patient's first fill of an opioid) and the incoming prescription drug is being filled for more than a 7-day supply, then the claim will reject with a message indicating that the patient can receive a 7-day supply or submit a prior authorization (PA) for additional quantities. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit. If the incoming prescription drug is being filled for less than a 7-day supply, then the initial quantity limit criteria will apply (see Column A in the Opioid Analgesics IR Quantity Limits Chart below).

INITIAL QUANTITY LIMIT:
Morphine milligram equivalent (MME) quantity limits for immediate-release opioids provide coverage for an initial amount of a quantity that corresponds to 90 MME or less per day. Coverage is provided for up to the initial quantity limit per Column A in the Opioid Analgesics IR Quantity Limits Chart below. Prior authorization review is required to determine coverage for additional quantities above the initial limit.

**Acute Pain Duration Limit logic will apply first, followed by initial quantity limit logic.*

Opioid Analgesics IR Quantity Limits Chart
Coverage is provided without prior authorization (for patients not identified as potential first fills) for a 30-day or 90-day supply of an immediate-release opioid for a daily dose that corresponds to ≤ 90 MME/day. Coverage for a daily dose that corresponds to ≤ 200 MME/day for a 30-day or 90-day supply is provided through prior authorization when criteria for approval are met. **Accumulation does not apply if limit is coded for daily dose.**

		COLUMN A	COLUMN B
Drug/Strength*	**Labeled Dosing**	**Daily Dose Initial Limit ≤ 90 MME/day**	**Daily Dose Post Limit ≤ 200 MME/day**
Codeine sulfate tab 15 mg	15 to 60 mg q4h. Max Daily Dose 360 mg.	6 tabs/day** (13.5 MME/day)	6 tabs/day** (13.5 MME/day)
Codeine sulfate tab 30 mg	15 to 60 mg q4h. Max Daily Dose 360 mg.	6 tabs/day** (27 MME/day)	6 tabs/day** (27 MME/day)
Codeine sulfate tab 60 mg	15 to 60 mg q4h. Max Daily Dose 360 mg.	6 tabs/day** (54 MME/day)	6 tabs/day** (54 MME/day)
Hydromorphone oral soln 5 mg/5 mL (1 mg/mL)	2.5 mg – 10 mg (2.5 mL to 10 mL) q3-6h	20 mL/day (80 MME/day)	50 mL/day (200 MME/day)
Hydromorphone supp 3 mg	1 supp q6-8h	4 supps/day (48 MME/day)	6 supps/day (72 MME/day)
Hydromorphone tab 2 mg	2-4 mg q4-6h	6 tabs/day (48 MME/day)	9 tabs/day (72 MME/day)
Hydromorphone tab 4 mg	2-4 mg q4-6h	5 tabs/day (80 MME/day)	7.5 tabs/day (120 MME/day)
Hydromorphone tab 8 mg	2-4 mg q4-6h	2 tabs/day (64 MME/day)	3 tabs/day (96 MME/day)
Levorphanol tab 1 mg	1-3 mg q6-8h	4 tabs/day (44 MME/day)	6 tabs/day (66 MME/day)
Levorphanol tab 2 mg	1-3 mg q6-8h	4 tabs/day (88 MME/day)	6 tabs/day (132 MME/day)
Levorphanol tab 3 mg	1-3 mg q6-8h	2 tabs/day (66 MME/day)	6 tabs/day (198 MME/day)
Meperidine oral soln 50 mg/5 mL	50-150 mg (5-15 mL) q3-4h	30 mL/day*** (30 MME/day)	30 mL/day*** (30 MME/day)
Meperidine tab 50 mg	50-150 mg q3-4h	6 tabs/day*** (30 MME/day)	6 tabs/day*** (30 MME/day)
Meperidine tab 100 mg	50-150 mg q3-4h	6 tabs/day*** (60 MME/day)	6 tabs/day*** (60 MME/day)
Morphine sulfate (conc) oral soln 20 mg/mL (100 mg/5 mL)	10-20 mg q4h	4.5 mL/day (90 MME/day)	9 mL/day (180 MME/day)
Morphine sulfate oral soln 10 mg/5 mL	10-20 mg q4h	30 mL/day (60 MME/day)	45 mL/day (90 MME/day)
Morphine sulfate oral soln 20 mg/5 mL	10-20 mg q4h	22.5 mL/day (90 MME/day)	45 mL/day (180 MME/day)
Morphine sulfate supp 5 mg	10-20 mg q4h	6 supps/day (30 MME/day)	9 supps/day (45 MME/day)
Morphine sulfate supp 10 mg	10-20 mg q4h	6 supps/day (60 MME/day)	9 supps/day (90 MME/day)
Morphine sulfate supp 20 mg	10-20 mg q4h	4 supps/day (80 MME/day)	9 supps/day (180 MME/day)
Morphine sulfate supp 30 mg	10-20 mg q4h	3 supps/day (90 MME/day)	6 supps/day (180 MME/day)
Morphine sulfate tab 15 mg	15-30 mg q4h	6 tabs/day (90 MME/day)	9 tabs/day (135 MME/day)
Morphine sulfate tab 30 mg	15-30 mg q4h	3 tabs/day (90 MME/day)	6 tabs/day (180 MME/day)
Oxycodone cap 5 mg	5-15 mg q4-6h	6 caps/day (45 MME/day)	9 caps/day (67.5 MME/day)
Oxycodone oral concentrate 100 mg/5 mL (20 mg/mL)	5-15 mg q4-6h	3 mL/day (90 MME/day)	6 mL/day (180 MME/day)
Oxycodone soln 5 mg/5 mL	5-15 mg q4-6h	30 mL/day (45 MME/day)	90 mL/day (135 MME/day)
Oxaydo 5 mg	5-15 mg q4-6h	6 tabs/day (45 MME/day)	9 tabs/day (67.5 MME/day)
Oxaydo 7.5 mg	5-15 mg q4-6h	6 tabs/day	9 tabs/day

		(67.5 MME/day)	(101.25 MME/day)
Oxycodone tab 5 mg	5-15 mg q4-6h	6 tabs/day (45 MME/day)	9 tabs/day (67.5 MME/day)
Oxycodone tab 10 mg	5-15 mg q4-6h	6 tabs/day (90 MME/day)	9 tabs/day (135 MME/day)
Oxycodone tab 15 mg	5-15 mg q4-6h	4 tabs/day (90 MME/day)	6 tabs/day (135 MME/day)
Oxycodone tab 20 mg	5-15 mg q4-6h	3 tabs/day (90 MME/day)	6 tabs/day (180 MME/day)
Oxycodone tab 30 mg	5-15 mg q4-6h	2 tabs/day (90 MME/day)	4 tabs/day (180 MME/day)
Oxymorphone tab 5 mg	10-20 mg q4-6h	6 tabs/day (90 MME/day)	12 tabs/day (180 MME/day)
Oxymorphone tab 10 mg	10-20 mg q4-6h	3 tabs/day (90 MME/day)	6 tabs/day (180 MME/day)
Pentazocine/naloxone 50/0.5 mg	1-2 tabs q3-4h. Total daily dose should not exceed 12 tablets.	4 tabs/day (74 MME/day)	10 tabs/day (185 MME/day)
RoxyBond 5 mg	5-15 mg q4-6h	6 tabs/day (45 MME/day)	9 tabs/day (67.5 MME/day)
RoxyBond 15 mg	5-15 mg q4-6h	4 tabs/day (90 MME/day)	6 tabs/day (135 MME/day)
RoxyBond 30 mg	5-15 mg q4-6h	2 tabs/day (90 MME/day)	4 tabs/day (180 MME/day)
Tapentadol oral soln 20 mg/mL	50 mg (2.5 mL) to 100 mg (5 mL) every 4 to 6 hours. Max daily dose is 700 mg on the first day and 600 mg on subsequent days.	10 mL/day (80 MME/day)	23.33 mL/day (186.7 MME/day)
Tapentadol tab 50 mg	50 mg, 75 mg, or 100 mg every 4 to 6 hours. Max daily dose is 700 mg on the first day and 600 mg on subsequent days.	4 tabs/day (80 MME/day)	8 tabs/day (160 MME/day)
Tapentadol tab 75 mg	50 mg, 75 mg, or 100 mg every 4 to 6 hours. Max daily dose is 700 mg on the first day and 600 mg on subsequent days.	3 tabs/day (90 MME/day)	6 tabs/day (180 MME/day)
Tapentadol tab 100 mg	50 mg, 75 mg, or 100 mg every 4 to 6 hours. Max daily dose is 700 mg on the first day and 600 mg on subsequent days.	2 tabs/day (80 MME/day)	4 tabs/day (160 MME/day)
Tramadol 50 mg	50-100 mg q4-6h, MAX = 400 mg/day	6 tabs/day (30 MME/day)	8 tabs/day (40 MME/day)
Tramadol 100 mg	50-100 mg q4-6h, MAX = 400 mg/day	3 tabs/day (30 MME/day)	4 tabs/day (40 MME/day)

**The limit criteria apply to both brand and generic, if available.*
*** The limit for codeine is set reflective of its questionable role in chronic or moderate to severe pain management as compared to other opioid medications. Therefore, the post limit quantity will be set as the same as the initial quantity limit.*
**** Although meperidine is commonly used for acute pain relief, use of this drug as first-line opiate therapy is discouraged because of central excitatory toxicity of the metabolite (normeperidine). Therefore, the post limit quantity will be set as the same as the initial quantity limit.*

REFERENCES

1. CareFirst Prior Authorization Approval Policy.

Written by: UM Development (CF/DS)
Date Written: 11/2019
Revised:
Reviewed: Medical Affairs: (DNC) 02/2020

DURATION LIMIT CRITERIA

DRUG CLASS	**ACETAMINOPHEN/ASPIRIN/IBUPROFEN CONTAINING OPIOID ANALGESICS (BRAND AND GENERIC)**
(generic)*	**(acetaminophen and benzhydrocodone)** **(acetaminophen and codeine)** **(acetaminophen and hydrocodone)** **(acetaminophen and oxycodone)** **(acetaminophen and tramadol)** **(acetaminophen, caffeine, and dihydrocodeine)** **(aspirin and oxycodone)** **(aspirin, caffeine, and dihydrocodeine)** **(ibuprofen and hydrocodone)** **(ibuprofen and oxycodone)**
Status: Client Requested Criteria	
Type: Initial Step; Duration Limit; Post Limit Criteria	***Ref # C17535-E***

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*
***C17535-E is used in combination with Opioids IR APAP-ASA-IBU Combo Products Limit CareFirst C17534-H. The Opioids IR APAP-ASA-IBU Combo Products Limit CareFirst C17534-H will be coded separately.*

INITIAL STEP THERAPY
If the patient has filled a prescription for at least a 1-day supply of a drug indicating the patient is being treated for cancer or sickle cell disease within the past 365 days under a prescription benefit administered by CVS Caremark, then the claim will proceed to the subsequent initial quantity limit criteria C17534-H.

If a claim is submitted with an ICD 10 diagnosis code indicating cancer, sickle cell disease, or palliative care under a prescription benefit administered by CVS Caremark, then the claim will proceed to the subsequent initial quantity limit criteria C17534-H.

If the patient has an ICD 10 diagnosis code indicating cancer, sickle cell disease, or palliative care in their member health profile in the past 365 days, then the claim will proceed to the subsequent initial quantity limit criteria C17534-H.

If a claim is submitted using a hospice patient residence code under a prescription benefit administered by CVS Caremark, then the claim will proceed to the subsequent initial quantity limit criteria C17534-H.

For patients with no prescription claims of a cancer drug or a sickle cell disease drug in the past 365 days, no ICD 10 diagnosis code indicating cancer, sickle cell disease, or palliative care submitted with their prescription claim, no ICD 10 diagnosis code indicating cancer, sickle cell disease, or palliative care in the member health profile in the past 365 days, or no hospice patient residence code submitted with their prescription claim:
If the patient has filled a prescription for at least a 7-day supply of an opioid agent indicated for the management of pain (immediate- or extended-release) within prescription claim history in the past 90 days under a prescription benefit administered by CVS Caremark, then the claim will proceed to the subsequent initial quantity limit criteria C17534-H.

If the patient does not have at least a 7-day supply of an opioid agent indicated for the management of pain (immediate- or extended-release) within prescription claim history in the past 90 days (i.e., this is the patient's first fill of an opioid), and the incoming prescription drug is being filled for more than a 7-day supply, then the claim will reject with a message indicating that the patient can receive a 7-day supply or submit a prior authorization (PA). The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit. When using this program in combination with Opioids IR APAP-ASA-IBU Combo Products Limit CareFirst C17534-H, then subsequent initial quantity limits would apply. If the incoming prescription drug is being filled for less than a 7-day supply, then the claim will proceed to the subsequent initial quantity limit criteria C17534-H.

LIMIT CRITERIA (DAY SUPPLY)**
Acute pain duration limits do not apply if the patient has a drug in claims history in the past year that indicates the patient is being treated for cancer or sickle cell disease. In addition, acute pain duration limits will not apply if a prescription claim is submitted with an ICD 10 diagnosis code indicating cancer, sickle cell disease, or palliative care, if the patient has an ICD 10 diagnosis code indicating cancer, sickle cell disease, or palliative care in their member health profile in the past 365 days, or if a prescription claim is submitted using a hospice patient residence code. When using this program in combination with Opioids IR APAP-ASA-IBU Combo Products Limit CareFirst C17534-H, the claim will proceed to the subsequent initial quantity limit criteria C17534-H.

If the patient has filled a prescription for at least a 7-day supply of an opioid agent indicated for the management of pain (immediate- or extended-release) within prescription claim history in the past 90 days under a prescription benefit administered by CVS Caremark, then the claim will proceed to the subsequent initial quantity limit criteria C17534-H.

If the patient does not have at least a 7-day supply of an opioid agent indicated for the management of pain (immediate- or extended-release) within prescription claim history in the past 90 days (i.e., this is the patient's first fill of an opioid), and the incoming prescription drug is being filled for more than a 7-day supply, then the claim will reject with a message indicating that the patient can receive a 7-day supply or submit a prior authorization (PA) for additional days supply. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit. When using this program in combination with Opioids IR APAP-ASA-IBU Combo Products Limit CareFirst C17534-H, then subsequent initial quantity limits would apply. If the incoming prescription drug is being filled for less than a 7-day supply, then the claim will proceed to the subsequent initial quantity limit criteria C17534-H.

***C17535-E may be used as a stand-alone criteria OR in combination with Opioids IR APAP-ASA-IBU Combo Products Limit CareFirst C17534-H. The Opioids IR APAP-ASA-IBU Combo Products Limit CareFirst C17534-H will be coded separately.*

REFERENCES

1. CareFirst Prior Authorization Approval Policy.

Written by: UM Development (CF/DS)
Date Written: 11/2019
Revised:
Reviewed: Medical Affairs: (DNC) 02/2020

QUANTITY LIMIT CRITERIA

DRUG CLASS	**ACETAMINOPHEN/ASPIRIN/IBUPROFEN CONTAINING OPIOID ANALGESICS**
(generic)*	**(acetaminophen and benzhydrocodone)** **(acetaminophen and codeine)** **(acetaminophen and hydrocodone)** **(acetaminophen and oxycodone)** **(acetaminophen and tramadol)** **(acetaminophen, caffeine, and dihydrocodeine)** **(aspirin and oxycodone)** **(aspirin, caffeine, and dihydrocodeine)** **(ibuprofen and hydrocodone)** **(ibuprofen and oxycodone)**

Status: Client Requested Criteria**

Type: Quantity Limit ***Ref # C17534-H***

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

***C17534-H is used in combination with Opioids IR APAP-ASA-IBU Combo Products – Acute Pain Duration Limit CareFirst C17535-E. The Opioids IR APAP-ASA-IBU Combo Products – Acute Pain Duration Limit CareFirst C17535-E will be coded separately.*

Opioid Analgesics IR Combo Products Quantity Limits Chart		
Coverage is provided without prior authorization for a 30-day or 90-day supply of an immediate-release combination product opioid for a daily quantity that does not exceed the maximum daily dose listed in product labeling. Quantities also do not exceed 90 MME/day (unless maximum FDA-labeled strength/dose/frequency exceeds 90 MME/day), 4 g/day of acetaminophen or aspirin, or 3200 mg/day of ibuprofen. If the patient is requesting more than the initial quantity limit, then the claim will reject with a message indicating that quantity limits are exceeded. **Accumulation does not apply if limit is coded for daily dose.**		
Drug/Strength	**Labeled Dosing**	**Daily Dose Initial Limit ≤ 90 MME/day* and ≤ 4 g APAP or ASA and**

CVS caremark™

		≤ 3200 mg IBU
APAP/codeine soln 120-12 mg/5 mL	15 mL q4h, MAX 360 mg codeine/day	90 mL/day (32.4 MME/day)
APAP/codeine susp 120-12 mg/5 mL	15 mL q4h, MAX 360 mg codeine/day	90 mL/day (32.4 MME/day)
APAP/codeine tab 300/15 mg	15-60 mg codeine q4h, MAX 360 mg codeine/day	13.33 tabs/day (30 MME/day)
APAP/codeine tab 300/30 mg	15-60 mg codeine q4h, MAX 360 mg codeine/day	12 tabs/day (54 MME/day)
APAP/codeine tab 300/60 mg	15-60 mg codeine q4h, MAX 360 mg codeine/day	6 tabs/day (54 MME/day)
APAP/caffeine/dihydrocodeine cap 320.5/30/16 mg	2 caps q4h, MAX 10 caps/day	10 caps/day (40 MME/day)
APAP/caffeine/dihydrocodeine tab 325/30/16 mg	2 tabs q4h, MAX 10 tabs/day	10 tabs/day (40 MME/day)
ASA/caffeine/dihydrocodeine cap 356.4/30/16 mg	2 caps q4h, MAX 10 caps/day	10 caps/day (40 MME/day)
Benzhydrocodone/APAP 4.08 mg/325 mg	1-2 tabs q4-6h, MAX 12 tabs/day	12 tabs/day (60 MME/day)
Benzhydrocodone/APAP 6.12 mg/325 mg	1-2 tabs q4-6h, MAX 12 tabs/day	12 tabs/day (90 MME/day)
Benzhydrocodone/APAP 8.16 mg/325 mg	1-2 tabs q4-6h, MAX 12 tabs/day	12 tabs/day (120 MME/day)
Hydrocodone/APAP tab 2.5/325 mg	1-2 tabs q 4-6h, MAX 12 tabs/day	12 tabs/day (30 MME/day)
Hydrocodone/APAP tab 5/300 mg	1-2 tabs q 4-6h, MAX 8 tabs/day	8 tabs/day (40 MME/day)
Hydrocodone/APAP tab 5/325 mg	1-2 tabs q 4-6h, MAX 8 tabs/day	8 tabs/day (40 MME/day)
Hydrocodone/APAP tab 7.5/300 mg	1 tab q4-6h, MAX 6 tabs/day	6 tabs/day (45 MME/day)
Hydrocodone/APAP tab 7.5/325 mg	1 tab q4-6h, MAX 6 tabs/day	6 tabs/day (45 MME/day)
Hydrocodone/APAP tab 10/300 mg	1 tab q4-6h, MAX 6 tabs/day	6 tabs/day (60 MME/day)
Hydrocodone/APAP tab 10/325 mg	1 tab q4-6h, MAX 6 tabs/day	6 tabs/day (60 MME/day)
Hydrocodone/APAP soln 7.5-325 mg/15 mL (5-217 mg/10 mL)	15 mL q4-6h, MAX 90 mL/day	90 mL/day (45 MME/day)
Hydrocodone/APAP elixir 10/300 mg/15 mL	11.25 mL q4-6h, MAX 67.5 mL/day	67.5 mL/day (45 MME/day)
Hydrocodone/APAP soln 10-325 mg/15 mL	15 mL q4-6h, MAX 90 mL/day	90 mL/day (60 MME/day)
Hydrocodone/ibuprofen tab 2.5/200 mg	1 tab q4-6h, MAX 5 tabs/day	5 tabs/day (12.5 MME/day)
Hydrocodone/ibuprofen tab 5/200 mg	1 tab q4-6h, MAX 5 tabs/day	5 tabs/day (25 MME/day)
Hydrocodone/ibuprofen tab 7.5/200 mg	1 tab q4-6h, MAX 5 tabs/day	5 tabs/day (37.5 MME/day)
Hydrocodone/ibuprofen tab 10/200 mg	1 tab q4-6h, MAX 5 tabs/day	5 tabs/day (50 MME/day)
Oxycodone/APAP soln 5/325 mg/5 mL	5 mL q6h, MAX 60 mL/day	60 mL/day (90 MME/day)

Oxycodone/APAP tab 2.5/300 mg	1-2 tabs q6h, MAX 12 tabs/day	12 tabs/day (45 MME/day)
Oxycodone/APAP tab 2.5/325 mg	1-2 tabs q6h, MAX 12 tabs/day	12 tabs/day (45 MME/day)
Oxycodone/APAP tab 5/300 mg	1 tab q6h, MAX 12 tabs/day	12 tabs/day (90 MME/day)
Oxycodone/APAP tab 5/325 mg	1 tab q6h, MAX 12 tabs/day	12 tabs/day (90 MME/day)
Oxycodone/APAP tab 7.5/300 mg	1 cap q6h, MAX 8 tabs/day	8 tabs/day (90 MME/day)
Oxycodone/APAP tab 7.5/325 mg	1 tab q6h, MAX 8 tabs/day	8 tabs/day (90 MME/day)
Oxycodone/APAP tab 10/300 mg	1 tab q6h, MAX 6 tabs/day	6 tabs/day (90 MME/day)
Oxycodone/APAP tab 10/325 mg	1 tab q6h, MAX 6 tabs/day	6 tabs/day (90 MME/day)
Oxycodone/ASA tab 4.8355/325 mg	1 tab q6h, MAX 12 tabs/day	12 tabs/day (87 MME/day)
Oxycodone/ibuprofen tab 5/400 mg	1 tab q6h, MAX 4 tabs/day	4 tabs/day (30 MME/day)
Tramadol/APAP 37.5/325 mg	2 tabs q4-6h, MAX 8 tabs/day. Use for 5 days only.	8 tabs/day (30 MME/day)

**Unless maximum FDA-labeled strength/dose/frequency exceeds 90 MME/day.*

REFERENCES

1. CareFirst Prior Authorization Approval Policy.

Written by: UM Development (CF/DS)
Date Written: 11/2019
Revised:
Reviewed: Medical Affairs: (DNC) 02/2020

PRIOR AUTHORIZATION CRITERIA

BRAND NAME*
(generic)

ONGENTYS
(opicapone)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization ***Ref # 5464-A***

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Ongentys is indicated as adjunctive treatment to levodopa/carbidopa in patients with Parkinson's disease (PD) experiencing "off" episodes.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed as adjunctive treatment to levodopa/carbidopa in a patient with Parkinson's disease (PD) experiencing "off" episodes

AND

- The patient has experienced an inadequate treatment response to a trial of generic carbidopa/levodopa/entacapone or generic entacapone used in combination with a generic levodopa/carbidopa product

OR

- The patient has experienced an intolerance to generic carbidopa/levodopa/entacapone or generic entacapone used in combination with a generic levodopa/carbidopa product

OR

- The patient has a contraindication that would prohibit a trial of generic carbidopa/levodopa/entacapone or generic entacapone used in combination with a generic levodopa/carbidopa product

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Ongentys is indicated as adjunctive treatment to levodopa/carbidopa in patients with Parkinson's disease (PD) experiencing "off" episodes.[1-3]

The efficacy of Ongentys for the adjunctive treatment to levodopa/carbidopa in patients with PD experiencing "off" episodes was evaluated in two double-blind, randomized, parallel-group, placebo- and active-controlled, or placebo-controlled studies of 14-15-week duration. All patients were treated with levodopa/ DOPA decarboxylase inhibitor (DDCI) alone or in combination with other PD medications. The double-blind period for each study began with a period for levodopa/DDCI dose adjustment (up to 3 weeks), followed by a stable maintenance period of 12 weeks. In Study 1, patients (n=600) were randomized to treatment with one of 3 doses of Ongentys. The intention to treat (ITT) population included patients treated with Ongentys 50 mg once daily (n=115) or placebo (n=120). The primary efficacy endpoint was the change in mean absolute off-time based on 24-hour patient diaries completed 3 days prior to each of the scheduled visits. Ongentys 50 mg significantly reduced mean absolute off-time compared to placebo. In Study 2, patients (n=427) were randomized to treatment with either one of two doses of Ongentys once daily (n=283) or placebo (n=144). The intention to treat (ITT) study population included patients treated with Ongentys 50 mg once daily (n=147) or placebo (n=135). Eighty-five percent of patients treated with Ongentys 50 mg compared to 81% of patients who received placebo used concomitant PD medications in addition to levodopa; the most commonly used were dopamine agonists (70%), amantadine (21%), MAO-B inhibitors (20%), and anticholinergics (12%). The primary efficacy endpoint was the change in mean absolute off-time based on 24-hour patient diaries completed 3 days prior to each of the scheduled visits. Ongentys 50 mg significantly reduced mean absolute off-time compared to placebo.[1]

Since its introduction in the late 1960s, carbidopa/levodopa has continued to be the gold standard for PD therapy. However, long-term treatment with carbidopa/levodopa can lead to motor fluctuations and carbidopa/levodopa induced dyskinesia. Motor fluctuations are alterations between periods marked by a positive response to carbidopa/levodopa ("on") and periods marked by reappearance of Parkinsonian symptoms ("off"). "Wearing off" near the end of the carbidopa/levodopa dose interval is often the first and most encountered motor fluctuation and linked to the short half-life of oral carbidopa/levodopa (60–90 min).[4] Strategies for reducing the risk of motor complications include adjusting the dosage of levodopa or adding other antiparkinsonian agents such as a catechol-o-methyl transferase (COMT) inhibitor. Adjunctive therapy with a COMT inhibitor prolongs the duration of action of levodopa and reduces peak-trough variations through inhibition of its metabolism. Other drugs in the COMT inhibitor class include entacapone and tolcapone. Due to the risk of potentially fatal hepatotoxicity, tolcapone is generally reserved for patients who are nonresponsive to or intolerant of other adjunctive antiparkinsonian agents.[2] Based on the clinical trials, 50 mg of opicapone once daily was shown to be noninferior to entacapone and reduced the mean off time by about 50 minutes when compared to placebo.[4] Therefore, coverage will be provided when the patient has tried and failed or has a contraindication or intolerance to generic carbidopa/levodopa/entacapone or generic entacapone used in combination with a generic levodopa/carbidopa product.

REFERENCES

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Written by:	UM Development (DRS)
Date Written:	07/2022
Revised:	08/2022 (no clinical changes)
Reviewed:	Medical Affairs (CHART) 07/21/2022, 08/25/2022 External Review: 10/2022 (FYI), 12/2022

CRITERIA FOR APPROVAL

1	Is the requested drug being prescribed as adjunctive treatment to levodopa/carbidopa in a patient with Parkinson's disease (PD) experiencing "off" episodes? [If yes, go to 2. If no, then no further questions.]	Yes	No
2	Has the patient experienced an inadequate treatment response to a trial of generic carbidopa/levodopa/entacapone or generic entacapone used in combination with a generic levodopa/carbidopa product? [If yes, then no further questions. If no, go to 3.]	Yes	No
3	Has the patient experienced an intolerance to generic carbidopa/levodopa/entacapone or generic entacapone used in combination with a generic levodopa/carbidopa product? [If yes, then no further questions. If no, go to 4.]	Yes	No
4	Does the patient have a contraindication that would prohibit a trial of generic carbidopa/levodopa/entacapone or generic entacapone used in combination with a generic levodopa/carbidopa product? [No further questions]	Yes	No

Mapping Instructions			
	Yes	**No**	**DENIAL REASONS**

1.	Go to 2	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you meet all of these conditions: - You have Parkinson's disease - You are having "off" episodes - The requested drug is being added on to levodopa/carbidopa Your request has been denied based on the information we have. [Short Description: No approvable diagnosis.]
2.	Approve, 12 Months	Go to 3	
3.	Approve, 12 Months	Go to 4	
4.	Approve, 12 Months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have tried generic carbidopa/levodopa/entacapone or generic entacapone used with a generic levodopa/carbidopa product and they did not work for you, or you cannot use them. Your request has been denied based on the information we have. [Short Description: No inadequate response, intolerance or contraindication to generic carbidopa/levodopa/entacapone or generic entacapone in combination with generic a levodopa/carbidopa product.]

Reference number(s)
1647-A

SPECIALTY GUIDELINE MANAGEMENT

Opsumit (macitentan)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Opsumit is an endothelin receptor antagonist (ERA) indicated for the treatment of pulmonary arterial hypertension (PAH, World Health Organization [WHO] Group 1) to reduce the risks of disease progression and hospitalization for PAH. Effectiveness was established in a long-term study in PAH patients with predominantly WHO Functional Class II-III symptoms treated for an average of 2 years. Patients had idiopathic and heritable PAH, PAH caused by connective tissue disorders, and PAH caused by congenital heart disease with repaired shunts.

All other indications are considered experimental/investigational and not medically necessary.

II. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with a pulmonologist or cardiologist.

III. CRITERIA FOR INITIAL APPROVAL

Pulmonary Arterial Hypertension (PAH)
Authorization of 12 months may be granted for treatment of PAH when ALL of the following criteria are met:
A. Member has PAH defined as WHO Group 1 class of pulmonary hypertension (refer to Appendix).
B. PAH was confirmed by either criterion (1) or criterion (2) below:
    1. Pretreatment right heart catheterization with all of the following results:
        i. Mean pulmonary arterial pressure (mPAP) > 20 mmHg
        ii. Pulmonary capillary wedge pressure (PCWP) ≤ 15 mmHg
        iii. Pulmonary vascular resistance (PVR) ≥ 3 Wood units in adult patients or pulmonary vascular resistance index (PVRI) ≥ 3 Wood units x m^2 in pediatric patients
    2. For infants less than one year of age, PAH was confirmed by Doppler echocardiogram if right heart catheterization cannot be performed.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for members with an indication listed in Section III who are currently receiving the requested medication through a paid pharmacy or medical benefit, and who are experiencing benefit from therapy as evidenced by disease stability or disease improvement.

V. APPENDIX

WHO Classification of Pulmonary Hypertension

1 PAH

1.1 Idiopathic (PAH)
1.2 Heritable PAH
1.3 Drug- and toxin-induced PAH
1.4. PAH associated with:
- 1.4.1 Connective tissue diseases
- 1.4.2 HIV infection
- 1.4.3 Portal hypertension
- 1.4.4 Congenital heart diseases
- 1.4.5 Schistosomiasis

1.5 PAH long-term responders to calcium channel blockers
1.6 PAH with overt features of venous/capillaries (PVOD/PCH) involvement
1.7 Persistent PH of the newborn syndrome

2 PH due to left heart disease

2.1 PH due to heart failure with preserved LVEF
2.2 PH due to heart failure with reduced LVEF
2.3 Valvular heart disease
2.4 Congenital/acquired cardiovascular conditions leading to post-capillary PH

3 PH due to lung diseases and/or hypoxia

3.1 Obstructive lung disease
3.2 Restrictive lung disease
3.3 Other lung disease with mixed restrictive/obstructive pattern
3.4 Hypoxia without lung disease
3.5 Developmental lung disorders

4 PH due to pulmonary artery obstruction

4.1 Chronic thromboembolic PH
4.2 Other pulmonary artery obstructions
- 4.2.1 Sarcoma (high or intermediate grade) or angiosarcoma
- 4.2.2 Other malignant tumors
  - Renal carcinoma
  - Uterine carcinoma
  - Germ cell tumours of the testis
  - Other tumours
- 4.2.3 Non-malignant tumours
  - Uterine leiomyoma
- 4.2.4 Arteritis without connective tissue disease
- 4.2.5 Congenital pulmonary artery stenosis
- 4.2.6 Parasites
  - Hydatidosis

5 PH with unclear and/or multifactorial mechanisms

5.1 Hematologic disorders: Chronic hemolytic anemia, myeloproliferative disorders
5.2 Systemic and metabolic disorders: Pulmonary Langerhans cell histiocytosis, Gaucher disease, glycogen storage disease, neurofibromatosis, sarcoidosis
5.3 Others: chronic renal failure with or without hemodialysis, fibrosing mediastinitis
5.4 Complex congenital heart disease

VI. REFERENCES

1. Opsumit [package insert]. Titusville, NJ: Actelion Pharmaceuticals US, Inc.; July 2022.
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3. McLaughlin VV, Archer SL, Badesch DB, et al. ACCF/AHA 2009 expert consensus document on pulmonary hypertension a report of the American College of Cardiology Foundation Task Force on Expert Consensus Documents and the American Heart Association developed in collaboration with the American College of Chest Physicians, American Thoracic Society, Inc., and the Pulmonary Hypertension Association. *J Am Coll Cardiol*. 2009;53(17):1573-1619.
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PRIOR AUTHORIZATION CRITERIA

BRAND NAME
(generic)

OPZELURA
(ruxolitinib cream)

Status: CVS Caremark® Criteria
Type: Initial Prior Authorization with Quantity Limit

POLICY

FDA-APPROVED INDICATIONS

Atopic Dermatitis
Opzelura is indicated for the topical short-term and non-continuous chronic treatment of mild to moderate atopic dermatitis in non-immunocompromised adult and pediatric patients 12 years of age and older whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable.

Nonsegmental Vitiligo
Opzelura is indicated for the topical treatment of nonsegmental vitiligo in adult and pediatric patients 12 years of age and older.

Limitation of Use:
Use of Opzelura in combination with therapeutic biologics, other JAK inhibitors or potent immunosuppressants such as azathioprine or cyclosporine is not recommended.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is NOT being prescribed in combination with therapeutic biologics, other janus kinase (JAK) inhibitors, or potent immunosuppressants such as azathioprine or cyclosporine

AND

- The requested drug is being prescribed for the topical treatment of nonsegmental vitiligo
  AND
  - The request is for an adult or pediatric patient 12 years of age or older
  AND
    - The request is NOT for continuation of therapy
    OR
    - The request is for continuation of therapy
      AND
      - The patient has achieved or maintained a positive clinical response as evidenced by improvement (e.g., meaningful repigmentation)
  AND
  - The requested drug will NOT be applied to affected areas of greater than 10% body surface area (BSA)

OR

- The requested drug is being prescribed for topical short-term and non-continuous chronic treatment of mild to moderate atopic dermatitis in a non-immunocompromised patient
  AND
  - The request is for an adult or pediatric patient 12 years of age or older

AND

- The request is NOT for continuation of therapy

  AND

  - The requested drug will be used on sensitive skin areas (e.g., face, genitals or skin folds)

    AND

    - The patient has experienced an inadequate treatment response, intolerance or has a contraindication to a topical calcineurin inhibitor

  OR

  - The patient has experienced an inadequate treatment response, intolerance or has a contraindication to a topical calcineurin inhibitor AND a medium or higher potency topical corticosteroid

OR

- The request is for continuation of therapy

  AND

  - The patient has achieved or maintained a positive clinical response as evidenced by improvement [(e.g., improvement in or resolution of any of the following signs and symptoms: erythema (redness), edema (swelling), xerosis (dry skin), erosions, excoriations (evidence of scratching), oozing and crusting, lichenification (epidermal thickening), OR pruritus (itching)]

AND

- The requested drug will NOT be applied to affected areas of greater than 20% body surface area (BSA)

AND

- If additional quantities are being requested, then the requested drug is being prescribed to treat a body surface area that requires more than 60 grams per 28 days

Quantity Limits apply.
60 grams per 21 days* or 180 grams per 63 days**
For larger BSA for Vitiligo: 180 grams per 21 days* or 540 grams per 63 days**
For larger BSA for Atopic Dermatitis: 240 grams per 21 days* or 720 grams per 63 days**
**The duration of 21 days is used for a 28-day fill period and 63 days is used for an 84-day fill period to allow time for refill processing.*
For new starts, the mail limit will be the same as the retail limit.* ***The intent is for prescriptions of the requested drug to be filled one month at a time for new starts, even if filled at mail order; there should be no 3-month supplies filled for new starts. *The duration of 21 days is used for a 28-day fill period to allow time for refill processing.*

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PRIOR AUTHORIZATION CRITERIA

DRUG CLASS	**ORAL/INTRANASAL FENTANYL PRODUCTS**
BRAND NAME* **(generic)**	**ABSTRAL** **(fentanyl citrate sublingual tablet)**
	ACTIQ **(fentanyl citrate oral transmucosal lozenge)**
	FENTORA **(fentanyl citrate buccal tablet)**
	LAZANDA **(fentanyl nasal spray)**
	SUBSYS **(fentanyl sublingual spray)**

Status: CVS Caremark Criteria
Type: Initial Prior Authorization with Quantity Limit* ***Ref # 288-C***

**Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*
*** No Tech Approval; criteria requires a pharmacist to approve.*

FDA-APPROVED INDICATIONS

Abstral
Abstral (fentanyl citrate sublingual tablet) is indicated for the management of breakthrough pain in cancer patients 18 years of age and older who are already receiving, and who are tolerant to, around-the-clock opioid therapy for their underlying persistent cancer pain.

Actiq
Actiq (fentanyl citrate oral transmucosal lozenge) is indicated for the management of breakthrough pain in cancer patients 16 years of age and older who are already receiving and who are tolerant to around-the-clock opioid therapy for their underlying persistent cancer pain.

Fentora
Fentora (fentanyl citrate buccal tablet) is indicated for the management of breakthrough pain in cancer patients 18 years of age and older who are already receiving and who are tolerant to around-the-clock opioid therapy for their underlying persistent cancer pain.

Lazanda
Lazanda (fentanyl nasal spray) is indicated for the management of breakthrough pain in cancer patients 18 years of age and older who are already receiving and who are tolerant to around-the clock opioid therapy for their underlying persistent cancer pain.

Subsys
Subsys (fentanyl sublingual spray) is indicated for the management of breakthrough pain in cancer patients 18 years of age and older who are already receiving and who are tolerant to around-the-clock opioid therapy for their underlying persistent cancer pain.

For All Oral/Intranasal Fentanyl Products:
Patients considered opioid tolerant are those who are taking around-the-clock medicine consisting of at least 60 mg of oral morphine per day, at least 25 mcg per hour of transdermal fentanyl, at least 30 mg of oral oxycodone per day, at least 60 mg of oral hydrocodone per day, at least 8 mg of oral hydromorphone per day, at least 25 mg of oral oxymorphone per day, or an equianalgesic dose of another opioid medication daily for one week or longer. Patients must remain on around-the-clock opioids when taking the requested oral/intranasal fentanyl product.
Limitations of Use
- Not for use in opioid non-tolerant patients.
- Not for use in the management of acute or postoperative pain, including headache/migraine, dental pain, or in the emergency department.
- As a part of the TIRF REMS Access program, oral/intranasal fentanyl products may be dispensed only to outpatients enrolled in the program. For inpatient administration of oral/intranasal fentanyl products (e.g., hospitals, hospices, and long-term care facilities that prescribe for inpatient use), patient and prescriber enrollment is not required.

COVERAGE CRITERIA
The requested drug will be covered with prior authorization when the following criteria are met:
- The requested drug is indicated for the treatment of breakthrough CANCER-related pain only. The requested drug is being prescribed for the management of breakthrough pain in a CANCER patient with underlying CANCER pain. The prescriber must submit chart notes or other documentation supporting a diagnosis of cancer-related pain and list the type of cancer. [Note: For drug coverage approval, ICD diagnosis code provided MUST support the CANCER-RELATED DIAGNOSIS.]
  AND
- Chart notes or other documentation supporting a diagnosis of cancer-related pain have been submitted to CVS Health
  AND
- The patient is currently receiving, and will continue to receive, around-the-clock opioid therapy for underlying CANCER pain
  AND
- The requested drug is intended only for use in opioid tolerant patients. The patient can safely take the requested dose based on their history of opioid use. [Note: Patients considered opioid tolerant are those who are taking around-the-clock medicine consisting of at least 60 mg of oral morphine per day, at least 25 mcg per hour of transdermal fentanyl, at least 30 mg of oral oxycodone per day, at least 60 mg of oral hydrocodone per day, at least 8 mg of oral hydromorphone per day, at least 25 mg of oral oxymorphone per day, or an equianalgesic dose of another opioid medication daily for one week or longer.]
  AND
- If additional quantities are being requested, then:
  - The patient's dose of a concomitant long-acting analgesic is being increased
    OR
  - Additional quantities of the requested drug are needed for breakthrough pain because the dose of the patient's long-acting analgesic is unable to be increased

  [Note: Ensure that the patient can safely take the requested dose based on their history of opioid use.]

Quantity Limits apply.

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Abstral, Actiq, Fentora, Lazanda, and Subsys are indicated for the management of breakthrough pain in cancer patients who are already receiving and who are tolerant to around-the-clock opioid therapy for their underlying persistent cancer pain. Patients considered opioid tolerant are those who are taking, for one week or longer, around-the-clock medicine consisting of at least 60 mg of oral morphine per day, at least 25 mcg per hour of transdermal fentanyl, at least 30 mg of oral oxycodone per day, at least 60 mg of oral hydrocodone per day, at least 8 mg of oral hydromorphone per day, at least 25 mg of oral oxymorphone per day, or an equianalgesic dose of another opioid medication daily for one week or longer. Patients must remain on around-the-clock opioids when taking the requested oral/intranasal fentanyl product. Oral/intranasal fentanyl products are not for use in opioid non-tolerant patients. Oral/intranasal fentanyl products are not for use in the management of acute or postoperative pain, including headache/migraine, dental pain, or in the emergency department. As a part of the Transmucosal Immediate-Release Fentanyl (TIRF) Risk Evaluation and Mitigation Strategies (REMS) Access program, oral/intranasal fentanyl products may be dispensed only to outpatients enrolled in the program. For inpatient administration of oral/intranasal fentanyl products (e.g., hospitals, hospices, and long-term care facilities that prescribe for inpatient use), patient and prescriber enrollment is not required.[1-7]

For patients who are tolerant to and currently receiving opioid therapy for persistent cancer pain, dosing should be individually titrated to provide adequate analgesia with minimal side effects. Oral/intranasal fentanyl products should be limited to four or fewer doses per day. When the breakthrough pain episode is not relieved after administration of one dose, an additional dose may be necessary. If the patient requires more than 1 dose per breakthrough pain episode for several consecutive episodes, dose titration may be necessary. Patients experiencing >4 breakthrough pain episodes/day should have the dose of their long-term opioid re-evaluated.[1-8] Prescribers should ensure that the patient can safely take the requested dose based on their history of opioid use.

Based on this information, a limit of four units per day, or 120 units per month, will be placed on Abstral, Actiq, Fentora, and Subsys 100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg. A limit of 240 sprays per month (i.e., 120 blisters per month) will be placed on Subsys 1200 mcg and 1600 mcg since two sprays of 600 mcg are needed to achieve the 1200 mcg dose and two sprays of 800 mcg are needed to achieve the 1600 mcg dose. A limit of 30 bottles per month will be placed on the Lazanda products since each bottle provides 8 sprays.

For patients undergoing dose titration (increase) of their concomitant long-acting analgesic or in situations where it is not clinically appropriate to increase the dose of the long-acting analgesic, an additional quantity may be available. This additional quantity will provide coverage for an amount sufficient for up to 4 episodes of breakthrough pain per day plus two additional doses per day. A limit of 6 units per day, or 180 units per month, will be placed on Abstral 100 mcg, 200 mcg, 300 mcg, 400 mcg, Actiq (all strengths), Fentora (all strengths), and Subsys 100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg. For Subsys 1200 mcg and 1600 mcg, a higher limit of 12 sprays per day (i.e., 6 blisters), or 360 sprays per month (i.e., 180 blisters), will be in place. For Lazanda 100 mcg, a higher limit of 12 sprays per day, or 45 bottles per month, will be in place.

Coverage for Abstral 600 mcg or 800 mcg and Lazanda 300 mcg or 400 mcg, is only provided for up to 4 units (Abstral), or 8 sprays (Lazanda) per day to avoid exceeding the labeled maximum dose.

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Written by:	UM Development (JG)
Date Written:	04/2002
Revised:	(MB) 08/2004; (NB) 08/2005; (CT) 08/2006; (NB) 11/2006 (Added Fentora); (RP) 03/2007 (update label); (CT) 07/2007; (AM) 08/2008; (SE) 08/2009; (RB/AH/SE) 06/2010; (SE) 01/2011 (Added Abstral; Clarified age restriction question), 08/2011, 01/2012 added Subsys (08-2011 (2)), 03/2012, 03/2013, 07/2013 (changed to commercial reference number); (SE/MT) 01/2014; (SE) 06/2014, 01/2015; (CF) 08/2015 (added Onsolis, additional cancer question, documentation/tech notes), 10/2015 (added questions for additional quantities), 01/2016 (added Lazanda questions for macro compatibility, no clinical changes), 06/2016 (new strength of Lazanda – 300 mcg), 12/2016 (updated denial reasons, no clinical changes); (JH/CF) 01/2017, 07/2017 (clarified qty for Subsys 1200 mcg and 1600 mcg), 01/2018, 06/2018 (added note); (CF/DS) 01/2019 (no clinical changes), 01/2020 (removed Onsolis); (DS) 01/2021 (updated questions to reflect updated REMS; updated document title); (PM) 08/2021 (updated denial verbiage); (DS) 01/2022 (no clinical changes)
Reviewed:	Medical Affairs: 04/2002; (MM) 08/2004, 08/2005, 08/2006; (WF) MD 07/2007, 08/2008, 08/2009; (KP) 06/2010, 01/2011, 08/2011, 01/2012, 03/2012; (DNC) 03/2013; (LMS) 07/2013; (KP) 01/2014; (SES) 06/2014, 01/2015; (ADA) 08/2015; (DNC) 10/2015; (ME) 06/2016; (DNC) 01/2017, 07/2017, 01/2018; (MC) 06/2018; (CHART) 01/30/2020, 01/28/2021, 02/03/2022
External Review:	12/2004, 12/2006, 02/2008, 12/2008, 09/2009, 12/2010, 10/2011, 1/2012, 02/2012, 08/2012, 06/2013, 06/2014, 04/2015, 12/2015, 04/2016, 04/2017, 08/2017, 04/2018, 04/2019, 04/2020, 04/2021, 04/2022

CRITERIA FOR APPROVAL

1	The requested drug is indicated for the treatment of breakthrough CANCER-related pain only. Is the requested drug being prescribed for the management of breakthrough pain in a CANCER patient with underlying CANCER pain? If yes, then prescriber MUST submit chart notes or other documentation supporting a diagnosis of cancer-related pain AND list type of cancer_____ [Note: For drug coverage approval, ICD diagnosis code provided MUST support the CANCER-RELATED DIAGNOSIS.] [If no, then no further questions.]	Yes	No
2	Have chart notes or other documentation supporting a diagnosis of cancer-related pain been submitted to CVS Health? [If no, then no further questions.] [Tech Note: If the PA is worked over the phone, then the prescriber still MUST submit physical chart notes or other documentation.] [RPh Note: MUST obtain a physical copy of chart notes or other documentation supporting a diagnosis of cancer-related pain AND verify that the prescriber has listed the type of cancer. If a physical copy of documentation of a diagnosis of cancer-related pain is not received, then the PA should be denied.]	Yes	No
3	Is the patient currently receiving, and will continue to receive, around-the-clock opioid therapy for underlying CANCER pain? [If no, then no further questions.]	Yes	No
4	The requested drug is intended only for use in opioid tolerant patients. Can the patient safely take the requested dose based on their current opioid use history? [Note: Patients considered opioid tolerant are those who are taking around-the-clock medicine consisting of at least 60 mg of oral morphine per day, at least 25 mcg per hour of transdermal fentanyl, at least 30 mg of oral oxycodone per day, at least 60 mg of oral hydrocodone per day, at least 8 mg of oral hydromorphone per day, at least 25 mg of oral oxymorphone per day, or an equianalgesic dose of another opioid medication daily for one week or longer.] [If no, then no further questions.]	Yes	No

5	Which drug is being requested? Please check the drug being requested. [Note: Ensure that the patient can safely take the requested dose based on their history of opioid use.] [] Abstral 600 mcg or 800 mcg (if checked, then go to 6) [] Abstral 100 mcg, 200 mcg, 300 mcg, 400 mcg (if checked, then go to 8) [] Actiq (all strengths) (if checked, then go to 8) [] Fentora (all strengths) (if checked, then go to 8) [] Lazanda 100 mcg (if checked, then go to 9) [] Lazanda 300 mcg or 400 mcg (if checked, then go to 7) [] Subsys 100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg (if checked, then go to 8) [] Subsys 1200 mcg, 1600 mcg (if checked, then go to 10)		
6	Coverage is provided for up to 120 units per month of Abstral 600 mcg, 800 mcg. Is MORE than this quantity needed to manage the patient's pain? [No further questions.] [RPh Note: If yes, then deny and enter a partial approval for up to 120 units per month of Abstral 600 mcg, 800 mcg.]	Yes	No
7	Coverage is provided for up to 240 sprays per month (i.e., 30 bottles per month) of Lazanda 300 mcg, 400 mcg. Is MORE than this quantity needed to manage the patient's pain? [No further questions.] [RPh Note: If yes, then deny and enter a partial approval for 240 sprays per month (i.e., 30 bottles per month) of Lazanda 300 mcg, 400 mcg.]	Yes	No
8	Coverage is provided for up to 120 units per month of the following: A) Abstral 100 mcg, 200 mcg, 300 mcg, 400 mcg, B) Actiq (all strengths), C) Fentora (all strengths), D) Subsys 100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg. If higher quantities are needed, then additional questions are required. Is MORE than this quantity needed to manage the patient's pain? [Note Subsys packaging: Supplied as 1 spray per blister for Subsys 100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg.] [If no, then no further questions.] [If yes, then skip to question 11.]	Yes	No
9	Coverage is provided for up to 240 sprays per month (i.e., 30 bottles per month) of Lazanda 100 mcg. If higher quantities are needed, then additional questions are required. Is MORE than this quantity needed to manage the patient's pain? [If no, then no further questions.] [If yes, then skip to question 11.]	Yes	No
10	Coverage is provided for up to 240 sprays per month (i.e., 120 blisters per month) of Subsys 1200 mcg or 1600 mcg. If higher quantities are needed, then additional questions are required. Is MORE than this quantity needed to manage the patient's pain? [Note Subsys packaging: Supplied as 2 sprays per blister for Subsys 1200 mcg and 1600 mcg.] [If no, then no further questions.]	Yes	No
11	Is the patient's dose of a concomitant long-acting analgesic being increased? [If yes, then skip to question 13.]	Yes	No

12	Are additional quantities of the requested drug needed for breakthrough pain because the dose of the patient's long-acting analgesic is unable to be increased? [If no, then no further questions.] [RPh Note: If no, then deny and enter a partial approval for the following: A) 120 units per month of Abstral, Actiq, Fentora, or Subsys 100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg, B) 240 sprays per month (i.e., 30 bottles per month) of Lazanda 100 mcg, C) 240 sprays per month (i.e., 120 blisters per month) of Subsys 1200 mcg or 1600 mcg.]	Yes	No
13	Which drug is being requested? Please check the drug being requested. [Note: Ensure that the patient can safely take the requested dose based on their history of opioid use.] [] Abstral 100 mcg, 200 mcg, 300 mcg, 400 mcg (if checked, then go to 14) [] Actiq (all strengths) (if checked, then go to 14) [] Fentora (all strengths) (if checked, then go to 14) [] Lazanda 100 mcg (if checked, then go to 15) [] Subsys 100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg (if checked, then go to 14) [] Subsys 1200 mcg, 1600 mcg (if checked, then go to 16)		
14	Does the patient's pain require use of MORE than 180 units per month of any of the following: A) Abstral 100 mcg, 200 mcg, 300 mcg, 400 mcg, B) Actiq (all strengths), C) Fentora (all strengths), D) Subsys 100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg? [Note Subsys packaging: Supplied as 1 spray per blister for Subsys 100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg.] [No further questions.] [RPh Note: If yes, then deny and enter a partial approval for 180 units per month of the following: A) Abstral 100 mcg, 200 mcg, 300 mcg, 400 mcg, B) Actiq (all strengths), C) Fentora (all strengths), D) Subsys 100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg.]	Yes	No
15	Does the patient's pain require use of MORE than 360 sprays per month (i.e., 45 bottles per month) of Lazanda 100 mcg? [No further questions.] [RPh Note: If yes, then deny and enter a partial approval for 360 sprays per month (i.e., 45 bottles per month) of Lazanda 100 mcg.]	Yes	No
16	Does the patient's pain require use of MORE than 360 sprays per month (i.e., 180 blisters per month) of Subsys 1200 mcg or 1600 mcg? [Note Subsys packaging: Supplied as 2 sprays per blister for Subsys 1200 mcg and 1600 mcg.] [RPh Note: If yes, then deny and enter a partial approval for 360 sprays per month (i.e., 180 blisters per month) of Subsys 1200 mcg or 1600 mcg.]	Yes	No

Mapping Instructions			
	Yes	**No**	**DENIAL REASONS – DO NOT USE FOR MEDICARE PART D**
1.	Go to 2	Deny	You do not meet the requirements of your plan.

			Your plan covers this drug when you are using it to manage your breakthrough cancer pain. Your request has been denied based on the information we have. [Short Description: No approvable diagnosis.]
2.	Go to 3	Deny	You do not meet the requirements of your plan. Your plan covers this drug when your prescriber submits your chart notes or other documentation that supports that you have pain due to cancer to CVS Health. Your request has been denied based on the information we have. [Short Description: Prescriber did not fax documentation to confirm cancer-related pain.]
3.	Go to 4	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you are currently taking, and will continue to take, opioid drugs around-the-clock for cancer pain. Your request has been denied based on the information we have. [Short Description: Not on around-the-clock opioids.]
4.	Go to 5	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you can safely take the drug based on your history of opioid use. Your request has been denied based on the information we have. [Short Description: Patient cannot safely take requested dose.]
5.	1=6; 2=8; 3=8; 4=8; 5=9; 6=7; 7=8; 8=10	N/A	
6.	Deny	Approve, 12 months 120 units per 25 days or 360 units per 75 days* of: Abstral 600 mcg, 800 mcg No Tech Approval	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 120 units per month of the requested drug and strength. Your request has been partially approved. You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity - Abstral.]
7.	Deny	Approve, 12 months 30 bottles per 25 days or 90 bottles per 75 days* of: Lazanda 300 mcg, 400 mcg No Tech Approval	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 240 sprays per month (i.e., 30 bottles per month) of the requested drug and strength. Your request has been partially approved. You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity - Lazanda.]
8.	Go to 11	Approve, 12 months 120 units per 25 days OR 360 units per 75 days* of: Abstral 100 mcg, 200 mcg, 300 mcg, 400 mcg Actiq (all strengths)	

		Fentora (all strengths) Subsys 100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg No Tech Approval	
9.	Go to 11	Approve, 12 months 30 bottles per 25 days or 90 bottles per 75 days* of: Lazanda 100 mcg No Tech Approval	
10.	Go to 11	Approve, 12 months 240 sprays (i.e., 120 blisters) per 25 days or 720 sprays (i.e., 360 blisters) per 75 days* of Subsys 1200 mcg or 1600 mcg No Tech Approval	
11.	Go to 13	Go to 12	
12.	Go to 13	Deny RPh Note: For the denial verbiage, only include the requested drug. Remove all the other drugs from the verbiage.	You have requested more than the quantity allowed by your plan. Current plan approved criteria cover up to: - 120 units per month of Abstral, Actiq, Fentora, or Subsys 100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg - 240 sprays per month (i.e., 30 bottles per month) of Lazanda 100 mcg - 240 sprays per month (i.e., 120 blisters per month) of Subsys 1200 mcg or 1600 mcg Your request has been partially approved. You have been approved for the quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied. Your plan covers additional quantities of this drug when you meet any of these conditions: - The dose of your long-acting opioid drug is being increased - The dose of your long-acting opioid drug is unable to be increased and you need more of the requested drug to manage your breakthrough pain Your use of this drug does not meet the requirement. This is based on the information we have. [Short Description: Over max quantity and patient does not meet requirements for additional quantities.]
13.	1=14; 2=14; 3=14; 4=15; 5=14; 6=16	N/A	
14.	Deny	Approve, 12 months 180 units per 25 days	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 180 units/month of the requested drug and strength. Your request has

		OR 540 units per 75 days* of: Abstral 100 mcg, 200 mcg, 300 mcg, 400 mcg Actiq (all strengths) Fentora (all strengths) Subsys 100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg No Tech Approval	been partially approved. You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity – Abstral, Subsys.]
15.	Deny	Approve, 12 months 45 bottles per 25 days or 135 bottles per 75 days* of: Lazanda 100 mcg No Tech Approval	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 45 bottles/month of the requested drug and strength. Your request has been partially approved. You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity – Lazanda dose adjustment.]
16.	Deny	Approve, 12 months 360 sprays (i.e., 180 blisters) per 25 days or 1080 sprays (i.e., 540 blisters) per 75 days* of Subsys 1200 mcg or 1600 mcg No Tech Approval	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 360 sprays (i.e., 180 blisters)/month of the requested drug and strength. Your request has been partially approved. You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity – Subsys dose adjustment.]

**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*

QUANTITY LIMIT CRITERIA

BRAND NAME*
(generic)

ORAVIG
(miconazole buccal tablet)

Status: CVS Caremark Criteria
Type: Quantity Limit ***Ref # 2946-H***

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Oravig is indicated for the local treatment of oropharyngeal candidiasis (OPC) in adults.

RATIONALE

Oravig is indicated for the local treatment of oropharyngeal candidiasis (OPC) in adults. The recommended dosing schedule for Oravig is the application of one 50 mg buccal tablet to the upper gum region (canine fossa) once daily for 14 consecutive days.[1-3]

The Infectious Diseases Society of America published the Clinical Practice Guideline for the Management of Candidiasis: 2016 Update by the Infectious Diseases Society of America. For oropharyngeal mild disease, the guidelines recommend clotrimazole troches 10 mg five times daily or miconazole mucoadhesive buccal 50 mg tablet (Oravig) applied to the mucosal surface over the canine fossa once daily for 7 to 14 days. For moderate to severe disease, oral fluconazole 100 mg to 200 mg daily for 7 to 14 days is recommended.[4] Similarly, the Guidelines for the Prevention and Treatment of Opportunistic Infections in HIV-Infected Adults and Adolescents recommend oral fluconazole 100 mg once a day for one to two weeks for the treatment of oropharyngeal candidiasis. Once daily miconazole in 50 mg mucoadhesive buccal tablets (Oravig) is recommended as an alternative to oral fluconazole.[5] Chronic suppressive therapy is usually unnecessary. If required for patients who have recurrent infection, then fluconazole 100 mg 3 times weekly is recommended.[4] Therefore, based on the recommended dosing schedule as well as applicable guidelines, there will be a limit of 14 Oravig tablets per 30 days.

If the patient is requesting more than the initial quantity limit, then the claim will reject with a message indicating that quantity limits are exceeded.

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Written by: UM Development (DS)
Date Written: 03/2019
Revised: 02/2020 (no clinical changes); (PM) 12/2020 (no clinical changes); (DS) 09/2021 (no clinical changes)
Reviewed: Medical Affairs: (GAD) 04/2019; (CHART) 02/27/2020, 12/31/2020, 09/30/2021
External Review: 06/2019, 06/2020, 04/2021, 12/2021

LIMIT CRITERIA

Drug	1 Month Limit*	3 Month Limit*
Oravig	14 tablets / 25 days	Does Not Apply**

** The duration of 25 days is used for a 30-day fill period to allow time for refill processing.*
*** This drug is for short-term acute use; therefore, the mail limit will be the same as the retail limit. The intent is for prescriptions of the requested drug to be filled one month at a time, even if filled at mail order; there should be no 3 month supplies filled.*

Reference number
2127-A

SPECIALTY GUIDELINE MANAGEMENT

ORENCIA (abatacept)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. Moderately to severely active rheumatoid arthritis in adults
   2. Moderately to severely active polyarticular juvenile idiopathic arthritis in patients 2 years of age or older
   3. Active psoriatic arthritis in adults
   4. Prophylaxis of acute graft versus host disease (aGVHD), in combination with a calcineurin inhibitor and methotrexate, in adults and pediatric patients 2 years of age and older undergoing hematopoietic stem cell transplantation (HSCT) from a matched or 1 allele-mismatched unrelated-donor

B. Compendial Uses
   1. Oligoarticular juvenile idiopathic arthritis
   2. Chronic graft versus host disease
   3. Immune checkpoint inhibitor-related toxicity

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

A. Rheumatoid arthritis (RA)
   1. For initial requests:
      i. Chart notes, medical record documentation, or claims history supporting previous medications tried (if applicable), including response to therapy. If therapy is not advisable, documentation of clinical reason to avoid therapy.
      ii. Laboratory results, chart notes, or medical record documentation of biomarker testing (i.e., rheumatoid factor [RF], anti-cyclic citrullinated peptide [anti-CCP], and C-reactive protein [CRP] and/or erythrocyte sedimentation rate [ESR]) (if applicable).
   2. For continuation requests: Chart notes or medical record documentation supporting positive clinical response.

B. Articular juvenile idiopathic arthritis
   1. Initial requests: Chart notes, medical record documentation, or claims history supporting previous medications tried (if applicable), including response to therapy.

2. Continuation requests: Chart notes or medical record documentation supporting positive clinical response.

C. Psoriatic arthritis (PsA): For continuation requests: Chart notes or medical record documentation supporting positive clinical response.

D. Chronic graft versus host disease: For initial requests: Chart notes, medical record documentation, or claims history supporting previous medications tried (if applicable), including response to therapy. If therapy is not advisable, documentation of clinical reason to avoid therapy.

III. CRITERIA FOR INITIAL APPROVAL

A. Moderately to severely active rheumatoid arthritis (RA)

1. Authorization of 12 months may be granted for members who have previously received a biologic or targeted synthetic DMARD (e.g., Rinvoq, Xeljanz) indicated for moderately to severely active rheumatoid arthritis.

2. Authorization of 12 months may be granted for treatment of moderately to severely active RA when all of the following criteria are met:
   i. Member meets either of the following criteria:
      a. Member has been tested for either of the following biomarkers and the test was positive:
         1. Rheumatoid factor (RF)
         2. Anti-cyclic citrullinated peptide (anti-CCP)
      b. Member has been tested for ALL of the following biomarkers:
         1. RF
         2. Anti-CCP
         3. C-reactive protein (CRP) and/or erythrocyte sedimentation rate (ESR)
   ii. Member meets either of the following criteria:
      a. Member has experienced an inadequate response to at least a 3-month trial of methotrexate despite adequate dosing (i.e., titrated to at least 15 mg/week).
      b. Member has an intolerance or contraindication to methotrexate (see Appendix A).

B. Moderately to severely active articular juvenile idiopathic arthritis

1. Authorization of 12 months may be granted for members who have previously received a biologic or targeted synthetic DMARD indicated for moderately to severely active articular juvenile idiopathic arthritis.

2. Authorization of 12 months may be granted for treatment of moderately to severely active articular juvenile idiopathic arthritis when any of the following criteria are met:
   i. The member had an inadequate response to methotrexate or another non-biologic DMARD administered at an adequate dose and duration.
   ii. The member has risk factors (see Appendix B) and the member also meets one of the following:
      a. High-risk joints are involved (e.g., cervical spine, wrist, or hip).
      b. High disease activity.
      c. Are judged to be at high risk for disabling joint disease.

C. Active psoriatic arthritis (PsA)

Authorization of 12 months may be granted for treatment of active psoriatic arthritis (PsA).

D. Prophylaxis of acute graft versus host disease
Authorization of 1 month may be granted for prophylaxis of acute graft versus host disease when both of the following criteria are met:
1. Member is undergoing hematopoietic stem cell transplantation (HSCT) from a matched or 1 allele-mismatched unrelated-donor
2. The requested medication will be used in combination with a calcineurin inhibitor (e.g., cyclosporine, tacrolimus) and methotrexate

E. Chronic graft versus host disease
Authorization of 12 months may be granted for treatment of chronic graft versus host disease when either of the following criteria is met:
1. Member has experienced an inadequate response to systemic corticosteroids.
2. Member has an intolerance or contraindication to corticosteroids.

F. Immune checkpoint inhibitor-related toxicity
Authorization of 1 month may be granted for treatment of immune checkpoint inhibitor-related toxicity when the member has cardiac toxicity.

IV. CONTINUATION OF THERAPY

A. Moderately to severely active rheumatoid arthritis (RA)
Authorization of 12 months may be granted for all members (including new members) who are using the requested medication for moderately to severely active RA and who achieve or maintain a positive clinical response as evidenced by disease activity improvement of at least 20% from baseline in tender joint count, swollen joint count, pain, or disability.

B. Moderately to severely active articular juvenile idiopathic arthritis
Authorization of 12 months may be granted for all members (including new members) who are using the requested medication for moderately to severely active articular juvenile idiopathic arthritis and who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition when there is improvement in any of the following from baseline:
1. Number of joints with active arthritis (e.g., swelling, pain, limitation of motion)
2. Number of joints with limitation of movement
3. Functional ability

C. Active psoriatic arthritis (PsA)
Authorization of 12 months may be granted for all members (including new members) who are using the requested medication for active psoriatic arthritis and who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition when there is improvement in any of the following from baseline:
1. Number of swollen joints
2. Number of tender joints
3. Dactylitis
4. Enthesitis
5. Skin and/or nail involvement

D. Prophylaxis of acute graft versus host disease, chronic graft versus host disease, and immune checkpoint inhibitor-related toxicity

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

V. OTHER

For all indications: Member has had a documented negative TB test (which can include a tuberculosis skin test [PPD], an interferon-release assay [IGRA], or a chest x-ray)* within 6 months of initiating therapy for persons who are naïve to biologic DMARDs or targeted synthetic DMARDs associated with an increased risk of TB.

* If the screening testing for TB is positive, there must be further testing to confirm there is no active disease. Do not administer the requested medication to members with active TB infection. If there is latent disease, TB treatment must be started before initiation of the requested medication.

For all indications: Member cannot use the requested medication concomitantly with any other biologic DMARD or targeted synthetic DMARD.

VI. DOSAGE AND ADMINISTRATION

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

VII. APPENDICES

Appendix A: Examples of Contraindications to Methotrexate

1. Clinical diagnosis of alcohol use disorder, alcoholic liver disease or other chronic liver disease
2. Breastfeeding
3. Blood dyscrasias (e.g., thrombocytopenia, leukopenia, significant anemia)
4. Elevated liver transaminases
5. History of intolerance or adverse event
6. Hypersensitivity
7. Interstitial pneumonitis or clinically significant pulmonary fibrosis
8. Myelodysplasia
9. Pregnancy or currently planning pregnancy
10. Renal impairment
11. Significant drug interaction

Appendix B: Risk factors for articular juvenile idiopathic arthritis

1. Positive rheumatoid factor
2. Positive anti-cyclic citrullinated peptide antibodies
3. Pre-existing joint damage

VIII. REFERENCES

1. Orencia [package insert]. Princeton, NJ: Bristol-Myers Squibb; December 2021.
2. Smolen JS, Landewé R, Bijlsma J, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2019 update. *Ann Rheum Dis.* 2020;*79*:685-699.

3. Singh JA, Saag KG, Bridges SL Jr, et al. 2015 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. *Arthritis Rheumatol.* 2016;68(1)1-26.
4. Saag KG, Teng GG, Patkar NM, et al. American College of Rheumatology 2008 recommendations for the use of nonbiologic and biologic disease-modifying antirheumatic drugs in rheumatoid arthritis. *Arthritis Rheum.* 2008;59(6):762-784.
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10. Smolen JS, Aletaha D. Assessment of rheumatoid arthritis activity in clinical trials and clinical practice. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. Available with subscription. URL: www.uptodate.com. Accessed March 19, 2021.
11. Fraenkel L, Bathon JM, England BR, et al. 2021 American College of Rheumatology guideline for the treatment of rheumatoid arthritis. *Arthrit Care Res*. 2021;0:1-16.

Reference number(s)
1643-A

SPECIALTY GUIDELINE MANAGEMENT

Orenitram
(treprostinil extended-release tablets)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Orenitram is indicated for the treatment of pulmonary arterial hypertension (PAH) (World Health Organization [WHO] Group 1) to delay disease progression and to improve exercise capacity. The studies that established effectiveness included predominately patients with WHO functional class II-III symptoms and etiologies of idiopathic or heritable PAH (66%) or PAH associated with connective tissue disease (26%).

All other indications are considered experimental/investigational and not medically necessary.

II. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with a pulmonologist or cardiologist.

III. CRITERIA FOR INITIAL APPROVAL

Pulmonary Arterial Hypertension (PAH)
Authorization of 12 months may be granted for treatment of PAH when ALL of the following criteria are met:
A. Member has PAH defined as WHO Group 1 class of pulmonary hypertension (refer to Appendix).
B. PAH was confirmed by either criterion (1) or criterion (2) below:
    1. Pretreatment right heart catheterization with all of the following results:
        i. Mean pulmonary arterial pressure (mPAP) > 20 mmHg
        ii. Pulmonary capillary wedge pressure (PCWP) ≤ 15 mmHg
        iii. Pulmonary vascular resistance (PVR) ≥ 3 Wood units in adult patients or pulmonary vascular resistance index (PVRI) ≥ 3 Wood units x m^2 in pediatric patients
    2. For infants less than one year of age, PAH was confirmed by Doppler echocardiogram if right heart catheterization cannot be performed.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for members with an indication listed in Section III who are currently receiving the requested medication through a paid pharmacy or medical benefit, and who are experiencing benefit from therapy as evidenced by disease stability or disease improvement.

V. APPENDIX

WHO Classification of Pulmonary Hypertension

1 PAH

1.1 Idiopathic (PAH)
1.2 Heritable PAH
1.3 Drug- and toxin-induced PAH
1.4. PAH associated with:
- 1.4.1 Connective tissue diseases
- 1.4.2 HIV infection
- 1.4.3 Portal hypertension
- 1.4.4 Congenital heart diseases
- 1.4.5 Schistosomiasis

1.5 PAH long-term responders to calcium channel blockers
1.6 PAH with overt features of venous/capillaries (PVOD/PCH) involvement
1.7 Persistent PH of the newborn syndrome

2 PH due to left heart disease

2.1 PH due to heart failure with preserved LVEF
2.2 PH due to heart failure with reduced LVEF
2.3 Valvular heart disease
2.4 Congenital/acquired cardiovascular conditions leading to post-capillary PH

3 PH due to lung diseases and/or hypoxia

3.1 Obstructive lung disease
3.2 Restrictive lung disease
3.3 Other lung disease with mixed restrictive/obstructive pattern
3.4 Hypoxia without lung disease
3.5 Developmental lung disorders

4 PH due to pulmonary artery obstruction

4.1 Chronic thromboembolic PH
4.2 Other pulmonary artery obstructions
- 4.2.1 Sarcoma (high or intermediate grade) or angiosarcoma
- 4.2.2 Other malignant tumors
  - Renal carcinoma
  - Uterine carcinoma
  - Germ cell tumours of the testis
  - Other tumours
- 4.2.3 Non-malignant tumours
  - Uterine leiomyoma
- 4.2.4 Arteritis without connective tissue disease
- 4.2.5 Congenital pulmonary artery stenosis
- 4.2.6 Parasites
  - Hydatidosis

5 PH with unclear and/or multifactorial mechanisms

5.1 Hematologic disorders: Chronic hemolytic anemia, myeloproliferative disorders
5.2 Systemic and metabolic disorders: Pulmonary Langerhans cell histiocytosis, Gaucher disease, glycogen storage disease, neurofibromatosis, sarcoidosis
5.3 Others: chronic renal failure with or without hemodialysis, fibrosing mediastinitis
5.4 Complex congenital heart disease

VI. REFERENCES

1. Orenitram [package insert]. Research Triangle Park, NC: United Therapeutics Corp.; February 2023.
2. Chin KM, Rubin LJ. Pulmonary arterial hypertension. *J Am Coll Cardiol*. 2008;51(16):1527-1538.
3. McLaughlin VV, Archer SL, Badesch DB, et al. ACCF/AHA 2009 expert consensus document on pulmonary hypertension a report of the American College of Cardiology Foundation Task Force on Expert Consensus Documents and the American Heart Association developed in collaboration with the American College of Chest Physicians, American Thoracic Society, Inc., and the Pulmonary Hypertension Association. *J Am Coll Cardiol*. 2009;53(17):1573-1619.
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Reference number(s)
4411-A

SPECIALTY GUIDELINE MANAGEMENT

ORGOVYX (relugolix)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication
Orgovyx is indicated for the treatment of adult patients with advanced prostate cancer.

B. Compendial Use
Prostate Cancer

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Prostate Cancer
Authorization of 12 months may be granted for treatment of prostate cancer when used as a single agent.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization who are experiencing clinical benefit to therapy (e.g., maintaining serum testosterone to less than 50ng/dL) and who have not experienced an unacceptable toxicity.

IV. REFERENCES

1. Orgovyx [package insert]. Brisbane, CA: Myovant Sciences, Inc; December 2020.
2. The NCCN Drugs & Biologics Compendium® © 2022 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed July 6, 2022.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME
(generic)

ORIAHNN
(elagolix/estradiol/norethindrone acetate)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

POLICY

FDA-APPROVED INDICATIONS

Oriahnn is indicated for the management of heavy menstrual bleeding associated with uterine leiomyomas (fibroids) in premenopausal women.

Limitation of Use:
Use of Oriahnn should be limited to 24 months due to the risk of continued bone loss, which may not be reversible.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for the management of heavy menstrual bleeding associated with uterine leiomyomas (fibroids) in a premenopausal patient

AND

- If the patient has previously received treatment with an elagolix-containing product (e.g., Oriahnn, Orilissa) or a relugolix-containing product (e.g., Myfembree), the patient has not already received ANY of the following: A) Greater than or equal to 24 cumulative months of treatment with elagolix-containing products (e.g., Oriahnn, Orilissa) and/or relugolix-containing products (e.g., Myfembree), B) Greater than or equal to 6 months of treatment with Orilissa 200 mg twice daily

Duration of Approval Limits apply.
Total cumulative duration: 24 months

REFERENCES

1. Myfembree [package insert]. Brisbane, CA: Myovant Sciences, Inc.; September 2022.
2. Oriahnn [package insert]. North Chicago, IL: AbbVie Inc.; August 2021.
3. Orilissa [package insert]. North Chicago, IL: AbbVie Inc.; February 2021.
4. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2022; Accessed November 22, 2022.
5. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed November 22, 2022.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME
(generic)

ORILISSA
(elagolix)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

POLICY

FDA-APPROVED INDICATIONS
Orilissa is indicated for the management of moderate to severe pain associated with endometriosis.

Limitations of Use:
Limit the duration of use based on the dose and coexisting condition.

COVERAGE CRITERIA
The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for the management of moderate to severe pain associated with endometriosis

AND

- The patient has not received the maximum recommended treatment course of 12 months of Lupron Depot or Lupaneta Pack OR 6 months of Synarel or Zoladex

AND

  - If the patient has not previously received treatment with an elagolix-containing product (e.g., Oriahnn, Orilissa) or a relugolix-containing product (e.g., Myfembree), the patient will receive 150 mg once daily of the requested drug OR 200 mg twice daily of the requested drug

  OR

  - If the patient has previously received treatment with an elagolix-containing product (e.g., Oriahnn, Orilissa) or a relugolix-containing product (e.g., Myfembree), the patient has not already received ANY of the following: A) Greater than or equal to 24 cumulative months of treatment with elagolix-containing products (e.g., Oriahnn, Orilissa) and/or relugolix-containing products (e.g., Myfembree), B) Greater than or equal to 6 months of treatment with Orilissa 200 mg twice daily

Duration of Approval Limits apply.
Total cumulative duration: 24 months

REFERENCES

1. Lupaneta Pack [package insert]. North Chicago, IL: AbbVie Inc.; June 2015.
2. Lupron Depot [package insert]. North Chicago, IL: AbbVie Inc.; July 2022.
3. Myfembree [package insert]. Brisbane, CA: Myovant Sciences, Inc.; September 2022.
4. Oriahnn [package insert]. North Chicago, IL: AbbVie Inc.; August 2021.
5. Orilissa [package insert]. North Chicago, IL: AbbVie Inc.; February 2021.
6. Synarel [package insert]. New York, NY: Pfizer Inc.; April 2022.
7. Zoladex [package insert]. Deerfield, IL: TerSera Therapeutics LLC; December 2020.
8. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2022; Accessed November 22, 2022.
9. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed November 22, 2022.

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12. Edi R, Cheng T. Endometriosis: Evaluation and Treatment. *Am Fam Physician*. 2022;106(4):397-404.

Reference number(s)
1885-A

SPECIALTY GUIDELINE MANAGEMENT

ORKAMBI (lumacaftor/ivacaftor)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Orkambi is a combination of lumacaftor and ivacaftor indicated for the treatment of cystic fibrosis (CF) in patients aged 1 year and older who are homozygous for the *F508del* mutation in the cystic fibrosis transmembrane conductance regulator (*CFTR*) gene. If the patient's genotype is unknown, an FDA-cleared CF mutation test should be used to detect the presence of the *F508del* mutation on both alleles of the *CFTR* gene.

Limitation of use: The efficacy and safety of Orkambi have not been established in patients with CF other than those homozygous for the *F508del* mutation.

All other indications are considered experimental/investigational and are not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: genetic testing report confirming the presence of the appropriate *CFTR* gene mutation.

III. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with a pulmonologist.

IV. CRITERIA FOR INITIAL APPROVAL

Cystic Fibrosis
Authorization of 12 months may be granted for treatment of cystic fibrosis when all of the following criteria are met:
A. Genetic testing was conducted to detect a mutation in the *CFTR* gene.
B. The member is positive for the *F508del* mutation on both alleles of the *CFTR* gene.
C. The member is at least 1 year of age.
D. Orkambi will not be used in combination with other medications containing ivacaftor.

V. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section IV who are experiencing benefit from therapy as evidenced by disease stability or disease improvement (e.g., improvement in FEV1 from baseline).

VI. REFERENCES

1. Orkambi [package insert]. Boston, MA: Vertex Pharmaceuticals Inc.; July 2019.

Reference number(s)
4400-A

SPECIALTY GUIDELINE MANAGEMENT

ORLADEYO (berotralstat)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Orladeyo is indicated for prophylaxis to prevent attacks of hereditary angioedema (HAE) in adults and pediatric patients 12 years and older.

Limitations of Use
Orladeyo should not be used for treatment of acute HAE attacks

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
A. For initial authorization, the following should be documented:
   1. C1 inhibitor functional and antigenic protein levels
   2. F12, angiopoietin-1, plasminogen, kininogen-1 (KNG1), heparan sulfate-glucosamine 3-O-sulfotransferase 6 (HS3ST6), or myoferlin (MYOF) gene mutation testing, if applicable
   3. Chart notes confirming family history of angioedema and the angioedema was refractory to a trial of high-dose antihistamine therapy, if applicable
B. For continuation of therapy, chart notes demonstrating a reduction in frequency of attacks

III. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with a prescriber who specializes in the management of HAE.

IV. CRITERIA FOR INITIAL APPROVAL

Hereditary angioedema (HAE)
Authorization of 6 months may be granted for prevention of hereditary angioedema attacks when the requested medication will not be used in combination with any other medication used for the prophylaxis of HAE attacks and either of the following criteria is met at the time of diagnosis:
A. Member has C1 inhibitor deficiency or dysfunction as confirmed by laboratory testing and meets one of the following criteria:
   1. C1 inhibitor (C1-INH) antigenic level below the lower limit of normal as defined by the laboratory performing the test, or

2. Normal C1-INH antigenic level and a low C1-INH functional level (functional C1-INH less than 50% or C1-INH functional level below the lower limit of normal as defined by the laboratory performing the test).

B. Member has normal C1 inhibitor as confirmed by laboratory testing and meets one of the following criteria:
   1. Member has an F12, angiopoietin-1, plasminogen, kininogen-1 (KNG1), heparan sulfate-glucosamine 3-O-sulfotransferase 6 (HS3ST6), or myoferlin (MYOF) gene mutation as confirmed by genetic testing, or
   2. Member has a documented family history of angioedema and the angioedema was refractory to a trial of high-dose antihistamine therapy (i.e., cetirizine at 40 mg per day or the equivalent) for at least one month.

V. CONTINUATION OF THERAPY

Authorization of 6 months may be granted for continuation of therapy when all of the following criteria are met:
A. Member meets the criteria for initial approval.
B. Member has experienced a significant reduction in frequency of attacks (e.g., ≥ 50%) since starting treatment.
C. Member has reduced the use of medications to treat acute attacks since starting treatment.

VI. REFERENCES

1. Orladeyo [package insert]. Durham, NC: BioCryst Pharmaceuticals, Inc.; December 2020.
2. Maurer M, Magerl M, Ansotegui I, et al. The international WAO/EAACI guideline for the management of hereditary angioedema – the 2021 revision and update. *Allergy*. 2022 Jan 10. doi: 10.1111/all. 15214. Online ahead of print.
3. Henao MP, Kraschnewski J, Kelbel T, Craig T. Diagnosis and screening of patients with hereditary angioedema in primary care. *Therapeutics and Clin Risk Management.* 2016; 12: 701-711.
4. Zuraw B, Lumry WR, Johnston DT, et al. Oral once-daily berotralstat for the prevention of hereditary angioedema attacks: A randomized, double-blind, placebo-controlled phase 3 trial. *J Allergy Clin Immunol*. 2020;S0091-6749(20)31484-6.
5. Busse PJ, Christiansen, SC, Riedl MA, et al. US HAEA Medical Advisory Board 2020 Guidelines for the Management of Hereditary Angioedema. *J Allergy Clin Immunol: In Practice.* 2021 Jan;9(1):132-150.e3.
6. Sharma J, Jindal AK, Banday AZ, et al. Pathophysiology of Hereditary Angioedema (HAE) Beyond the SERPING1 Gene [published online ahead of print, 2021 Jan 14] [published correction appears in Clin Rev Allergy Immunol. 2021 Feb 17]. *Clin Rev Allergy Immunol*. 2021;10.1007/s12016-021-08835-8. Doi:10.1007/s12016-021-08835-8.
7. Kanani, A., Schellenberg, R. & Warrington, R. Urticaria and angioedema. *All Asth Clin Immun* 7, S9 (2011), Table 2.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME*
(generic)

OSPHENA
(ospemifene)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

POLICY

FDA-APPROVED INDICATIONS

Osphena is indicated for:

- The treatment of moderate to severe dyspareunia, a symptom of vulvar and vaginal atrophy, due to menopause.
- The treatment of moderate to severe vaginal dryness, a symptom of vulvar and vaginal atrophy, due to menopause.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for the treatment of any of the following: A) Moderate to severe dyspareunia (pain during sexual intercourse) due to menopause, B) Moderate to severe vaginal dryness due to menopause

REFERENCES

1. Osphena [package insert]. Florham Park, NJ: Shionogi Inc.; January 2019.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2021; Accessed December 2, 2021.
3. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed December 2, 2021.

Reference number(s)
2002-A

SPECIALTY GUIDELINE MANAGEMENT

OTEZLA (apremilast)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

A. Adult patients with plaque psoriasis who are candidates for phototherapy or systemic therapy
B. Adults with active psoriatic arthritis
C. Adults with oral ulcers associated with Behcet's disease

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

A. Plaque psoriasis
    1. Initial requests:
        i. Chart notes, medical record documentation, or claims history supporting previous medications tried (if applicable), including response to therapy. If therapy is not advisable, documentation of clinical reason to avoid therapy.
    2. Continuation requests: Chart notes or medical record documentation of improvement in signs and symptoms.

B. Psoriatic arthritis: For continuation requests: Chart notes or medical record documentation supporting positive clinical response.

C. Behcet's disease (initial requests only): Chart notes, medical record documentation, or claims history supporting previous medications tried, including response to therapy (if applicable).

III. CRITERIA FOR INITIAL APPROVAL

A. Plaque psoriasis (PsO)

1. Authorization of 12 months may be granted for the treatment of plaque psoriasis in members when one of the following criteria is met:
    i. Member has previously received a biologic indicated for the treatment of plaque psoriasis.
    ii. Member has had an inadequate response or intolerance to ONE of the following:
        a. Phototherapy (e.g., UVB, PUVA)

b. Topical therapies (e.g., medium or higher potency topical corticosteroids [see Appendix A], calcineurin inhibitors, vitamin D analogs)

iii. Member has a contraindication or clinical reason to avoid BOTH of the following:
   a. Phototherapy (e.g., UVB, PUVA)
   b. Topical therapies (e.g., medium or higher potency topical corticosteroids, calcineurin inhibitors, vitamin D analogs)

iv. Member has had an inadequate response to or intolerance to pharmacological treatment with ONE of the following medications: methotrexate, cyclosporine, or acitretin.

v. Member has a clinical reason to avoid pharmacological treatment with ALL of the following medications: methotrexate, cyclosporine, and acitretin (see Appendix B).

B. Active psoriatic arthritis (PsA)

Authorization of 12 months may be granted for treatment of active psoriatic arthritis.

C. Behcet's disease

1. Authorization of 12 months may be granted for members who have previously received a biologic indicated for the treatment of Behcet's disease.
2. Authorization of 12 months may be granted for the treatment of oral ulcers associated with Behcet's disease when the member has had an inadequate response to at least one nonbiologic medication for Behcet's disease (e.g., colchicine, systemic glucocorticoids, azathioprine).

IV. CONTINUATION OF THERAPY

A. Plaque psoriasis (PsO)

Authorization of 12 months may be granted for all members (including new members) who are using the requested medication for plaque psoriasis and who achieve or maintain positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition when any of the following is met:

1. Reduction in body surface area (BSA) affected from baseline
2. Improvement in signs and symptoms from baseline (e.g., itching, redness, flaking, scaling, burning, cracking, pain)

B. Active psoriatic arthritis (PsA)

Authorization of 12 months may be granted for all members (including new members) who are using the requested medication for active psoriatic arthritis and who achieve or maintain positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition when there is improvement in any of the following from baseline:

1. Number of swollen joints
2. Number of tender joints
3. Dactylitis
4. Enthesitis
5. Skin and/or nail involvement

C. Behcet's disease

Authorization of 12 months may be granted for all members (including new members) who achieve or maintain positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition.

V. OTHER

For all indications: Member cannot use the requested medication concomitantly with any other biologic DMARD or targeted synthetic DMARD.

VI. DOSAGE AND ADMINISTRATION

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

VII. APPENDIX

A. Table. Relative potency of select topical corticosteroid products

Potency	Drug	Dosage form	Strength
I. Super-high potency (group 1)	Augmented betamethasone dipropionate	Ointment, Lotion, Gel	0.05%
	Clobetasol propionate	Cream, Gel, Ointment, Solution, Cream (emollient), Lotion, Shampoo, Foam, Spray	0.05%
	Fluocinonide	Cream	0.1%
	Flurandrenolide	Tape	4 mcg/cm^2
	Halobetasol propionate	Cream, Lotion, Ointment, Foam	0.05%
II. High potency (group 2)	Amcinonide	Ointment	0.1%
	Augmented betamethasone dipropionate	Cream	0.05%
	Betamethasone dipropionate	Ointment	0.05%
	Clobetasol propionate	Cream	0.025%
	Desoximetasone	Cream, Ointment, Spray	0.25%
		Gel	0.05%
	Diflorasone diacetate	Ointment, Cream (emollient)	0.05%
	Fluocinonide	Cream, Ointment, Gel, Solution	0.05%
	Halcinonide	Cream, Ointment	0.1%
	Halobetasol propionate	Lotion	0.01%
Potency	**Drug**	**Dosage form**	**Strength**
III. High potency (group 3)	Amcinonide	Cream, Lotion	0.1%
	Betamethasone dipropionate	Cream, hydrophilic emollient	0.05%
	Betamethasone valerate	Ointment	0.1%
		Foam	0.12%
	Desoximetasone	Cream, Ointment	0.05%
	Diflorasone diacetate	Cream	0.05%
	Fluocinonide	Cream, aqueous emollient	0.05%
	Fluticasone propionate	Ointment	0.005%
	Mometasone furoate	Ointment	0.1%
	Triamcinolone acetonide	Cream, Ointment	0.5%
IV. Medium potency (group 4)	Betamethasone dipropionate	Spray	0.05%
	Clocortolone pivalate	Cream	0.1%
	Fluocinolone acetonide	Ointment	0.025%

Potency	Drug	Dosage form	Strength
	Flurandrenolide	Ointment	0.05%
	Hydrocortisone valerate	Ointment	0.2%
	Mometasone furoate	Cream, Lotion, Solution	0.1%
	Triamcinolone acetonide	Cream	0.1%
		Ointment	0.05% and 0.1%
		Aerosol Spray	0.2 mg per 2-second spray
V. Lower-mid potency (group 5)	Betamethasone dipropionate	Lotion	0.05%
	Betamethasone valerate	Cream	0.1%
	Desonide	Ointment, Gel	0.05%
	Fluocinolone acetonide	Cream	0.025%
	Flurandrenolide	Cream, Lotion	0.05%
	Fluticasone propionate	Cream, Lotion	0.05%
	Hydrocortisone butyrate	Cream, Lotion, Ointment, Solution	0.1%
	Hydrocortisone probutate	Cream	0.1%
	Hydrocortisone valerate	Cream	0.2%
	Prednicarbate	Cream (emollient), Ointment	0.1%
	Triamcinolone acetonide	Lotion	0.1%
		Ointment	0.025%
VI. Low potency (group 6)	Alclometasone dipropionate	Cream, Ointment	0.05%
	Betamethasone valerate	Lotion	0.1%
	Desonide	Cream, Lotion, Foam	0.05%
	Fluocinolone acetonide	Cream, Solution, Shampoo, Oil	0.01%
	Triamcinolone acetonide	Cream, lotion	0.025%
VII. Least potent (group 7)	Hydrocortisone (base, less than 2%)	Cream, Ointment, Solution	2.5%
		Lotion	2%
		Cream, Ointment, Gel, Lotion, Spray, Solution	1%
		Cream, Ointment	0.5%
	Hydrocortisone acetate	Cream	2.5%
		Lotion	2%
		Cream	1%

B. Examples of Clinical Reasons to Avoid Pharmacologic Treatment with Methotrexate, Cyclosporine or Acitretin

1. Clinical diagnosis of alcohol use disorder, alcoholic liver disease, or other chronic liver disease
2. Breastfeeding
3. Drug interaction
4. Cannot be used due to risk of treatment-related toxicity
5. Pregnancy or currently planning pregnancy
6. Significant comorbidity prohibits use of systemic agents (examples include liver or kidney disease, blood dyscrasias, uncontrolled hypertension)

VIII. REFERENCES

1. Otezla [package insert]. Thousand Oaks, CA: Amgen Inc.; December 2021.
2. Coates LC, Kavanaugh A, Mease PJ, et al. Group for research and assessment of psoriasis and psoriatic arthritis 2015 treatment recommendation for psoriatic arthritis. *Arthritis Rheumatol*. 2016 May;68(5):1060-71.
3. Menter A, Gelfand JM, Connor C, et al. Joint AAD-NPF guidelines of care for the management of psoriasis with systemic nonbiologic therapies. *J Am Acad Dermatol.* 2020;82(6):1445-1486
4. Gossec L, Baraliakos X, Kerschbaumer A, et al. European League Against Rheumatism (EULAR) recommendations for the management of psoriatic arthritis with pharmacological therapies: 2019 update. *Ann Rheum Dis*. 2020;79(6):700-712.
5. Singh JA, Guyatt G, Ogdie A, et al. 2018 American College of Rheumatology/National Psoriasis Foundation Guideline for the Treatment of Psoriatic Arthritis. *Arthritis Rheum.* 2018;71:5-32
6. Hatemi G, Christensen R, Bodaghi, et al. 2018 update of the EULAR recommendations for the management of Behcet's syndrome. Ann Rheum Dis. 2018.; 77: 808-818.
7. ClinicalTrials.gov. National Library of Medicine (US). Identifier NCT03721172, Apremilast as a direct treatment for mild-to-moderate plaque psoriasis versus placebo: an analysis of clinical safety and efficacy (ADVANCE). Available from: https://www.clinicaltrials.gov/ct2/show/NCT03721172.
8. Elmets CA, Korman NJ, Prater EF, et al. Joint AAD-NPF Guidelines of care for the management and treatment of psoriasis with topical therapy and alternative medicine modalities for psoriasis severity measures. *J Am Acad Dermatol.* 2021;84(2):P432-470.
9. Topical Corticosteroids. *Drug Facts and Comparisons.* Facts & Comparisons [database online]. St. Louis, MO: Wolters Kluwer Health Inc; January 15, 2020. Accessed January 27, 2022.

Reference number(s)
2019-A

SPECIALTY GUIDELINE MANAGEMENT

OTREXUP (methotrexate injection)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

1. Rheumatoid Arthritis (RA) including Polyarticular Juvenile Idiopathic Arthritis (pJIA)
   Otrexup is indicated in the management of selected adults with severe, active rheumatoid arthritis (RA) or children with active polyarticular juvenile idiopathic arthritis (pJIA), who have had an insufficient therapeutic response to, or are intolerant of, an adequate trial of first-line therapy including full dose non-steroidal anti-inflammatory agents (NSAIDs).
2. Psoriasis
   Otrexup is indicated in adults for the symptomatic control of severe, recalcitrant, disabling psoriasis that is not adequately responsive to other forms of therapy, but only when the diagnosis has been established, as by biopsy and/or after dermatologic consultation. It is important to ensure that a psoriasis "flare" is not due to an undiagnosed concomitant disease affecting immune responses.

   Limitations of use: *Otrexup is not indicated for the treatment of neoplastic diseases*

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

A. Chart notes, medical record documentation, or claims history supporting previous use of generic oral methotrexate and inadequate response or intolerance to therapy.
B. Chart notes or medical record documentation of member's inability to prepare and administer generic injectable methotrexate.

III. CRITERIA FOR INITIAL APPROVAL

Authorization of 12 months may be granted for treatment of rheumatoid arthritis (RA), polyarticular juvenile idiopathic arthritis (pJIA), or psoriasis when BOTH of the following criteria are met:
A. Member has tried and had an inadequate response or intolerance to generic oral methotrexate.
B. Member has inability to prepare and administer generic injectable methotrexate.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for all members (including new members) who meet ALL initial authorization criteria and achieve or maintain positive clinical response after at least 3 months of therapy with Otrexup as evidenced by low disease activity or improvement in signs and symptoms of the condition.

V. REFERENCES

1. Otrexup [package insert]. Ewing, NJ: Antares Pharma, Inc.; December 2019.
2. Fraenkel L, Bathon JM, England BR, et al. 2021 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. *Arthritis Care Res (Hoboken).* 2021;73(7):924-939.
3. Smolen JS, Landewé R, Billsma J, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2019 update. *Ann Rheum Dis.* 2020*;79*:685-699.
4. Ringold, S, Angeles-Han, S, Beukelman, T, et al. 2019 American College of Rheumatology recommendations for the treatment of juvenile idiopathic arthritis: Therapeutic approaches for non-systemic polyarthritis, sacroilitis, and enthesitis. *Arthritis Care Res*. 2019;71(6):717-734.
5. Menter A, Korman NJ, Elmets CA, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis. Section 4: Guidelines of care for the management and treatment of psoriasis with traditional systemic agents. *J Am Acad Dermatol.* 2009;61:451-485.

STEP THERAPY CRITERIA

BRAND NAME
(generic)

OVIDE
(malathion)

Status: CVS Caremark Criteria
Type: Initial Step Therapy; Post Step Therapy Prior Authorization

POLICY

FDA-APPROVED INDICATIONS
Ovide Lotion is indicated for patients infected with *Pediculus humanus capitis* (head lice and their ova) of the scalp hair.

INITIAL STEP THERAPY*
**Include Rx and OTC products unless otherwise stated.*

If the patient has filled a prescription for at least a 1 day supply of permethrin 1% within the past 60 days under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit. If the patient does not meet the initial step therapy criteria, then the claim will reject with a message indicating that a prior authorization (PA) is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

COVERAGE CRITERIA
The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for the treatment of *Pediculus humanus capitis* (head lice and their ova) of the scalp hair
  AND
  - The patient has experienced an inadequate treatment response to permethrin 1%
    OR
  - The patient has experienced an intolerance to permethrin 1%
    OR
  - The patient has a contraindication that would prohibit a trial of permethrin 1%
    OR
  - There is a local pattern of known or suspected resistance to permethrin 1%

REFERENCES

1. Ovide [package insert]. Hawthorne, NY: Taro Pharmaceuticals U.S.A., Inc.; March 2017.
2. Nix [package insert]. Tarrytown NY: Insight Pharmaceuticals LLC.; April 2020.
3. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2023; Accessed January 25,2023.
4. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed January 25, 2023.
5. Devore CD, Schutze GE. Council on School Health and Committee on Infectious Diseases, American Academy of Pediatrics. Head lice. *Pediatrics*. 2015;135(5):e1355-65. Erratum in: *Pediatrics.* 2015;136(4):781-2.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME
(generic)

(oxandrolone)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

POLICY

FDA-APPROVED INDICATIONS

Oxandrolone tablets are indicated as adjunctive therapy to promote weight gain after weight loss following extensive surgery, chronic infections, or severe trauma, and in some patients who without definite pathophysiologic reasons fail to gain or to maintain normal weight, to offset the protein catabolism associated with prolonged administration of corticosteroids, and for the relief of bone pain frequently accompanying osteoporosis.

Compendial Uses
Cachexia associated with AIDS (HIV wasting)[2-4]
To enhance growth in patients with Turner Syndrome[3-5]

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for any of the following: A) As adjunctive therapy to promote weight gain after weight loss following extensive surgery, chronic infections or severe trauma, B) To offset the protein catabolism associated with prolonged administration of corticosteroids, C) For the relief of bone pain accompanying osteoporosis, D) Cachexia associated with acquired immunodeficiency syndrome (AIDS) (human immunodeficiency virus [HIV] wasting)
  OR
- The requested drug is being prescribed to enhance growth in patients with Turner Syndrome

REFERENCES

1. Oxandrolone [package insert]. Maple Grove, MN: Upsher-Smith Laboratories, LLC; June 2020.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2022; Accessed December 11, 2022.
3. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed December 11, 2022.
4. Orphan Products Designations and Approvals. Available at: https://www.accessdata.fda.gov/scripts/opdlisting/oopd/Detailed.cfm. Accessed December 2022.
5. Gravholt CH, Andersen NH, Conway GS, et al. Clinical practice guidelines for the care of girls and women with Turner syndrome: proceedings from the 2016 Cincinnati International Turner Syndrome Meeting. *Eur J Endocrinol*. 2017;177(3):G1–G170. Available at: http://www.eje-online.org/content/177/3/G1.full. (Endorsed on September 2017 by the American Academy of Pediatrics. *Pediatrics.* 2017;140(5): e20172626).

Reference number(s)
3426-A

SPECIALTY GUIDELINE MANAGEMENT

OXBRYTA (voxelotor)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Oxbryta is indicated for the treatment of sickle cell disease (SCD) in adults and pediatric patients 4 years of age and older.

All other indications are considered experimental/investigational and not medically necessary.

II. PRESCRIBER SPECIALTIES

Oxbryta must be prescribed by or in consultation with a hematologist or specialist in sickle cell disease.

III. CRITERIA FOR INITIAL APPROVAL

Sickle cell disease (SCD)
Authorization of 6 months may be granted for treatment of sickle cell disease in members 4 years of age or older with a pretreatment hemoglobin level of 10.5 g/dL or less, when either of the following criteria is met:

A. Member has sickle hemoglobin C (HbSC) or sickle β^+-thalassemia (HbSβ^+) genotype
B. Member has homozygous hemoglobin S (HbSS) or sickle β^0-thalassemia (HbSβ^0) genotype AND meets any of the following:
    1. Has experienced, at any time in the past, an inadequate response or intolerance to a trial of hydroxyurea.
    2. Has a contraindication to hydroxyurea.
    3. Will be using Oxbryta with concurrent hydroxyurea therapy.

Note: Requirements regarding pretreatment hemoglobin level exclude values due to a recent transfusion.

IV. CONTINUATION OF THERAPY

Sickle cell disease (SCD)
Authorization of 12 months may be granted for continued treatment in members experiencing benefit from therapy demonstrated by increased hemoglobin levels or maintenance of increased hemoglobin levels since starting treatment.

V. REFERENCES

1. Oxbryta [package insert]. South San Francisco, CA: Global Blood Therapeutics, Inc.; December 2021.

2. Vichinsky E, Hoppe CC, Ataga KI, et al. A phase 3 randomized trial of voxelotor in sickle cell disease. *N Engl J Med.* 2019 Aug 8;381(6):509-519.

Reference number(s)
2869-A

SPECIALTY GUIDELINE MANAGEMENT

OXERVATE (cenegermin-bkbj)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Oxervate is a recombinant human nerve growth factor indicated for the treatment of neurotrophic keratitis.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Neurotrophic keratitis
Authorization of 8 weeks total per eye may be granted for treatment of Stage 2 and Stage 3 neurotrophic keratitis when all of the following criteria are met:

A. The member must experience persistent epithelial defects (PED) or corneal ulceration of at least 2 weeks duration refractory to one or more conventional non-surgical treatments (e.g., preservative free artificial tears).
B. There is evidence of decreased corneal sensitivity (less than or equal to 4 cm using the Cochet-Bonnet aesthesiometer) within the area of the PED or corneal ulcer and outside of the area of the defect in at least one corneal quadrant.
C. The member has not received a previous 8-week course of Oxervate in the affected eye.

REFERENCES

1. Oxervate [package insert]. Boston, MA: Dompe U.S. Inc.; October 2019.
2. Evaluation of Safety and Efficacy of rhNGF in Patients With Stage 2 and 3 Neurotrophic Keratitis. (REPARO). Available at: https://clinicaltrials.gov/ct2/show/NCT01756456. Accessed October 19, 2021.

Reference number(s)
2585-A

SPECIALTY GUIDELINE MANAGEMENT

PALYNZIQ (pegvaliase-pqpz)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Palynziq is indicated to reduce blood phenylalanine (Phe) concentrations in adult patients with phenylketonuria who have uncontrolled blood Phe concentrations greater than 600 micromol/L on existing management.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: blood phenylalanine concentration greater than 600 micromol/L or genetic testing results supporting diagnosis.

III. CRITERIA FOR INITIAL APPROVAL

Phenylketonuria (PKU)
Authorization of 6 months may be granted for members when baseline blood phenylalanine concentration, prior to initiation of the requested medication, is greater than 600 micromol/L.

Note: If Palynziq is initiated in a member currently receiving Kuvan for phenylketonuria (PKU), then Kuvan will be discontinued after an appropriate period of overlap.

IV. CONTINUATION OF THERAPY

Phenylketonuria (PKU)
A. Authorization of 12 months may be granted for members who have achieved a clinical response as evidenced by achieving a blood phenylalanine concentration of less than or equal to 600 micromol/L.
B. Authorization of 6 months may be granted for members who have not achieved an adequate clinical response to treatment with Palynziq of blood phenylalanine concentration less than or equal to 600 micromol/L and the member meets one of the following requirements:
    1. Member has not been titrated to the maximum allowed dose of 60 mg once daily.
    2. Member has received less than 16 weeks of continuous treatment at the maximum allowed dose of 60 mg once daily.

Note: Palynziq should not be used concomitantly with Kuvan for phenylketonuria (PKU).

V. REFERENCES

1. Palynziq [package insert]. Novato, CA: BioMarin Pharmaceutical Inc.; November 2020.

PRIOR AUTHORIZATION CRITERIA

DRUG CLASS	**PANCREATIC ENZYMES**
BRAND NAME* **(generic)**	**CREON (pancrelipase)**
	PANCREAZE (pancrelipase)
	PERTZYE (pancrelipase)
	VIOKACE (pancrelipase)
	ZENPEP (pancrelipase)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization ***Ref # 3134-A***

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Creon
Creon (pancrelipase) is indicated for the treatment of exocrine pancreatic insufficiency due to cystic fibrosis, chronic pancreatitis, pancreatectomy, or other conditions.

Pancreaze, Pertzye, Zenpep
Pancreaze, Pertzye, and Zenpep (pancrelipase) are indicated for the treatment of exocrine pancreatic insufficiency due to cystic fibrosis or other conditions.

Viokace
Viokace (pancrelipase) tablets, in combination with a proton pump inhibitor, is indicated in adults for the treatment of exocrine pancreatic insufficiency due to chronic pancreatitis or pancreatectomy.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for the treatment of exocrine pancreatic insufficiency due to cystic fibrosis, chronic pancreatitis, pancreatectomy, or other conditions
  AND
- If the request is for Viokace, the patient will take with a proton pump inhibitor (PPI)

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Creon (pancrelipase) is indicated for the treatment of exocrine pancreatic insufficiency due to cystic fibrosis, chronic pancreatitis, pancreatectomy, or other conditions.[1] Pancreaze, Pertzye, and Zenpep (pancrelipase) are indicated for the treatment of exocrine pancreatic insufficiency due to cystic fibrosis or other conditions.[2,3,5] Viokace (pancrelipase) tablets, in combination with a proton pump inhibitor, is indicated in adults for the treatment of exocrine pancreatic insufficiency due to chronic pancreatitis or pancreatectomy.[4] Pancrelipase is not effective in the treatment of functional digestive disorders unrelated to pancreatic insufficiency.[6]

REFERENCES

1. Creon [package insert]. North Chicago, IL: AbbVie Inc.; March 2020.
2. Pancreaze [package insert]. Campbell, CA: Vivus, Inc.; April 2021.
3. Pertzye [package insert]. Bethlehem, PA: Digestive Care, Inc.; March 2020.
4. Viokace [package insert]. Madison, NJ: Allergan USA, Inc.; March 2020.
5. Zenpep [package insert]. Madison, NJ: Allergan USA, Inc.; March 2020.
6. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2021; Accessed September 13, 2021.
7. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed September 13, 2021.

Written by: UM Development (KC)
Date Written: 07/2019
Revised: (KC) 09/2019 (no clinical changes), (MAC) 09/2020 (no clinical changes), (JK) 09/2021 (no clinical changes)
Reviewed: Medical Affairs (CHART) 08/08/19, 09/26/19, 09/24/20, 09/30/21
External Review: 08/2019, 12/2019, 12/2020, 12/2021

CRITERIA FOR APPROVAL

1	Is the requested drug being prescribed for the treatment of exocrine pancreatic insufficiency due to cystic fibrosis, chronic pancreatitis, pancreatectomy, or other conditions? [If no, then no further questions.]	Yes	No
2	Is this request for Viokace (pancrelipase)? [If no, then no further questions.]	Yes	No
3	Will the patient take Viokace (pancrelipase) with a proton pump inhibitor (PPI)?	Yes	No

Mapping Instructions			
	Yes	**No**	**DENIAL REASONS – DO NOT USE FOR MEDICARE PART D**
1.	Go to 2	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you meet the following condition: - You have pancreatic insufficiency caused by another condition Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]
2.	Go to 3	Approve, 12 months	
3.	Approve, 12 months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you will be taking a proton pump inhibitor (PPI) with Viokace. Your request has been denied based on the information we have. [Short Description: Not taking Viokace with a PPI]

Reference number(s)
2574-A

SPECIALTY GUIDELINE MANAGEMENT

PCSK9i
PRALUENT (alirocumab), REPATHA (evolocumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
A. Members with established atherosclerotic cardiovascular disease.
B. Members with an untreated LDL-C of greater than, or equal to, 190 mg/dL.
C. Members with familial hypercholesterolemia.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Clinical atherosclerotic cardiovascular disease (ASCVD)
Authorization of 12 months may be granted for treatment of ASCVD when all of the following criteria are met:
1. The member has a history of clinical atherosclerotic cardiovascular disease or has experienced a cardiovascular event
2. The member has a current LDL-C level greater than, or equal to, 70 mg/dL
3. The member is receiving maximally tolerated statin therapy or is statin intolerant

B. Primary hyperlipidemia
Authorization of 12 months may be granted for treatment of primary hyperlipidemia when all of the following criteria are met:
1. The member had an untreated (before any lipid lowering therapy) LDL-C level greater than, or equal to, 190 mg/dL
2. The member has a current LDL-C level greater than, or equal to, 100 mg/dL
3. The member is receiving maximally tolerated statin therapy or is statin intolerant

C. Familial hypercholesterolemia
Authorization of 12 months may be granted for treatment of heterozygous familial hypercholesterolemia (HeFH) or homozygous familial hypercholesterolemia (HoFH) when all of the following criteria are met:
1. The member meets one of the following criteria:
   a. The member is 18 years of age or older and had an untreated (before any lipid lowering therapy) LDL-C level greater than, or equal to, 190 mg/dL
   b. The member is less than 18 years of age and had an untreated (before any lipid lowering therapy) LDL-C level greater than, or equal to, 160 mg/dL
2. The member has a current LDL-C level greater than, or equal to, 100 mg/dL
3. The member is receiving maximally tolerated statin therapy or is statin intolerant

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for members who are continuing therapy with a PCSK9i.

IV. REFERENCES

1. Repatha [package insert]. Thousand Oaks, CA: Amgen, Inc.; September 2021.
2. Praluent [package insert]. Tarrytown, NY: Regeneron Pharmaceuticals, Inc.; April 2021.
3. Stone NJ, Robinson JG, Lichtenstein AH, et al. 2013 ACC/AHA guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation. 2014;129:S1-S45.
4. Lloyd-Jones DM, Morris PB, Ballantybe CM, et al. 2017 Focused Update of the 2016 ACC expert consensus decision pathway on the role of non-statin therapies for LDL-cholesterol lowering in the management of atherosclerotic cardiovascular disease risk: a report of the American College of Cardiology Task Force on Clinical Expert Consensus Documents. J Am Coll Cardiol. 2017;70:1785-822.
5. Cannon CP, Blazing MA, Giugliano RP, et al. Ezetimibe added to statin therapy after acute coronary syndromes. N Engl J Med. 2015;372:2387-97.
6. Jacobson TA, Ito MK, Maki KC, et al. National Lipid Association recommendations for patient-centered management of dyslipidemia: part 1 — full report. J Clin Lipidol. 2015;9:129–169.
7. Nordestgaard BG, Chapman MJ, Humphries SE, et al. Familial hypercholesterolaemia is underdiagnosed and undertreated in the general population: guidance for clinicians to prevent coronary heart disease. Consensus Statement of the European Atherosclerosis Society. Eur Heart J. 2013;34:3478–3490.
8. Cuchel M, Bruckert E, Ginsberg HN, et al. Homozygous familial hypercholesterolaemia: new insights and guidance for clinicians to improve detection and clinical management. A position paper from the Consensus Panel on Familial Hypercholesterolaemia of the European Atherosclerosis Society. Eur Heart J. 2014;35:2146-2157.
9. Raal FJ, Honarpour N, Blom DJ, et al. Inhibition of PCSK9 with evolocumab in homozygous familial hypercholesterolaemia (TESLA Part B): a randomised, double-blind, placebo-controlled trial. Lancet. 2015;385:341-350.
10. Banach M, Rizzo M, Toth PP, et al. Statin intolerance – an attempt at a unified definition. Position paper from an International Lipid Expert Panel. Arch Med Sci. 2015;11:1-23.
11. Sabatine MC, Giugliano RP, Keech AC, et al. Evolocumab and clinical outcomes in patients with cardiovascular disease. New England Journal of Medicine. 2017; Published online before print.
12. Hulten EA, Carbonaro S, Petrillo SP, et al. Prognostic value of cardiac computed tomography angiography. Journal of the American College of Cardiology. 2011;57(10):1237-1247.
13. Min JK, Labounty TM, Gomez MJ, et al. Incremental prognostic value of coronary computed tomographic angiography over coronary artery calcium score for risk predication of major adverse cardiac events in asymptomatic diabetic individuals. Atherosclerosis. 2014;232(2):298-304.
14. Robinson, J. G., Rogers, W. J., Nedergaard, B. S., Fialkow, J., Neutel, J. M., Ramstad, D., Somaratne, R., Legg, J. C., Nelson, P., Scott, R., Wasserman, S. M. and Weiss, R. (2014), Rationale and Design of LAPLACE-2: A Phase 3, Randomized, Double-Blind, Placebo- and Ezetimibe-Controlled Trial Evaluating the Efficacy and Safety of Evolocumab in Subjects With Hypercholesterolemia on Background Statin Therapy. Clin Cardiol, 37: 195–203.
15. Grundy SM, Stone NJ, Bailey AL, et al. 2018 AHA/ACC guideline on the management of blood cholesterol: report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *J Am Coll Cardiol* 2018.
16. McGowan MP, Hosseini Dehkordi SH, Moriarty PM, et al. Diagnosis and Treatment of Heterozygous Familial Hypercholesterolemia. *J Am Heart Assoc*. 2019; 8:e013225. DOI: 10.1161/JAHA119.013225.

Reference number(s)
2139-A

SPECIALTY GUIDELINE MANAGEMENT

PEGASYS (peginterferon alfa-2a)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
1. Chronic Hepatitis C
   Pegasys, as part of a combination regimen with other hepatitis C virus (HCV) antiviral drugs, is indicated for the treatment of adults with chronic hepatitis C (CHC) and compensated liver disease. Pegasys in combination with ribavirin is indicated for treatment of pediatric patients 5 years of age and older with CHC and compensated liver disease. Pegasys monotherapy is only indicated for the treatment of patients with CHC and compensated liver disease if there are contraindications or significant intolerance to other HCV antiviral drugs.
2. Chronic Hepatitis B
   Pegasys is indicated for the treatment of adult patients with HBeAg-positive and HBeAg-negative chronic hepatitis B (CHB) infection who have compensated liver disease and evidence of viral replication and liver inflammation. Pegasys is indicated for the treatment of HBeAG-positive CHB in non-cirrhotic pediatric patients 3 years of age and older with evidence of viral replication and elevations in serum alanine aminotransferase (ALT).

B. Compendial Uses
1. Myeloproliferative neoplasm (essential thrombocythemia, polycythemia vera, symptomatic lower-risk myelofibrosis)
2. Systemic mastocytosis
3. Adult T-cell leukemia/lymphoma
4. Mycosis fungoides/Sezary syndrome
5. Primary cutaneous CD30+ T-cell lymphoproliferative disorders
6. Hairy cell leukemia
7. Erdheim-Chester disease
8. Chronic myeloid leukemia

All other indications are considered experimental/investigational and not medically necessary.

II. INITIAL CRITERIA FOR APPROVAL

A. Chronic hepatitis C virus (HCV) infection
Refer to the SGM of requested regimen for the specific criteria for approval and approval durations.

B. Chronic hepatitis B virus (HBV) infection (including hepatitis D virus [HDV] coinfection)
Authorization of up to 48 weeks total may be granted for treatment of chronic HBV infection, including HDV coinfection.

C. Myeloproliferative neoplasm
Authorization of 12 months may be granted for treatment of myeloproliferative neoplasm (essential thrombocythemia, polycythemia vera, symptomatic lower-risk myelofibrosis).

D. Systemic mastocytosis
Authorization of 12 months may be granted for treatment of systemic mastocytosis.

E. Adult T-cell leukemia/lymphoma
Authorization of 12 months may be granted for treatment of adult T-cell leukemia/lymphoma.

F. Mycosis fungoides/Sezary syndrome
Authorization of 12 months may be granted for treatment of mycosis fungoides/Sezary syndrome.

G. Primary cutaneous CD30+ T-cell lymphoproliferative disorders
Authorization of 12 months may be granted for the treatment of primary cutaneous CD30+ T-cell lymphoproliferative disorders.

H. Hairy cell leukemia
Authorization of 12 months may be granted for treatment of hairy cell leukemia.

I. Erdheim-Chester disease
Authorization of 12 months may be granted for treatment of Erdheim-Chester disease.

J. Chronic myeloid leukemia
Authorization of 12 months may be granted for treatment of chronic myeloid leukemia in pregnancy.

III. CONTINUATION OF THERAPY

A. Chronic HCV infection and chronic HBV infection (including HDV coinfection)
All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

B. Myeloproliferative neoplasm
Authorization of 12 months may be granted if the member is experiencing benefit from therapy as evidenced by improvement in symptoms and/or disease markers (e.g., morphological response, reduction or stabilization in spleen size, improvement of thrombocytosis/leukocytosis, etc.).

C. Systemic mastocytosis
Authorization of 12 months may be granted if the member is experiencing benefit from therapy as evidenced by improvement in symptoms and/or disease markers (e.g., reduction in serum and urine metabolites of mast cell activation, improvement in cutaneous lesions, skeletal disease, bone marrow mast cell burden, etc.).

D. All other indications
Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for all other indications in Section II, not previously listed, when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

IV. REFERENCES

1. Pegasys [package insert]. South San Francisco, CA: Genentech, Inc; March 2021.
2. The NCCN Drugs & Biologics Compendium® © 2023 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed March 6, 2023.
3. Sovaldi [package insert]. Foster City, CA: Gilead Sciences, Inc.; March 2020.
4. AASLD/IDSA. HCV guidance: Recommendations for testing, managing, and treating hepatitis C. http://www.hcvguidelines.org. Last changes made October 24, 2022. Accessed March 3, 2023.

5. Terrault NA, Bzowej NH, Chang KM, et al. AASLD guidelines for treatment of chronic hepatitis B. *Hepatology*. 2016;63(1):261-283.
6. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology™ Myeloproliferative Neoplasms (Version 3.2022). http://www.nccn.org. Accessed March 8, 2023.
7. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology™ Systemic Mastocytosis (Version 2.2022). http://www.nccn.org. Accessed March 8, 2023.

Reference number(s)
3822-A

SPECIALTY GUIDELINE MANAGEMENT

PEMAZYRE (pemigatinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication
   1. Treatment of adults with previously treated, unresectable locally advanced or metastatic cholangiocarcinoma with a fibroblast growth factor receptor 2 (FGFR2) fusion or other rearrangement as detected by an FDA-approved test.
   2. Treatment of adults with relapsed or refractory myeloid/lymphoid neoplasms (MLNs) with fibroblast growth factor receptor 1 (FGFR1) rearrangement.

B. Compendial Uses
   1. Cholangiocarcinoma
   2. Myeloid/lymphoid neoplasms with eosinophilia and FGFR1 rearrangement in chronic phase or blast phase

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: Documentation of FGFR2 fusion or rearrangement or FGFR1 rearrangement (where applicable)

III. CRITERIA FOR INITIAL APPROVAL

A. Cholangiocarcinoma
Authorization of 12 months may be granted for subsequent treatment of progressive, unresectable or metastatic cholangiocarcinoma with a FGFR2 fusion or rearrangement, when used as a single agent.

B. Myeloid/Lymphoid Neoplasms
Authorization of 12 months may be granted for treatment of myeloid/lymphoid neoplasms with FGFR1 rearrangement.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

V. REFERENCES

1. Pemazyre [package insert]. Wilmington, DE: Incyte Corporation; August 2022.
2. The NCCN Drugs & Biologics Compendium® © 2022 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed July 8, 2022.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME
(generic)

(diclofenac sodium topical solution 1.5%)

PENNSAID
(diclofenac sodium topical solution 2%)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization with Quantity Limit

POLICY

FDA-APPROVED INDICATIONS

Diclofenac Sodium Topical Solution 1.5%
Diclofenac sodium topical solution 1.5% is indicated for the treatment of signs and symptoms of osteoarthritis of the knee(s).

Pennsaid
Pennsaid is indicated for the treatment of the pain of osteoarthritis of the knee(s).

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has osteoarthritis pain of the knee(s)

AND

- Treatment with the requested drug is necessary due to concern about intolerance to oral nonsteroidal anti-inflammatory drugs (NSAIDs)

OR

- Treatment with the requested drug is necessary due to a contraindication to oral nonsteroidal anti-inflammatory drugs (NSAIDs)

Quantity Limits apply.

QUANTITY LIMIT

Drug	4 Week Limit*	12 Week Limit*
Pennsaid (diclofenac sodium topical solution 2%)	224gm (2 bottles, 112 gm each) / 21 days	672 gm (6 bottles, 112gm each) / 63 days
(diclofenac sodium topical solution 1.5%)	300 mL (2 bottles, 150mL each) / 21 days	900 mL (6 bottles, 150mL each) / 63 days

** The duration of 21 days is used for a 28-day fill period and 63 days is used for an 84-day fill period to allow time for refill processing.*

REFERENCES

1. Pennsaid [package insert]. Deerfield, IL: Horizon Therapeutics USA, Inc.; January 2022.
2. Diclofenac Sodium Topical Solution 1.5% [package insert]. Baton Rouge, LA: SOLA Pharmaceuticals, LLC; June 2021.

3. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2022; Accessed May 12, 2022.
4. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed May 12, 2022.
5. Kolasinski SL, Neogi T, Hockberg MC, et al. 2019 American College of Rheumatology/Arthritis Foundation Guideline for the Management of Osteoarthritis of the Hand, Hip and Knee. *Arthritic Care & Research* 2020;72(2):149-162.
6. American Academy of Orthopaedic Surgeons. Management of Osteoarthritis of the Knee (Non-Arthroplasty) Evidence-Based Clinical Practice Guideline (3rd Edition). August 31, 2021.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME
(generic)

CUPRIMINE
(penicillamine)

CUVRIOR
(trientine tetrahydrochloride)

DEPEN
(penicillamine)

SYPRINE
(trientine hydrochloride)

Status: CVS Caremark® Criteria
Type: Initial Prior Authorization

POLICY

FDA-APPROVED INDICATIONS

Cuprimine
Cuprimine is indicated in the treatment of Wilson's disease, cystinuria, and in patients with severe, active rheumatoid arthritis who have failed to respond to an adequate trial of conventional therapy. Available evidence suggests that Cuprimine is not of value in ankylosing spondylitis.

Cuvrior
Cuvrior is indicated for the treatment of adult patients with stable Wilson's disease who are de-coppered and tolerant to penicillamine.

Depen
Depen is indicated in the treatment of Wilson's disease, cystinuria, and in patients with severe, active rheumatoid arthritis who have failed to respond to an adequate trial of conventional therapy. Available evidence suggests that Depen is not of value in ankylosing spondylitis.

Syprine
Syprine is indicated in the treatment of patients with Wilson's disease who are intolerant of penicillamine. Clinical experience with Syprine is limited and alternate dosing regimens have not been well-characterized; all endpoints in determining an individual patient's dose have not been well defined. Syprine and penicillamine cannot be considered interchangeable. Syprine should be used when continued treatment with penicillamine is no longer possible because of intolerable or life endangering side effects.
Unlike penicillamine, Syprine is not recommended in cystinuria or rheumatoid arthritis. The absence of a sulfhydryl moiety renders it incapable of binding cystine and, therefore, it is of no use in cystinuria. In 15 patients with rheumatoid arthritis, Syprine was reported not to be effective in improving any clinical or biochemical parameter after 12 weeks of treatment. Syprine is not indicated for treatment of biliary cirrhosis.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The request is for Cuprimine (penicillamine capsules) or Depen (penicillamine tablets)
  AND
  - The requested drug is being prescribed for the treatment of Wilson's disease
  OR
  - The requested drug is being prescribed for the treatment of cystinuria
  OR
  - The requested drug is being prescribed for the treatment of severe, active rheumatoid arthritis in a patient who has failed to respond to an adequate trial of conventional therapy
    [Note: Conventional therapy for rheumatoid arthritis may include disease-modifying antirheumatic drugs (DMARDs) such as methotrexate, leflunomide, hydroxychloroquine, or sulfasalazine.]

OR

- The request is for trientine hydrochloride (e.g., Syprine)
  AND
  - The requested drug is being prescribed for the treatment of Wilson's disease
  AND
  - The patient has experienced an intolerance to penicillamine

OR

- The request is for Cuvrior (trientine tetrahydrochloride) for the treatment of stable Wilson's disease
  AND
  - The patient is de-coppered
  AND
  - The patient is tolerant to penicillamine

REFERENCES

1. Cuprimine [package insert]. Bridgewater, New Jersey: Bausch Health US, LLC; October 2020.
2. Cuvrior [package insert]. Chicago, Illinois: Orphalan SA; April 2022.
3. Depen [package insert]. Somerset, New Jersey: Meda Pharmaceuticals Inc; January 2019.
4. Syprine [package insert]. Bridgewater, New Jersey: Bausch Health US, LLC; September 2020.
5. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Waltham, MA: UpToDate, Inc.; 2023. https://online.lexi.com. Accessed March 3, 2023.
6. Micromedex (electronic version). Merative, Ann Arbor, Michigan, USA. Available at: https://www.micromedexsolutions.com/ (cited: 03-03-2023).
7. Fraenkel L, Bathon JM, England BR, et al. 2021 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. *Arthritis Care Res*. 2021;73(7):924-939.

Reference number(s)
2121-A

SPECIALTY GUIDELINE MANAGEMENT

BUPHENYL (sodium phenylbutyrate)
PHEBURANE (sodium phenylbutyrate)
sodium phenylbutyrate (generic)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

A. Buphenyl is indicated as adjunctive therapy in the chronic management of patients with urea cycle disorders involving deficiencies of carbamylphosphate synthetase (CPS), ornithine transcarbamylase (OTC), or argininosuccinic acid synthetase (AS). It is indicated in all patients with neonatal-onset deficiency (complete enzymatic deficiency, presenting within the first 28 days of life). It is also indicated in patients with late-onset disease (partial enzymatic deficiency, presenting after the first month of life) who have a history of hyperammonemic encephalopathy. It is important that the diagnosis be made early, and treatment initiated immediately to improve survival. Any episode of acute hyperammonemia should be treated as a life-threatening emergency.

B. Pheburane is indicated as adjunctive therapy to standard of care, which includes dietary management, for the chronic management of adult and pediatric patients with urea cycle disorders (UCDs), involving deficiencies of carbamylphosphate synthetase (CPS), ornithine transcarbamylase (OTC) or argininosuccinic acid synthetase (AS).

Compendial Use

Arginase deficiency

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

A. Initial requests:
   1. Enzyme assay, biochemical, or genetic testing results supporting diagnosis; and
   2. Lab results documenting baseline plasma ammonia levels.

B. Continuation of therapy requests: lab results documenting a reduction in plasma ammonia levels from baseline.

III. CRITERIA FOR INITIAL APPROVAL

Authorization of 12 months may be granted for chronic management of urea cycle disorder (UCD) including arginase deficiency, when both of the following criteria are met:

1. The diagnosis is confirmed by enzymatic, biochemical, or genetic testing.

2. The member has elevated plasma ammonia levels at baseline.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for chronic management of a urea cycle disorder (UCD) including arginase deficiency, who are experiencing benefit from therapy as evidenced by a reduction in plasma ammonia levels from baseline.

V. REFERENCES

1. Buphenyl [package insert]. Lake Forest, IL: Horizon Pharma USA, Inc.; March 2021.
2. Mew NA, Lanpher BC. Urea Cycle Disorders Overview. In: Pagon RA, Adam MP, Ardinger HH, et. al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2017 [updated June 22, 2017]. Available at: https://www.ncbi.nlm.nih.gov/books/NBK1217/?report=printable.
3. Häberle J, Boddaert N, Burlina A, et al. Suggested guidelines for the diagnosis and management of urea cycle disorders. *J Inherit Metab Dis*. 2019;42(6):1192-1230.
4. Wong D, Cederbaum S, Crombez, E. Arginase Deficiency. *GeneReviews*. August 2014; http://www.ncbi.nlm.nih.gov/books/NBK1159/.
5. Clinical Consult: CVS Caremark. Clinical Programs Review. Focus on Enzyme Disorders Programs; January 2021.
6. Pheburane [package insert]. Bryn Mawr, PA: Medunik USA, Inc.; June 2022

Reference number(s)
3089-A

SPECIALTY GUIDELINE MANAGEMENT

PIQRAY (alpelisib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication
Piqray is indicated in combination with fulvestrant for the treatment of postmenopausal women, and men, with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, PIK3CA-mutated, advanced or metastatic breast cancer as detected by an FDA-approved test following progression on or after an endocrine-based regimen.

B. Compendial Uses
Breast cancer: Therapy for recurrent HR-positive, HER2-negative, PIK3CA mutated disease

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
A. Documentation of test confirming presence of PIK3CA mutation
B. Documentation of HR and HER2 status

III. CRITERIA FOR INITIAL APPROVAL

Breast cancer
Authorization of 12 months may be granted for treatment of HR-positive, HER2-negative, PIK3CA-mutated recurrent, advanced or metastatic breast cancer when all of the following criteria are met:
A. The requested drug is used in combination with fulvestrant
B. Disease has progressed while on or after an endocrine-based regimen

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

V. REFERENCES

1. Piqray [package insert]. East Hanover, NJ: Novartis; July 2021.

2. The NCCN Drugs & Biologics Compendium® © 2021 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed December 6, 2021.

Reference number(s)
1881-A

SPECIALTY GUIDELINE MANAGEMENT

ESBRIET (pirfenidone)
pirfenidone (generic)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Indicated for the treatment of idiopathic pulmonary fibrosis (IPF).

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review (where applicable):
A. Result of a chest high-resolution computed tomography (HRCT) study.
B. If a lung biopsy is conducted, submit the associated pathology report.

III. CRITERIA FOR INITIAL APPROVAL

Idiopathic Pulmonary Fibrosis (IPF)
Authorization of 12 months may be granted for treatment of idiopathic pulmonary fibrosis when the member has undergone a diagnostic work-up which includes the following:[2]
A. Other known causes of interstitial lung disease (e.g., domestic and occupational environmental exposures, connective tissue disease, drug toxicity) have been excluded AND
B. The member has completed a high-resolution computed tomography (HRCT) study of the chest or a lung biopsy which reveals a result consistent with the usual interstitial pneumonia (UIP) pattern, OR has completed an HRCT study of the chest which reveals a result other than the UIP pattern (e.g., probable UIP, indeterminate for UIP) and the diagnosis is supported by a lung biopsy. If a lung biopsy has not been previously conducted, the diagnosis is supported by a multidisciplinary discussion between a radiologist and pulmonologist who are experienced in IPF.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for members with an indication listed in Section III who are currently receiving treatment with the requested medication, excluding when the requested medication is obtained as samples or via manufacturer's patient assistance programs.

V. OTHER

Note: If the member is a current smoker, they should be counseled on the harmful effects of smoking on pulmonary conditions and available smoking cessation options.

VI. REFERENCES

1. Esbriet [package insert]. South San Francisco, CA: Genentech USA, Inc.; February 2022.
2. Pirfenidone [package insert.] Berkeley Heights, NJ: Laurus Labs Limited; July 2022
3. Raghu G, Remy-Jardin M, Myers JL, et al. Diagnosis of Idiopathic Pulmonary Fibrosis. An Official ATS/ERS/JRS/ALAT Clinical Practice Guideline. *Am J Respir Crit Care Med*. 2018 Sep 1;198(5):e44-e68.
4. Vancheri C, Kreuter M, Richeldi L, et al. Nintedanib with add-on pirfenidone in idiopathic pulmonary fibrosis: results of the Injourney trial. *Am J Respir Crit Care Med.* 2017 Sept 10. doi: 10.1164/rccm.201706-1301OC. [Epub ahead of print].

Reference number(s)
1844-A

SPECIALTY GUIDELINE MANAGEMENT

PLEGRIDY (peginterferon beta-1a)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Plegridy is indicated for the treatment of patients with relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.

All other indications are considered experimental/investigational and not medically necessary.

II. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with a neurologist.

III. CRITERIA FOR INITIAL APPROVAL

A. Relapsing forms of multiple sclerosis
Authorization of 12 months may be granted to members who have been diagnosed with a relapsing form of multiple sclerosis (including relapsing-remitting and secondary progressive disease for those who continue to experience relapse).

B. Clinically isolated syndrome
Authorization of 12 months may be granted to members for the treatment of clinically isolated syndrome of multiple sclerosis.

IV. CONTINUATION OF THERAPY

For all indications: Authorization of 12 months may be granted for members who are experiencing disease stability or improvement while receiving Plegridy.

V. OTHER

Members will not use Plegridy concomitantly with other disease modifying multiple sclerosis agents (Note: Ampyra and Nuedexta are not disease modifying).

VI. REFERENCE

1. Plegridy [package insert]. Cambridge, MA: Biogen, Inc.; March 2022.

Reference number(s)
2234-A

SPECIALTY GUIDELINE MANAGEMENT

POMALYST (pomalidomide)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
1. Treatment of multiple myeloma, in combination with dexamethasone, in adult patients who have received at least two prior therapies including lenalidomide and a proteasome inhibitor and have demonstrated disease progression on or within 60 days of completion of their last therapy
2. Treatment of adult patients with AIDS-related Kaposi sarcoma (KS) after failure of highly active antiretroviral therapy (HAART) or in adult patients with KS who are HIV-negative

B. Compendial Uses
1. Systemic light chain amyloidosis
2. Primary central nervous system lymphoma
3. POEMS (polyneuropathy, organomegaly, endocrinopathy, monoclonal protein, skin changes) syndrome
4. Multiple myeloma

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Multiple myeloma

Authorization of 12 months may be granted for treatment of multiple myeloma when any of the following criteria are met:
1. The member has previously received at least two prior therapies for multiple myeloma including an immunomodulatory agent and proteasome inhibitor and the requested medication will be used in one of the following regimens:
    i. In combination with elotuzumab and dexamethasone
    ii. In combination with ixazomib and dexamethasone
    iii. In combination with bortezomib and dexamethasone
    iv. In combination with cyclophosphamide and dexamethasone
    v. In combination with isatuximab-irfc and dexamethasone
    vi. In combination with dexamethasone
    vii. In combination with selinexor and dexamethasone
    viii. As a single agent
2. The member has previously received at least one prior therapy for multiple myeloma including an immunomodulatory agent and a proteasome inhibitor and the requested medication will be used in combination with daratumumab and dexamethasone
3. The member has previously received at least one prior therapy for multiple myeloma and the requested medication will be used in combination with carfilzomib and dexamethasone

B. Systemic light chain amyloidosis
Authorization of 12 months may be granted for treatment of relapsed or refractory systemic light chain amyloidosis in combination with dexamethasone.

C. Kaposi Sarcoma
Authorization of 12 months may be granted for the treatment of Kaposi sarcoma when either of the following criteria are met:
1. The requested medication will be used in combination with antiretroviral therapy for the treatment of AIDS-related Kaposi sarcoma
2. Member is HIV-negative

D. Primary central nervous system lymphoma
Authorization of 12 months may be granted for treatment of primary central nervous system lymphoma as a single agent.

E. POEMS syndrome
Authorization of 12 months may be granted for treatment of POEMS syndrome in combination with dexamethasone.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

IV. REFERENCES

1. Pomalyst [package insert]. Summit, NJ: Celgene Corporation; October 2021.
2. The NCCN Drugs & Biologics Compendium® © 2022 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed October 4, 2022.

Reference number(s)
4631-A

SPECIALTY GUIDELINE MANAGEMENT

PONVORY (ponesimod)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Ponvory is indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Relapsing Forms of Multiple Sclerosis
Authorization of 12 months may be granted to members who have been diagnosed with a relapsing form of multiple sclerosis (including relapsing-remitting and secondary progressive disease for those who continue to experience relapse).

B. Clinically Isolated Syndrome
Authorization of 12 months may be granted to members for the treatment of clinically isolated syndrome of multiple sclerosis.

III. CONTINUATION OF THERAPY

For all indications: Authorization of 12 months may be granted to members who are experiencing disease stability or improvement while receiving Ponvory.

IV. OTHER

Members will not use Ponvory concomitantly with other disease modifying multiple sclerosis agents (Note: Ampyra and Nuedexta are not disease modifying).

V. REFERENCES

1. Ponvory [package insert]. Titusville, NJ: Janssen Pharmaceuticals, Inc; March 2021.

QUANTITY LIMIT CRITERIA

DRUG CLASS **PROTON PUMP INHIBITORS**

BRAND NAME (generic)

ACIPHEX (rabeprazole)

ACIPHEX SPRINKLES (rabeprazole)

DEXILANT (dexlansoprazole)

(esomeprazole strontium)

KONVOMEP (omeprazole/sodium bicarbonate)

NEXIUM (esomeprazole)

PREVACID (lansoprazole)

PRILOSEC (omeprazole)

PROTONIX (pantoprazole)

ZEGERID (omeprazole/sodium bicarbonate)

Status: CVS Caremark® Criteria
Type: Quantity Limit

POLICY

FDA APPROVED INDICATIONS

Indication	AcipHex (rabeprazole)	AcipHex Sprinkles (rabeprazole)	Dexilant (dexlansoprazole)	Konvomep (omeprazole/ sodium bicarbonate)	Nexium (esomeprazole) Esomeprazole strontium	Prevacid (lansoprazole)	Prilosec (omeprazole)	Protonix (pantoprazole)	Zegerid (omeprazole/ sodium bicarbonate)
Short-term treatment of	✓					✓	✓		✓

active duodenal ulcer									
Helicobacter pylori eradication to reduce the risk of ulcer recurrence*	✓				✓	✓	✓		
Maintenance of healing of duodenal ulcers						✓			
Short-term treatment of gastric ulcer				✓		✓	✓		✓
Short-term treatment of symptoms associated with GERD	✓	✓	✓		✓	✓	✓	✓	✓
Short-term treatment of erosive esophagitis / GERD	✓		✓		✓	✓	✓	✓	✓
Maintenance healing of erosive esophagitis	✓		✓		✓	✓	✓	✓	✓
Pathological hypersecretory conditions	✓				✓	✓	✓	✓	
Short-term treatment of NSAID-associated gastric ulcer						✓			
Risk reduction of NSAID-associated gastric ulcer					✓	✓			
Risk reduction of upper GI bleeding in critically ill patients				✓					✓ Suspension

*The PPI is used in conjunction with antibiotics.

LIMIT CRITERIA

Limits should accumulate across all drugs and strengths (accumulation does not apply if limit is coded for daily dose).

Drug	Limit*
All products in the PPI drug class, all strengths	90 units of therapy total per 365 days

**If the patient requires more than 90 units of therapy per 365 days, then please refer to the PPI Post Limit PA*

REFERENCES

1. Aciphex [package insert]. Wixom, MI: Woodward Pharma Services LLC; March 2022.
2. Aciphex Sprinkles [package insert]. Rockville, MD: Atyu Therapeutics, LLC/Cerecor, Inc.; December 2020.
3. Dexilant [package insert]. Lexington, MA: Takeda Pharmaceuticals America, Inc.; March 2022.
4. Esomeprazole Strontium [package insert]. Ripley, MS: Sterling Knight Pharmaceuticals LLC; April 2020.
5. Konvomep [package insert]. Woburn, MA: Azurity Pharmaceuticals, Inc.; December 2022.

6. Nexium [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; March 2022.
7. Omeprazole Capsules [package insert]. East Windsor, NJ: Aurobindo Pharma USA, Inc.; February 2022.
8. Prevacid, Prevacid SoluTab [package insert]. Lexington, MA: Takeda Pharmaceuticals America, Inc.; March 2022.
9. Prilosec Granules [package insert]. Zug, Switzerland: Covis Pharma; March 2022.
10. Protonix [package insert]. Philadelphia, PA: Wyeth Pharmaceuticals LLC; March 2022.
11. Zegerid [package insert]. Bridgewater, NJ: Salix Pharmaceuticals; March 2022.
12. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Waltham, MA: UpToDate, Inc.; 2023. https://online.lexi.com. Accessed February 22, 2023.
13. Micromedex (electronic version). Merative, Ann Arbor, Michigan, USA. Available at: https://www.micromedexsolutions.com/ (cited: 02/22/2023).

PRIOR AUTHORIZATION CRITERIA

DRUG CLASS **PROTON PUMP INHIBITORS**

BRAND NAME (generic)

ACIPHEX (rabeprazole)

ACIPHEX SPRINKLES (rabeprazole)

DEXILANT (dexlansoprazole)

(esomeprazole strontium)

KONVOMEP (omeprazole/sodium bicarbonate)

NEXIUM (esomeprazole)

PREVACID (lansoprazole)

PRILOSEC (omeprazole)

PROTONIX (pantoprazole)

ZEGERID (omeprazole/sodium bicarbonate)

Status: CVS Caremark® Criteria
Type: Post Limit Prior Authorization

POLICY

FDA-APPROVED INDICATIONS

Indication	AcipHex (rabeprazole)	AcipHex Sprinkles (rabeprazole)	Dexilant (dexlansoprazole)	Konvomep (omeprazole/ sodium bicarbonate)	Nexium (esomeprazole) Esomeprazole strontium	Prevacid (lansoprazole)	Prilosec (omeprazole)	Protonix (pantoprazole)	Zegerid (omeprazole/ sodium bicarbonate)
Short-term treatment of	✓					✓	✓		✓

active duodenal ulcer									
Helicobacter pylori eradication to reduce the risk of ulcer recurrence*	✓				✓	✓	✓		
Maintenance of healing of duodenal ulcers						✓			
Short-term treatment of gastric ulcer				✓		✓	✓		✓
Short-term treatment of symptoms associated with GERD	✓	✓	✓		✓	✓	✓	✓	✓
Short-term treatment of erosive esophagitis / GERD	✓		✓		✓	✓	✓	✓	✓
Maintenance healing of erosive esophagitis	✓		✓		✓	✓	✓	✓	✓
Pathological hypersecretory conditions	✓				✓	✓	✓	✓	
Short-term treatment of NSAID-associated gastric ulcer						✓			
Risk reduction of NSAID-associated gastric ulcer					✓	✓			
Risk reduction of upper GI bleeding in critically ill patients				✓					✓ Suspension

*The PPI is used in conjunction with antibiotics.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for any of the following: A) Barrett's esophagus as confirmed by biopsy, B) Hypersecretory syndrome, such as Zollinger-Ellison, confirmed with a diagnostic test

OR

- The requested drug is being prescribed for any of the following: A) Endoscopically verified peptic ulcer disease, B) Frequent and severe symptoms of chronic gastroesophageal reflux disease (GERD), C) Atypical symptoms or complications of GERD

OR

- The patient is at high risk for gastrointestinal (GI) adverse events
  [Note: Risk factors for serious GI adverse events include, but are not limited to, the following: chronic nonsteroidal anti-inflammatory drug (NSAID) therapy, history of peptic ulcer disease and/or GI bleeding, treatment with oral corticosteroids, treatment with anticoagulants, poor general health status, or advanced age.]

REFERENCES

1. Aciphex [package insert]. Wixom, MI: Woodward Pharma Services LLC; March 2022.
2. Aciphex Sprinkles [package insert]. Rockville, MD: Atyu Therapeutics, LLC/Cerecor, Inc.; December 2020.
3. Dexilant [package insert]. Lexington, MA: Takeda Pharmaceuticals America, Inc.; March 2022.
4. Esomeprazole Strontium [package insert]. Ripley, MS: Sterling Knight Pharmaceuticals LLC; April 2022.
5. Konvomep [package insert]. Woburn, MA: Azurity Pharmaceuticals, Inc.; December 2022.
6. Nexium [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; March 2022.
7. Omeprazole Capsules [package insert]. East Windsor, NJ: Aurobindo Pharma USA, Inc.; February 2022.
8. Prevacid, Prevacid SoluTab [package insert]. Lexington, MA: Takeda Pharmaceuticals America, Inc.; March 2022.
9. Prilosec Granules [package insert]. Zug, Switzerland: Covis Pharma; March 2022.
10. Protonix [package insert]. Philadelphia, PA: Wyeth Pharmaceuticals LLC; March 2022.
11. Zegerid [package insert]. Bridgewater, NJ: Salix Pharmaceuticals; March 2022.
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13. Micromedex (electronic version). Merative, Ann Arbor, Michigan, USA. Available at: https://www.micromedexsolutions.com/ (cited: 02/22/2023).
14. Shaheen N, Falk G, Iyer P, et al. Diagnosis and Management of Barrett's Esophagus: An Updated ACG Guideline. *Am J Gastroenterol*. 2022; 117:559-587.
15. Katz P, Dunbar K, Schnoll-Sussman F, et al. ACG Clinical Guideline for the Diagnosis and Management of Gastroesophageal Reflux Disease. *Am J Gastroenterol*. 2022; 117:27-56.
16. Falconi M, Eriksson B, Kaltsas G, et al. Consensus guidelines update for the management of functional p-NETs (F-p-NETs) and non-functional p-NETs (NF-p-NETs). Neuroendocrinology. 2016; 103(2): 153–171.
17. Kavitt R, Lipowska A, Anyane-Yeboa A, et al. Diagnosis and Treatment of Peptic Ulcer Disease. The American Journal of Medicine (2019) 132:447−456
18. Lanza FL, Chan F, Quigley E, et al. Guidelines for Prevention of NSAID-Related Ulcer Complications. *Am J Gastroenterol* 2009; 104: 728-738.

Reference number(s)
2519-A

ENHANCED SPECIALTY GUIDELINE MANAGEMENT

PRALUENT (alirocumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

A. Praluent is indicated to reduce the risk of myocardial infarction, stroke, and unstable angina requiring hospitalization in adults with established cardiovascular disease.
B. Praluent is indicated as an adjunct to diet, alone or in combination with other low-density lipoprotein cholesterol (LDL-C)-lowering therapies, in adults with primary hyperlipidemia, including heterozygous familial hypercholesterolemia, to reduce LDL-C.
C. Praluent is indicated as an adjunct to other LDL-C-lowering therapies in adult patients with homozygous familial hypercholesterolemia (HoFH) to reduce LDL-C.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

A. Current LDL-C level for both initial requests and continuation requests. The level must be dated within the six months preceding the authorization request.
B. Untreated (before any lipid lowering therapy) LDL-C level if requesting Praluent to treat primary hyperlipidemia, heterozygous or homozygous familial hypercholesterolemia.
C. Chart notes confirming clinical atherosclerotic cardiovascular disease (ASCVD) if requesting Praluent to treat clinical ASCVD. (See Appendix A).
D. If member has contraindication or intolerance to statins, chart notes confirming the contraindication or intolerance. (See Appendix B and C).

III. CRITERIA FOR INITIAL APPROVAL

A. Clinical atherosclerotic cardiovascular disease (ASCVD)

Authorization of 6 months may be granted for treatment of clinical atherosclerotic cardiovascular disease when both of the following criteria are met:

1. Member has a history of clinical ASCVD (See Appendix A).
2. Member meets at least one of the following criteria:
   a. Member has a current LDL-C level ≥ 70 mg/dL after at least three months of treatment with a high-intensity statin dose in combination with ezetimibe. If the member is unable to tolerate a high-intensity statin dose, a moderate-intensity statin dose may be used.
   b. Member has a current LDL-C level ≥ 70 mg/dL with contraindication or intolerance to statins (See Appendix B and C).

B. Primary hyperlipidemia including heterozygous familial hypercholesterolemia (HeFH)
Authorization of 6 months may be granted for treatment of primary hyperlipidemia including heterozygous familial hypercholesterolemia (HeFH) when both of the following criteria are met:
1. Member had an untreated (before any lipid lowering therapy) LDL-C level ≥ 190 mg/dL in the absence of a secondary cause.
2. Member meets at least one of the following criteria:
   a. Member has a current LDL-C level ≥ 100 mg/dL after at least three months of treatment with a high-intensity statin dose in combination with ezetimibe. If the member is unable to tolerate a high-intensity statin dose, a moderate-intensity statin dose may be used.
   b. Member has a current LDL-C level ≥ 100 mg/dL with contraindication or intolerance to statins (See Appendix B and C).

C. Homozygous familial hypercholesterolemia (HoFH)
Authorization of 6 months may be granted for treatment of homozygous familial hypercholesterolemia when both of the following criteria are met:
1. Member had an untreated (before any lipid lowering therapy) LDL-C level ≥ 190 mg/dL in the absence of a secondary cause.
2. Member meets at least one of the following criteria:
   a. Member has a current LDL-C level ≥ 100 mg/dL after at least three months of treatment with a high-intensity statin dose in combination with ezetimibe. If the member is unable to tolerate a high-intensity statin dose, a moderate-intensity statin dose may be used.
   b. Member has a current LDL-C level ≥ 100 mg/dL with a contraindication or intolerance to statins (See Appendix B and C).

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III who achieve or maintain an LDL-C reduction (e.g., LDL-C is now at goal, robust lowering of LDL-C).

V. APPENDICES

APPENDIX A. Clinical ASCVD
- Acute coronary syndromes
- Myocardial infarction
- Stable or unstable angina
- Coronary or other arterial revascularization procedure (e.g., percutaneous coronary intervention [PCI], coronary artery bypass graft [CABG] surgery)
- Stroke of presumed atherosclerotic origin
- Transient ischemic attack (TIA)
- Non-cardiac peripheral arterial disease of presumed atherosclerotic origin (e.g., carotid artery stenosis, lower extremity PAD)
- Obstructive coronary artery disease (defined as fifty percent or greater stenosis on cardiac computed tomography angiogram or catheterization)
- Coronary Artery Calcium (CAC) Score ≥ 1000

APPENDIX B. Statin-associated muscle symptoms (SAMS) and statin re-challenge

- Score of 7 or higher on the Statin-Associated Muscle Symptom Clinical Index (SAMS-CI)
- Statin-associated elevation in creatine kinase (CK) level ≥ 10 times upper limit of normal (ULN)
  NOTE: Statin re-challenge is NOT required for members who have experienced an elevation of CK level ≥10 times ULN after receiving lipid-lowering therapy (LLT) with a statin.

APPENDIX C. Contraindications to statins

- Active liver disease, including unexplained persistent elevations in hepatic transaminase levels (e.g., alanine transaminase (ALT) level ≥ 3 times ULN)
- Pregnancy or planned pregnancy
- Breastfeeding

VI. REFERENCES

1. Praluent [package insert]. Tarrytown, NY: Regeneron Pharmaceuticals, Inc.; April 2021.
2. Lloyd-Jones DM, Morris PB, Ballantybe CM, et al. 2017 Focused Update of the 2016 ACC expert consensus decision pathway on the role of non-statin therapies for LDL-cholesterol lowering in the management of atherosclerotic cardiovascular disease risk: a report of the American College of Cardiology Task Force on Clinical Expert Consensus Documents. *J Am Coll Cardiol*. 2017;70:1785-822.
3. Cannon CP, Blazing MA, Giugliano RP, et al. Ezetimibe added to statin therapy after acute coronary syndromes. *N Engl J Med*. 2015;372:2387-97.
4. Jacobson TA, Ito MK, Maki KC, et al. National Lipid Association recommendations for patient-centered management of dyslipidemia: part 1 — full report. *J Clin Lipidol*. 2015;9:129–169.
5. Nordestgaard BG, Chapman MJ, Humphries SE, et al. Familial hypercholesterolaemia is underdiagnosed and undertreated in the general population: guidance for clinicians to prevent coronary heart disease. Consensus Statement of the European Atherosclerosis Society. *Eur Heart J*. 2013;34:3478–3490.
6. Cuchel M, Bruckert E, Ginsberg HN, et al. Homozygous familial hypercholesterolaemia: new insights and guidance for clinicians to improve detection and clinical management. A position paper from the Consensus Panel on Familial Hypercholesterolaemia of the European Atherosclerosis Society. *Eur Heart J*. 2014;35:2146-2157.
7. Banach M, Rizzo M, Toth PP, et al. Statin intolerance – an attempt at a unified definition. Position paper from an International Lipid Expert Panel. *Arch Med Sci.* 2015;11:1-23.
8. Sabatine MC, Giugliano RP, Keech AC, et al. Evolocumab and clinical outcomes in patients with cardiovascular disease. *New Engl J Med.* 2017; Published online before print.
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12. Grundy SM, Stone NJ, Bailey AL, et al. 2018 AHA/ACC guideline on the management of blood cholesterol: report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *J Am Coll Cardiol* 2018.
13. Beavers CJ, Kelly MS. Dyslipidemia.In: Murphy Je, Lee MW,eds. Pharmacotherapy Self-Assessment Program, 2019 Book 1. Cardiology. Lenexa, KS: American College of Clinical Pharmacy, 2019:41-42.
14. Blom DJ, Harada-Shiba M, Rubba P, et al. Efficacy and Safety of Alirocumab in Adults With Homozygous Familial Hypercholesterolemia: The ODYSSEY HoFH Trial. J Am Coll Cardiol. 2020 Jul 14;76(2):131-142. doi: 10.1016/j.jacc.2020.05.027. PMID: 32646561.

Reference number(s)
C17990-A

CareFirst: PrEP HIV
Truvada (emtricitabine, tenofovir disoproxil fumarate)
Descovy (emtricitabine, tenofovir alafenamide)

Client Requested: The intent of the criteria is to ensure that patients follow selection elements as established by CareFirst.

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines.

Preexposure prophylaxis (PrEP) is a way for individuals who do not have HIV but who are at very high risk of getting HIV through sex or injection drug use to prevent HIV infection. When taken as a daily pill, PrEP is highly effective at preventing HIV, as they can keep the virus from establishing a permanent infection if individuals are exposed.

In general, first-line therapy for PrEP should be Truvada (emtricitabine / tenofovir disoproxil fumarate [TDF]), due to established efficacy in all persons at risk through sex or injection drug use. Descovy (emtricitabine / tenofovir alafenamide [TAF]) is indicated for PrEP in select populations, excluding those who are at risk from receptive vaginal sex due to lack of efficacy in this population.

Descovy does not provide a clinically significant advantage over Truvada regarding adverse reactions. Both Truvada and Descovy have Warnings/Precautions related to renal toxicity due to the tenofovir component. Patients with preexisting renal impairment and those taking nephrotoxic agents are at increased risk. Truvada is not recommended for PrEP in patients with CrCl <60mL/min; Descovy is not recommended with CrCl <30mL/min. The tenofovir component of both Truvada and Descovy also decreases bone mineral density (BMD) through disruption in vitamin D metabolism. The incidence and negative impact that Descovy [TAF] has on BMD is less than that observed with Truvada [TDF], but may not be clinically significant due to the low incidence of fracture in this patient population. A higher incidence of dyslipidemia has been reported with Descovy [TAF] compared to Truvada [TDF].

Descovy should be reserved for patients with established HIV-1 infection, or for PrEP in individuals who have otherwise had clinically significant adverse reactions to Truvada.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has confirmed positive HIV-1 infection
  OR
- The patient is at risk for sexually acquired HIV-1 infection
  AND
- The patient is not at risk from receptive vaginal sex
  AND
- The patient has a diagnosis of Low Bone Mineral Density, Osteoporosis, Osteopenia, or an estimated CrCl less than 60mL/min
  OR
- The patient has experienced an intolerance to TRUVADA (emtricitabine / tenofovir disoproxil fumarate) for PrEP [documentation required]

Reference number(s)
C17990-A

REFERENCES

1. Descovy [package insert]. Foster City, CA: Gilead Sciences, Inc.; January 2020.
2. Truvada [package insert]. Foster City, CA: Gilead Sciences, Inc.; May 2018.
3. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. http://online.lexi.com/. Accessed June 2020.
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Document History

Created:	Specialty Clinical Development (JL) 02/2020
Revised:	JL 07/2020, 10/2020
Reviewed:	CDPR/ LMS 03/2020, SNG 07/2020, AN 10/2020

The Participating Group signed below hereby accepts and adopts as its own the criteria for use with Prior Authorization, as administered by CVS Caremark.

_____ _____

Signature Date

_____

Client Name

Reference number
2095-A

SPECIALTY GUIDELINE MANAGEMENT

PROCYSBI (cysteamine bitartrate delayed-release)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Procysbi is indicated for the treatment of nephropathic cystinosis in adults and pediatric patients 1 year of age and older.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

A. Initial requests: assay detecting increase cystine concentration in leukocytes or genetic testing results supporting diagnosis.
B. Continuation requests: lab results or chart notes documenting a positive response to therapy (e.g., improvement, stabilization, or slowing of disease progression for serum creatinine, calculated creatinine clearance, leukocyte cystine concentration, or maintained growth [height]).

III. CRITERIA FOR INITIAL APPROVAL

Nephropathic cystinosis
Authorization of 12 months may be granted for treatment of nephropathic cystinosis when all of the following criteria are met:

A. Diagnosis of cystinosis was confirmed by the presence of increased cystine concentration in leukocytes or by genetic testing; and
B. Member is 1 year of age or older; and
C. Member will not use Procysbi in combination with Cystagon.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for nephropathic cystinosis who are responding to therapy (e.g., improvement, stabilization, or slowing of disease progression for serum creatinine, calculated creatinine clearance, leukocyte cystine concentration, or maintained growth [height]).

V. REFERENCES

1. Procysbi [package insert]. Deerfield, IL: Horizon Therapeutics USA Inc; March 2021.
2. Ivanova E, De Leo MG, De Matteis MA, Levtchenko E. Cystinosis: clinical presentation, pathogenesis, and treatment. *Pediatr Endocrinol Rev.* 2014;12(1):176-184.

Reference number(s)
1928-A

SPECIALTY GUIDELINE MANAGEMENT

PROMACTA (eltrombopag)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
1. Treatment of thrombocytopenia in adult and pediatric patients 1 year and older with persistent or chronic immune thrombocytopenia (ITP) who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy
2. Treatment of thrombocytopenia in patients with chronic hepatitis C to allow the initiation and maintenance of interferon-based therapy
3. First-line treatment of severe aplastic anemia in adult and pediatric patients 2 years and older in combination with standard immunosuppressive therapy
4. Treatment of patients with severe aplastic anemia who have had an insufficient response to immunosuppressive therapy

B. Compendial Uses
1. MYH9-related disease with thrombocytopenia
2. Myelodysplastic syndromes, for lower risk disease in patients with severe or refractory thrombocytopenia following disease progression or no response to hypomethylating agents, immunosuppressive therapy, or clinical trial.
3. Myelodysplastic syndromes, in combination with equine anti-thymocyte globulin with or without cyclosporine, for treatment of lower risk disease in select patients (generally ≤60 years old and with ≤5% marrow blasts, or those with hypocellular marrows, PNH clone positivity, or STAT-3 mutant cytotoxic T-cell clones) with clinically relevant thrombocytopenia or neutropenia.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
A. Chronic or persistent immune thrombocytopenia: pretreatment and current platelet counts
B. Aplastic anemia continuation of therapy: current platelet counts

III. EXCLUSIONS

Coverage will not be provided for members with the following exclusion: concomitant use of Promacta with other thrombopoietin receptor agonists (e.g., Nplate, Doptelet, Mulpleta) or with spleen tyrosine kinase inhibitors (e.g., Tavalisse)

IV. PRESCRIBER SPECIALTIES

A. For diagnosis of persistent or chronic thrombocytopenia, severe aplastic anemia, MYH9-related disease with thrombocytopenia and myelodysplastic syndromes, this medication must be prescribed by or in consultation with a hematologist or oncologist.
B. For diagnosis of hepatitis C, this medication must be prescribed by or in consultation with a hepatologist, gastroenterologist, or infectious disease specialist.

V. CRITERIA FOR INITIAL APPROVAL

A. Chronic or persistent immune thrombocytopenia (ITP)
Authorization of 6 months may be granted for treatment of chronic or persistent ITP when both of the following criteria are met:
1. Inadequate response or intolerance to prior therapy with corticosteroids, immunoglobulins, or splenectomy
2. Untransfused platelet count at any point prior to the initiation of the requested medication is less than $30x10^9$/L OR $30x10^9$/L to $50x10^9$/L with symptomatic bleeding (e.g., significant mucous membrane bleeding, gastrointestinal bleeding or trauma) or risk factors for bleeding (see Section VII).

B. Thrombocytopenia associated with chronic hepatitis C
Authorization of 6 months may be granted to members who are prescribed Promacta for the initiation and maintenance of interferon-based therapy for the treatment of thrombocytopenia associated with chronic hepatitis C.

C. Aplastic anemia
1. Authorization of 6 months may be granted for first-line treatment of severe aplastic anemia when Promacta will be used in combination with standard immunosuppressive therapy (e.g., horse antithymocyte globulin (h-ATG) and cyclosporine).
2. Authorization of 6 months may be granted for treatment of aplastic anemia which had an insufficient response to immunosuppressive therapy.

D. MYH9-related disease with thrombocytopenia
Authorization of 12 months may be granted to members with thrombocytopenia associated with MYH9-related disease.

E. Myelodysplastic Syndromes
1. Authorization of 12 months may be granted for treatment of myelodysplastic syndromes with severe or refractory thrombocytopenia when both of the following criteria are met:
   i. Member has lower risk disease defined as Revised International Prognostic Scoring System (IPSS-R) (Very Low, Low, Intermediate), International Prognostic Scoring System (IPSS) (Low/Intermediate-1), WHO classification-based Prognostic Scoring System (WPSS) (Very Low, Low, Intermediate).
   ii. Member has severe or refractory thrombocytopenia following disease progression or no response to hypomethylating agents (such as azacitidine and decitabine), immunosuppressive therapy, or clinical trial.
2. Authorization of 12 months may be granted for treatment of myelodysplastic syndromes when all of the following criteria are met:
   i. Member has lower risk disease defined as Revised International Prognostic Scoring System (IPSS-R) (Very Low, Low, Intermediate), International Prognostic Scoring System (IPSS) (Low/Intermediate-1), WHO classification-based Prognostic Scoring System (WPSS) (Very Low, Low, Intermediate).
   ii. Member has clinically relevant thrombocytopenia or neutropenia.

iii. Promacta will be used in combination with equine anti-thymocyte globulin.

VI. CONTINUATION OF THERAPY

A. Chronic or persistent ITP

1. Authorization of 3 months may be granted to members with current platelet count less than $50x10^9$/L for whom the platelet count is not sufficient to prevent clinically important bleeding and who have not received a maximal Promacta dose for at least 4 weeks.
2. Authorization of 12 months may be granted to members with current platelet count less than $50x10^9$/L for whom the current platelet count is sufficient to prevent clinically important bleeding.
3. Authorization of 12 months may be granted to members with current platelet count of $50x10^9$/L to $200x10^9$/L.
4. Authorization of 12 months may be granted to members with current platelet count greater than $200x10^9$/L to less than or equal to $400x10^9$/L for whom Promacta dosing will be adjusted to achieve a platelet count sufficient to avoid clinically important bleeding.

B. Thrombocytopenia associated with chronic hepatitis C

Authorization of 6 months may be granted to members who are continuing to receive interferon-based therapy.

C. Aplastic anemia

1. Authorization of up to 16 weeks total may be granted to members with current platelet count less than $50x10^9$/L who have not received appropriately titrated therapy with Promacta for at least 16 weeks.
2. Authorization of up to 16 weeks total may be granted to members with current platelet count less than $50x10^9$/L who are transfusion-independent.
3. Authorization of 12 months may be granted to members with current platelet count of $50x10^9$/L to $200x10^9$/L.
4. Authorization of 12 months may be granted to members with current platelet count greater than 200 $x10^9$/L to less than or equal to $400x10^9$/L for whom Promacta dosing will be adjusted to achieve and maintain an appropriate target platelet count.

D. MYH9-related disease with thrombocytopenia

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

E. Myelodysplastic Syndromes

Authorization of 12 months may be granted for continued treatment of myelodysplastic syndromes in members who experience benefit from therapy (e.g., increased platelet counts, decreased bleeding events, reduced need for platelet transfusions).

VII. APPENDIX

<u>Examples of risk factors for bleeding (not all inclusive)</u>

- Undergoing a medical or dental procedure where blood loss is anticipated
- Comorbidity (e.g., peptic ulcer disease, hypertension)
- Mandated anticoagulation therapy
- Profession (e.g., construction worker) or lifestyle (e.g., plays contact sports) that predisposes member to trauma

VIII. REFERENCES

1. Promacta [package insert]. Research Triangle Park, NC: GlaxoSmithKline; October 2021.
2. Pecci A, Gresele P, Klersy C, et al. Eltrombopag for the treatment of the inherited thrombocytopenia deriving from MYH9 mutations. *Blood.* 2010;116(26):5832-7.
3. The NCCN Drugs & Biologics Compendium® © 2020 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed June 15, 2022.
4. The NCCN Clinical Practice Guidelines in Oncology® Myelodysplastic Syndrome (Version 3.2022). © 2020 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed June 15, 2022.
5. Nuenert C, Terrel DR, Arnold DM, et al. American Society of Hematology 2019 guidelines for immune thrombocytopenia. *Blood Adv* 2019;3(23):3829–3866.
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8. Rodeghiero F, Stasi R, Gernsheimer T, et al. Standardization of terminology, definitions and outcome criteria in immune thrombocytopenic purpura of adults and children: report from an international working group. *Blood*. 2009;113(11):2386-2393.
9. Olnes MJ, Scheinberg P, Calvo KR, et al. Eltrombopag and improved hematopoiesis in refractory aplastic anemia. *N Engl J Med*. 2012;367(1):11-19.
10. Townsley DM, Scheinberg P, Winkler T, et al. Eltrombopag added to standard immunosuppression for aplastic anemia. *N Engl J Med* 2017;376:1540-1550.

STEP THERAPY CRITERIA

BRAND NAME
(generic)

PROTOPIC
(tacrolimus)

Status: CVS Caremark Criteria
Type: Initial Step Therapy; Post Step Therapy Prior Authorization

POLICY

FDA-APPROVED INDICATIONS

Protopic Ointment, both 0.03% and 0.1% for adults, and only 0.03% for children aged 2 to 15 years, is indicated as *second-line therapy* for the short-term and non-continuous chronic treatment of moderate to severe atopic dermatitis in non-immunocompromised adults and children who have failed to respond adequately to other topical prescription treatments for atopic dermatitis, or when those treatments are not advisable.
Protopic ointment is not indicated for children younger than 2 years of age.

Compendial Uses
Psoriasis[3] - on the face, genitals, or skin folds[5]
Vitiligo on the head or neck[3,6,7]
Atopic Dermatitis for patients under 2 years of age (Protopic 0.03%)[3,4]

INITIAL STEP THERAPY

**Include Rx and OTC products unless otherwise stated.*

For Protopic (tacrolimus) 0.1%, the patient must be at least 16 years of age. For Protopic (tacrolimus) 0.03%, there is no age restriction. Additionally, if the patient has filled a prescription for at least a 14 day supply of at least one corticosteroid of medium or higher potency within the past 180 days (see examples in Table 1) under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit. If the patient does not meet the initial step therapy criteria, then the system will reject with a message indicating that a prior authorization (PA) is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

TABLE 1: EXAMPLES OF TOPICAL CORTICOSTEROIDS FOR TREATMENT OF ATOPIC DERMATITIS [2,3,4]	
Medium Potency	betamethasone dipropionate lotion, spray 0.05%
	betamethasone valerate crm/lotion 0.1%/foam 0.12%
	clocortolone pivalate crm 0.1%
	desonide lotion, ointment 0.05%
	desoximetasone crm 0.05%
	fluocinolone acetonide crm/oint/kit 0.025%
	flurandrenolide crm/oint/lotion 0.05%
	fluticasone propionate crm/lotion 0.05%/oint 0.005%
	hydrocortisone butyrate cream/lipocream/lotion/oint/soln 0.1%
	hydrocortisone probutate crm 0.1%
	hydrocortisone valerate crm/oint 0.2%
	mometasone furoate crm/lotion/solution 0.1%
	prednicarbate crm/oint 0.1%
	triamcinolone acetonide crm/oint/lotion/kit 0.1%
	triamcinolone acetonide crm/oint/lotion 0.025%
	triamcinolone acetonide ointment 0.05%
High Potency	amcinonide crm/oint/lotion 0.1%
	betamethasone dipropionate crm/oint 0.05%
	betamethasone dipropionate augmented crm/lotion 0.05%

	betamethasone valerate oint 0.1%
	desoximetasone crm/oint/spray 0.25%/gel/oint 0.05%
	diflorasone diacetate crm (emollient base) 0.05% diflorasone cream 0.05%
	halcinonide crm/oint 0.1%
	fluocinonide crm/emulsified cream/oint/gel/soln 0.05%
	mometasone furoate oint 0.1%
	triamcinolone acetonide crm/oint 0.5%
	triamcinolone acetonide aerosol soln 0.147 mg/g
Very High Potency	betamethasone dipropionate augmented oint/gel 0.05%
	clobetasol propionate crm/oint/foam/shampoo/gel/lotion/soln/spray 0.05%/cream 0.025%
	diflorasone diacetate oint 0.05%
	flurandrenolide tape 4mcg/cm^2
	halobetasol propionate crm/oint/lotion/kit 0.05%
	fluocinonide crm 0.1%

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The request is for Protopic (tacrolimus) 0.03% ointment
  OR
- The request is for Protopic (tacrolimus) 0.1% ointment **AND**
  - The patient is 16 years of age or older

AND

- The requested drug is being prescribed for psoriasis on the face, genitals, or skin folds OR vitiligo on the head or neck
  OR
- The requested drug is being prescribed for moderate to severe atopic dermatitis (eczema) **AND**
  - The patient is less than 2 years of age
    OR
  - The requested drug will be used on sensitive skin areas (e.g., face, genitals, or skin folds)
    OR
  - The patient has experienced an inadequate treatment response, intolerance, or contraindication to at least one first line therapy agent (e.g., medium or higher potency topical corticosteroid)

REFERENCES

1. Protopic [package insert]. Madison, NJ: Leo Pharma US, Inc.; February 2019.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2022; Accessed February 17, 2022.
3. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed February 17, 2022.
4. Eichenfield L, Tom W, et al. Guidelines of Care for the Management of Atopic Dermatitis. *J Am Acad Dermatol.* 2014;71:116-32.
5. Elmets CA, Korman NJ, Prater EF, et al. Joint AAD-NPF Guidelines of care for the management and treatment of psoriasis with topical therapy and alternative medicine modalities for psoriasis severity measures. *J Am Acad Dermatol*. 2021 Feb;84(2):432-470.
6. Kubelis-López DE, Zapata-Salazar NA, et al. Updates and new medical treatments for vitiligo (Review). *Exp Ther Med.* 2021;22(2):797.
7. Eleftheriadou V, Atkar R, et al. British Association of Dermatologists guidelines for the management of people with vitiligo 2021. *The British Journal of Dermatology*. 2021;186(1):18-29.

PRIOR AUTHORIZATION CRITERIA

DRUG CLASS	**NARCOLEPSY AGENTS**
BRAND NAME (generic)	**PROVIGIL (modafinil)**

Status: CVS Caremark Criteria
Type: Initial Prior Authorization with Quantity Limit

POLICY

FDA-APPROVED INDICATIONS
Provigil is indicated to improve wakefulness in adult patients with excessive sleepiness associated with narcolepsy, obstructive sleep apnea, or shift work disorder.

Limitations of Use
In obstructive sleep apnea (OSA), Provigil is indicated to treat excessive sleepiness and not as treatment for the underlying obstruction. If continuous positive airway pressure (CPAP) is the treatment of choice for a patient, a maximal effort to treat with CPAP for an adequate period of time should be made prior to initiating and during treatment with Provigil for excessive sleepiness.

Compendial Uses/Limited Treatment Option
Fatigue related to multiple sclerosis[8,9]
Idiopathic hypersomnia[6]

COVERAGE CRITERIA
The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has a diagnosis of narcolepsy
  AND
  - The request is for continuation of therapy
    AND
  - The patient had a positive response to treatment

  OR
  - The requested drug is being prescribed by, or in consultation with, a sleep specialist
    AND
  - The diagnosis is confirmed by sleep lab evaluation

OR

- The patient has a diagnosis of shift work disorder (SWD)
  AND
  - The request is for continuation of therapy
    AND
  - The patient had a positive response to treatment
    AND
  - The patient is still a shift-worker

  OR
  - The requested drug is being prescribed by, or in consultation with, a sleep specialist
    AND

- A sleep log and actigraphy monitoring have been completed for at least 14 days and show a disrupted sleep and wake pattern
  AND
- Symptoms have been present for 3 or more months

OR

- The patient has a diagnosis of obstructive sleep apnea (OSA)
  AND
  - The request is for continuation of therapy
    AND
  - The patient had a positive response to treatment
    AND
  - The patient is compliant with using continuous positive airway pressure (CPAP) or bilevel positive airway pressure (BIPAP)

  OR
  - The requested drug is being prescribed by, or in consultation with, a sleep specialist
    AND
  - The diagnosis has been confirmed by polysomnography
    AND
  - The patient has been receiving treatment for the underlying airway obstruction (continuous positive airway pressure [CPAP] or bilevel positive airway pressure [BIPAP]) for at least one month
    AND
  - Treatment with continuous positive airway pressure (CPAP) or bilevel positive airway pressure (BIPAP) will continue

OR

- The requested drug is being prescribed for idiopathic hypersomnia
  AND
  - The request is for continuation of therapy
    AND
  - The patient had a positive response to treatment

  OR
  - The requested drug is being prescribed by, or in consultation with, a sleep specialist
    AND
  - The patient has experienced the presence of daytime lapses into sleep or daily irrepressible periods of need to sleep for at least 3 months
    AND
  - Insufficient sleep syndrome has been ruled out such as by lack of improvement of sleepiness after an adequate trial of increased nocturnal time in bed, preferably confirmed by at least a week of sleep log with wrist actigraphy
    AND
  - A multiple sleep latency test (MSLT) documented fewer than two sleep onset rapid eye movement periods (SOREMPs) or no SOREMPs if the REM latency on the preceding polysomnogram was less than or equal to 15 minutes
    AND
  - Sleep lab evaluation showed at least ONE of the following: A) mean sleep latency on multiple sleep latency test (MLST) of less than or equal to 8 minutes, B) total 24-hour sleep time of greater than or equal to 660 minutes on 24-hour polysomnographic monitoring after correcting any chronic sleep deprivation or by wrist actigraphy in association with a sleep log and averaged over at least 7 days of unrestricted sleep
    AND
  - The patient does not have cataplexy
    AND
  - Hypersomnolence or multiple sleep latency test (MSLT) results are not better explained by ANY of the following: A) another sleep disorder, B) other medical or psychiatric disorder, C) use of drugs or medications
  -

OR

- The requested drug is being prescribed for multiple sclerosis-related fatigue

Quantity Limits Apply. The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.

REFERENCES

1. Provigil [package insert]. North Wales, Pennsylvania: Teva Pharmaceuticals USA, Inc.; November 2018.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2022; Accessed January 26, 2022.
3. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed January 26, 2022.
4. American Academy of Sleep Medicine. *International Classification of Sleep Disorders: Diagnostic and Coding Manual*. 3rd edition. Westchester, IL: American Academy of Sleep Medicine; 2014.
5. Morgenthaler TJ, Kapur VK, Brown T, et al. Practice parameters for the treatment of narcolepsy and other hypersomnias of central origin. *Sleep.* 2007; 30(12):1705-1711.
6. Maski K, Trotti LM, Kotagal S, et al. Treatment of central disorders of hypersomnolence: an American Academy of Sleep Medicine clinical practice guideline. *J Clin Sleep Med.* 2021;17(9):1881-1893.
7. Maski K, Trotti LM, Kotagal S, et al. Treatment of central disorders of hypersomnolence: an American Academy of Sleep Medicine systematic review, meta-analysis, and GRADE assessment. *J Clin Sleep Med.* 2021;17(9):1895-1945.
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10. Brown JN, Howard CA, Kemp DW. Modafinil for the treatment of multiple sclerosis-related fatigue. *Ann Pharmacother*. 2010 Jun; 44(6):1098-103.
11. Zifko UA, Rupp M, Schwarz S, et al. Modafinil in treatment of fatigue in multiple sclerosis. Results of an open-label study. *J Neurol*. 2002; 249:983-987.

PRIOR AUTHORIZATION CRITERIA

DRUG CLASS	**NARCOLEPSY AGENTS**
BRAND NAME (generic)	**PROVIGIL (modafinil)**

Status: CVS Caremark Criteria
Type: Initial Prior Authorization with Quantity Limit

POLICY

FDA-APPROVED INDICATIONS
Provigil is indicated to improve wakefulness in adult patients with excessive sleepiness associated with narcolepsy, obstructive sleep apnea, or shift work disorder.

Limitations of Use
In obstructive sleep apnea (OSA), Provigil is indicated to treat excessive sleepiness and not as treatment for the underlying obstruction. If continuous positive airway pressure (CPAP) is the treatment of choice for a patient, a maximal effort to treat with CPAP for an adequate period of time should be made prior to initiating and during treatment with Provigil for excessive sleepiness.

Compendial Uses/Limited Treatment Option
Fatigue related to multiple sclerosis[8,9]
Idiopathic hypersomnia[6]

COVERAGE CRITERIA
The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has a diagnosis of narcolepsy
  AND
  - The request is for continuation of therapy
    AND
  - The patient had a positive response to treatment

  OR
  - The requested drug is being prescribed by, or in consultation with, a sleep specialist
    AND
  - The diagnosis is confirmed by sleep lab evaluation

OR

- The patient has a diagnosis of shift work disorder (SWD)
  AND
  - The request is for continuation of therapy
    AND
  - The patient had a positive response to treatment
    AND
  - The patient is still a shift-worker

  OR
  - The requested drug is being prescribed by, or in consultation with, a sleep specialist
    AND

- A sleep log and actigraphy monitoring have been completed for at least 14 days and show a disrupted sleep and wake pattern
  AND
- Symptoms have been present for 3 or more months

OR

- The patient has a diagnosis of obstructive sleep apnea (OSA)
  AND
  - The request is for continuation of therapy
    AND
  - The patient had a positive response to treatment
    AND
  - The patient is compliant with using continuous positive airway pressure (CPAP) or bilevel positive airway pressure (BIPAP)

  OR
  - The requested drug is being prescribed by, or in consultation with, a sleep specialist
    AND
  - The diagnosis has been confirmed by polysomnography
    AND
  - The patient has been receiving treatment for the underlying airway obstruction (continuous positive airway pressure [CPAP] or bilevel positive airway pressure [BIPAP]) for at least one month
    AND
  - Treatment with continuous positive airway pressure (CPAP) or bilevel positive airway pressure (BIPAP) will continue

OR

- The requested drug is being prescribed for idiopathic hypersomnia
  AND
  - The request is for continuation of therapy
    AND
  - The patient had a positive response to treatment

  OR
  - The requested drug is being prescribed by, or in consultation with, a sleep specialist
    AND
  - The patient has experienced the presence of daytime lapses into sleep or daily irrepressible periods of need to sleep for at least 3 months
    AND
  - Insufficient sleep syndrome has been ruled out such as by lack of improvement of sleepiness after an adequate trial of increased nocturnal time in bed, preferably confirmed by at least a week of sleep log with wrist actigraphy
    AND
  - A multiple sleep latency test (MSLT) documented fewer than two sleep onset rapid eye movement periods (SOREMPs) or no SOREMPs if the REM latency on the preceding polysomnogram was less than or equal to 15 minutes
    AND
  - Sleep lab evaluation showed at least ONE of the following: A) mean sleep latency on multiple sleep latency test (MLST) of less than or equal to 8 minutes, B) total 24-hour sleep time of greater than or equal to 660 minutes on 24-hour polysomnographic monitoring after correcting any chronic sleep deprivation or by wrist actigraphy in association with a sleep log and averaged over at least 7 days of unrestricted sleep
    AND
  - The patient does not have cataplexy
    AND
  - Hypersomnolence or multiple sleep latency test (MSLT) results are not better explained by ANY of the following: A) another sleep disorder, B) other medical or psychiatric disorder, C) use of drugs or medications
  -

OR

- The requested drug is being prescribed for multiple sclerosis-related fatigue

Quantity Limits Apply. The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.

REFERENCES

1. Provigil [package insert]. North Wales, Pennsylvania: Teva Pharmaceuticals USA, Inc.; November 2018.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2022; Accessed January 26, 2022.
3. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed January 26, 2022.
4. American Academy of Sleep Medicine. *International Classification of Sleep Disorders: Diagnostic and Coding Manual*. 3rd edition. Westchester, IL: American Academy of Sleep Medicine; 2014.
5. Morgenthaler TJ, Kapur VK, Brown T, et al. Practice parameters for the treatment of narcolepsy and other hypersomnias of central origin. *Sleep.* 2007; 30(12):1705-1711.
6. Maski K, Trotti LM, Kotagal S, et al. Treatment of central disorders of hypersomnolence: an American Academy of Sleep Medicine clinical practice guideline. *J Clin Sleep Med.* 2021;17(9):1881-1893.
7. Maski K, Trotti LM, Kotagal S, et al. Treatment of central disorders of hypersomnolence: an American Academy of Sleep Medicine systematic review, meta-analysis, and GRADE assessment. *J Clin Sleep Med.* 2021;17(9):1895-1945.
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9. Epstein LJ, Kristo D, Strollo PJ et al. Clinical Guidelines for the Evaluation, Management and Long-term Care of Obstructive Sleep Apnea in Adults. *J Clin Sleep Med.* 2009:5(3):263-276.
10. Brown JN, Howard CA, Kemp DW. Modafinil for the treatment of multiple sclerosis-related fatigue. *Ann Pharmacother*. 2010 Jun; 44(6):1098-103.
11. Zifko UA, Rupp M, Schwarz S, et al. Modafinil in treatment of fatigue in multiple sclerosis. Results of an open-label study. *J Neurol*. 2002; 249:983-987.

QUANTITY LIMIT PRIOR AUTHORIZATION CRITERIA

BRAND NAME
(generic)

PRUDOXIN
(doxepin)

ZONALON
(doxepin)

Status: CVS Caremark Criteria
Type: Quantity Limit; Post Limit Prior Authorization

POLICY

FDA-APPROVED INDICATIONS
Prudoxin and Zonalon are indicated for the short-term (up to 8 days) management of moderate pruritus in adult patients with atopic dermatitis or lichen simplex chronicus.

INITIAL QUANTITY LIMIT**

LIMIT CRITERIA*
Limits should accumulate across all drugs and strengths up to highest quantity listed depending on the order the claims are processed.

Drug	1 Month Limit*	3 Month Limit*
Prudoxin (doxepin)	45 grams / 25 days	Does Not Apply*
Zonalon (doxepin)	45 grams / 25 days	Does Not Apply*

** The duration of 25 days is used for a 30-day fill period to allow time for refill processing.*

* ***These drugs are for short-term acute use; therefore, the mail limit will be the same as the retail limit. The intent is for prescriptions of the requested drug to be filled one month at a time, even if filled at mail order; there should be no 3 month supplies filled.***

**If the patient is requesting more than the initial quantity limit, the claim will reject with a message indicating that a prior authorization is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

COVERAGE CRITERIA
The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for the management of moderate pruritus in an adult patient with atopic dermatitis or lichen simplex chronicus
  AND
- The requested drug being prescribed for short-term use (up to 8 days)

Quantity limits apply.
[90 grams per 30 days]

REFERENCES
1. Prudoxin [package insert]. Newtown, PA: Prestium Pharma, Inc.; June 2017.

2. Zonalon [package insert]. Newtown, PA: Prestium Pharma, Inc.; June 2017.
3. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, Ohio: UpToDate, Inc.; 2022; Accessed April 30, 2022.
4. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed April 30, 2022.
5. Eichenfield L, Tom W, Berger T, et al. Guidelines of Care for the Management of Atopic Dermatitis Section 2. Management and treatment of atopic dermatitis with topical therapies. *J Am Acad Dermatol* 2014; 71:116-32.

Reference number(s)
1886-A

SPECIALTY GUIDELINE MANAGEMENT

PULMOZYME (dornase alfa)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Pulmozyme is indicated, in conjunction with standard therapies, for the management of pediatric and adult patients with cystic fibrosis (CF) patients to improve pulmonary function.

In CF patients with an FVC ≥ 40% of predicted, daily administration of Pulmozyme has also been shown to reduce the risk of respiratory tract infections requiring parenteral antibiotics.

All other indications are considered experimental/investigational and are not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Cystic Fibrosis
Authorization of 12 months may be granted for treatment of cystic fibrosis when Pulmozyme will be used in conjunction with standard therapies for cystic fibrosis.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II who are experiencing benefit from therapy as evidenced by disease stability or disease improvement.

IV. REFERENCES

1. Pulmozyme [package insert]. South San Francisco, CA: Genentech, Inc.; July 2021.
2. Mogayzel PJ, Naureckas ET, Robinson KA, et al. Cystic fibrosis pulmonary guidelines. Chronic medications for maintenance of lung health. *Am J Respir Crit Care Med.* 2013;187:680-689.
3. Cohen-Cymberknoh M, Shoseyov D, Kerem E. Managing cystic fibrosis: strategies that increase life expectancy and improve quality of life. *Am J Respir Crit Care Med*. 2011;183:1463-1471.

Reference number(s)
2982-A

SPECIALTY GUIDELINE MANAGEMENT

PURIXAN (mercaptopurine)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
Purixan is indicated for the treatment of patients with acute lymphoblastic leukemia (ALL) as part of a combination chemotherapy maintenance regimen.

B. Compendial Uses
1. ALL / Lymphoblastic lymphoma (LL)
2. Acute promyelocytic leukemia (APL)
3. Moderate to Severe Crohn's Disease (CD)

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: Documentation supporting an intolerable adverse event with the generic alternative mercaptopurine (the adverse event was not an expected adverse event attributed to the active ingredient as described in the prescribing information).

III. CRITERIA FOR INITIAL APPROVAL

A. Acute lymphoblastic leukemia (ALL)/ Lymphoblastic lymphoma (LL)
Authorization of 12 months may be granted for treatment of ALL/LL when either of the following criteria is met:
1. Member has a documented intolerable adverse event with the generic alternative mercaptopurine and the adverse event was not an expected adverse event attributed to the active ingredient as described in the prescribing information, OR
2. Member is unable to swallow the tablet formulation.

B. Acute promyelocytic leukemia (APL)
Authorization of 12 months may be granted for treatment of APL when either of the following criteria is met:
1. Member has a documented intolerable adverse event with the generic alternative mercaptopurine and the adverse event was not an expected adverse event attributed to the active ingredient as described in the prescribing information, OR

2. Member is unable to swallow the tablet formulation

C. Moderate to Severe Crohn's Disease (CD)

Authorization of 12 months may be granted for treatment of moderate to severe CD when either of the following criteria is met:

1. Member has a documented intolerable adverse event with the generic alternative mercaptopurine and the adverse event was not an expected adverse event attributed to the active ingredient as described in the prescribing information, OR
2. Member is unable to swallow the tablet formulation

IV. CONTINUATION OF THERAPY

A. ALL/LL and APL

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for ALL/LL or APL when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

B. Moderate to Severe Crohn's Disease (CD)

1. Authorization of 12 months may be granted for all members (including new members) who are using the requested medication for moderately to severely active CD and who achieve or maintain remission.
2. Authorization of 12 months may be granted for all members (including new members) who are using the requested medication for moderately to severely active CD and who achieve or maintain a positive clinical response as evidenced by low disease or improvement in signs and symptoms of the condition where there is improvement in any of the following from baseline:
   i. Abdominal pain or tenderness
   ii. Diarrhea
   iii. Body weight
   iv. Abdominal mass
   v. Hematocrit
   vi. Endoscopic appearance of the mucosa
   vii. Improvement on a disease activity scoring tool (e.g., Crohn's Disease Activity Index [CDAI] score)

V. REFERENCES

1. Purixan [package insert]. Franklin, TN: Rare Disease Therapeutics, Inc.; April 2020.
2. The NCCN Drugs & Biologics Compendium® © 2023 National Comprehensive Cancer Network, Inc. Available at: https://www.nccn.org. Accessed June 12, 2023.
3. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Acute Lymphoblastic Leukemia. Version 1.2023. https://www.nccn.org/professionals/physician_gls/pdf/ped_all.pdf. Accessed June 12, 2023.
4. IBM Micromedex® DRUGDEX ® (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at https://www.micromedexsolutions.com (Accessed: June 12, 2023).
5. Lichtenstein GR, Loftus Jr EV, Isaacs KI, et al. ACG Clinical Guideline: Management of Crohn's Disease in Adults. Am J Gastroenterol. 2018;113:481-517.

Reference number(s)
3901-A

SPECIALTY GUIDELINE MANAGEMENT

QINLOCK (ripretinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication
Qinlock is indicated for the treatment of adult patients with advanced gastrointestinal stromal tumor (GIST) who have received prior treatment with 3 or more kinase inhibitors, including imatinib.

B. Compendial Uses
Gastrointestinal stromal tumor (GIST)

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Gastrointestinal Stroma Tumor (GIST)
Authorization of 12 months may be granted as a single agent for treatment of advanced, unresectable, recurrent/progressive, or metastatic GIST when any of the following criteria are met:
1. Member has received prior treatment with 3 or more kinase inhibitors, including imatinib
2. Member has disease progression on avapritinib and dasatinib

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

IV. REFERENCE

1. Qinlock [package insert]. Waltham, MA: Deciphera Pharmaceuticals, LLC; June 2021.
2. The NCCN Drugs & Biologics Compendium® © 2022 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed March 8, 2022.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME
(generic)

QLOSI
(pilocarpine hydrochloride ophthalmic solution)

VUITY
(pilocarpine hydrochloride ophthalmic solution)

Status: CVS Caremark® Criteria
Type: Initial Prior Authorization with Quantity Limit

POLICY

FDA-APPROVED INDICATIONS
Qlosi
Qlosi is indicated for the treatment of presbyopia in adults.

Vuity
Vuity is indicated for the treatment of presbyopia in adults.

COVERAGE CRITERIA
The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for the treatment of presbyopia in an adult patient
  AND
  - The patient has NOT been receiving the requested drug for at least 14 days
    AND
    - The presbyopia impacts the patient's activities of daily living to the point where pharmacologic intervention is required. [Documentation is required for approval]

  OR
  - The patient has been receiving the requested drug for at least 14 days
    AND
    - The patient has demonstrated improvement from baseline presbyopia including gaining 3 lines or more in binocular distance corrected near visual acuity, without losing more than 1 line of corrected distance visual acuity. [Documentation is required for approval.]

Quantity Limits apply.

QUANTITY LIMIT

Drug	1 Month Limit	3 Month Limit***
Qlosi 0.4% Ophthalmic Solution (pilocarpine hydrochloride ophthalmic solution)	60 single-patient use vials (12 pouches) / 25 days*	180 single-patient use vials (36 pouches) / 75 days*
Vuity 1.25% Ophthalmic Solution (pilocarpine hydrochloride ophthalmic solution)	5 mL / 19 days**	15 mL / 57 days**

**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*
***The duration of 19 days is used for a 25-day fill period and 57 days is used for a 75-day fill period to allow time for refill processing.*
****For new starts, the mail limit will be the same as the retail limit.* ***The intent is for prescriptions of the requested drug to be filled one fill at a time for new starts, even if filled at mail order; there should be no 3-month supplies filled for new starts.***

Duration of Approval (DOA):

- 5054-C: Initial therapy DOA: 2 months; Continuation of therapy DOA: 12 months

REFERENCES

1. Qlosi [package insert]. Ponte Vedra, FL: Orasis Pharmaceuticals, Ltd.; October 2023.
2. Vuity [package insert]. North Chicago, IL: AbbVie Inc.; March 2023.
3. Lexicomp Online, Lexi-Drugs Online, Hudson, Ohio: UpToDate, Inc.; 2022; Accessed September 21, 2022.
4. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed September 21, 2022.
5. Chuck RS, Jacobs DS, Lee JK, et al. Refractive Errors & Refractive Surgery Preferred Practice Pattern. *Ophthalmology*. 2018;125(1):P1-P104.
6. Pharmacy Auditing and Dispensing Job Aid: Billing Other Dosage Forms. Centers for Medicare and Medicaid Services. December 2015.
7. Waring GO 4th, Price FW Jr, Wirta D, et al. Safety and Efficacy of AGN-190584 in Individuals With Presbyopia: The GEMINI 1 Phase 3 Randomized Clinical Trial. *JAMA Ophthalmol*. 2022;140(4):363-371.
8. Clinicaltrials.gov. Allergan. Phase 3 Efficacy Study of AGN-190584 in Participants with Presbyopia. Last Updated September 2021. Retrieved from: https://clinicaltrials.gov/ct2/show/NCT03857542?term=NCT03857542. Accessed October 4, 2022.
9. Clinicaltrials.gov. Allergan. Study to Assess Safety and Efficacy in Participants Age 40 to 55 with Presbyopia (Old Eye) Who Receive AGN-190584 in Both Eyes Twice Daily (Virgo). Last Updated: March 2023. Retrieved from: https://clinicaltrials.gov/ct2/show/NCT04983589. Accessed April 17, 2023.

PRIOR AUTHORIZATION CRITERIA

DRUG CLASS	**WEIGHT LOSS MANAGEMENT**
BRAND NAME (generic)	**QSYMIA (phentermine and topiramate extended-release)**

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

POLICY

FDA-APPROVED INDICATIONS
Qsymia is indicated as an adjunct to a reduced-calorie diet and increased physical activity for chronic weight management in:

- Adults with an initial body mass index (BMI) of:
  - 30 kg/m^2 or greater (obese), or
  - 27 kg/m^2 or greater (overweight) in the presence of at least one weight related comorbidity such as hypertension, type 2 diabetes mellitus, or dyslipidemia
- Pediatric patients aged 12 years and older with an initial BMI in the 95th percentile or greater standardized for age and sex.

Limitations of Use
- The effect of Qsymia on cardiovascular morbidity and mortality has not been established.
- The safety and effectiveness of Qsymia in combination with other products intended for weight loss, including prescription drugs, over-the-counter drugs, and herbal preparations, have not been established.

COVERAGE CRITERIA
The requested drug will be covered with prior authorization when the following criteria are met:
- The requested drug will not be used in a patient who is also using Fintepla (fenfluramine)

AND
- The requested drug will be used with a reduced calorie diet and increased physical activity for chronic weight management

AND
- The patient has not completed at least 12 weeks of therapy with Qsymia 7.5 mg/46 mg or 15 mg/92 mg
  AND
- The patient has participated in a comprehensive weight management program that encourages behavioral modification, reduced calorie diet and increased physical activity with continuing follow-up for at least 6 months prior to using drug therapy
  AND
- The patient is 18 years of age or older
  AND
  - The patient has a body mass index (BMI) greater than or equal to 30 kilogram per square meter
  OR
  - The patient has a body mass index (BMI) greater than or equal to 27 kilogram per square meter AND has at least one weight related comorbid condition (e.g., hypertension, type 2 diabetes mellitus or dyslipidemia)

  OR
- The patient is 12 to 17 years of age

AND

- The patient has an initial body mass index (BMI) in the 95th percentile or greater standardized for age and sex

OR

- The patient has completed at least 12 weeks of Qsymia 15 mg/92 mg therapy
  AND
  - The patient lost at least 5 percent of baseline body weight (for adults) or the patient experienced a reduction of at least 5 percent of baseline body mass index (BMI) (for pediatrics). [Documentation is required for approval.]
    OR
  - The patient has continued to maintain their initial 5 percent weight loss (for adults) or the patient has continued to maintain their initial reduction of 5 percent of baseline body mass index (BMI) (for pediatrics). [Documentation is required for approval.]

OR

- The patient has completed at least 12 weeks of Qsymia 7.5 mg/46 mg therapy
  AND
  - The patient lost at least 3 percent of baseline body weight (for adults) or the patient experienced a reduction of at least 3 percent of baseline body mass index (BMI) (for pediatrics). [Documentation is required for approval.]
    OR
  - The patient has continued to maintain their initial 3 percent weight loss (for adults) or the patient has continued to maintain their initial reduction of 3 percent of baseline body mass index (BMI) (for pediatrics). [Documentation is required for approval.]
    OR
  - The patient has not lost at least 3 percent of baseline body weight (for adults) or the patient has not experienced a reduction of at least 3 percent of baseline body mass index (BMI) (for pediatrics) OR the patient has not continued to maintain their initial 3 percent weight loss (for adults) or their initial reduction of 3 percent BMI (for pediatrics)
    AND
    - The patient's dose has been escalated to Qsymia 11.25 mg/69 mg and will follow the appropriate dose escalation schedule. [Documentation is required for approval.]

REFERENCES

1. Qsymia [package insert]. Campbell, CA: Vivus, Inc.; June 2022.
2. Lexicomp Online, Lexi-Drugs (Adult and Pediatric) Online. Hudson, Ohio: UpToDate, Inc.; 2022; Accessed May 12, 2022.
3. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com/. Accessed May 12, 2022.
4. Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents. National Heart, Lung, and Blood Institute. NIH Publication No. 12-7486. October 2012. http://www.nhlbi.nih.gov/guidelines/cvd_ped/peds_guidelines_full.pdf. 141-159. Accessed May 17, 2022.
5. Pharmacological Management of Obesity: An Endocrine Society Clinical Practice Guideline. The Journal of Clinical Endocrinology & Metabolism, Volume 100, Issue 2, 1 February 2015, Pages 342–362. https://academic.oup.com/jcem/article/100/2/342/2813109. Accessed May 17, 2022.
6. Jensen MD, et al. 2013 AHA/ACC/TOS guideline for the management of overweight and obesity in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and The Obesity Society. *Circulation.* 2013; 129:S102–S138.
7. FDA Announces Withdrawal Fenfluramine and Dexfenfluramine (Fen-Phen). July 2005. Available at: https://wayback.archive-it.org/7993/20170723090512/https://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm179871.htm. Accessed May 17, 2022.

STEP THERAPY CRITERIA

BRAND NAME*
(generic)

RANEXA
(ranolazine extended-release)

Status: CVS Caremark Criteria
Type: Initial Step Therapy; Post Step Therapy Prior Authorization ***Ref # 658-D***

** Drugs that are listed in the target drug box include both brand and generic and all dosages forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS
Ranexa is indicated for the treatment of chronic angina.

Ranexa may be used with beta-blockers, nitrates, calcium channel blockers, anti-platelet therapy, lipid-lowering therapy, ACE inhibitors, and angiotensin receptor blockers.

INITIAL STEP THERAPY
If the patient has filled a prescription for at least a 30 day supply of a beta blocker in combination with either a calcium channel blocker or long-acting nitrate within the past 365 days under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit. If the patient does not meet the initial step therapy criteria, then the claim will reject with a message indicating that a prior authorization (PA) is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

COVERAGE CRITERIA
The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for the treatment of chronic angina

AND

- The patient has experienced an inadequate treatment response, intolerance, or has a contraindication to a beta blocker used in combination with either a calcium channel blocker or long-acting nitrate

RATIONALE
If the patient has filled a prescription for at least a 30 day supply of a beta blocker in combination with either a calcium channel blocker or long-acting nitrate within the past 365 days under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit.

If the patient does not meet the initial step therapy criteria, then prior authorization is required.

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Ranexa is indicated for the treatment of chronic angina. Ranexa may be used with beta-blockers, nitrates, calcium channel blockers, anti-platelet therapy, lipid-lowering therapy, ACE inhibitors, and angiotensin receptor blockers.[1-3]

The ACCF/AHA/ACP/AATS/PCNA/SCAI/STS Guideline for the Diagnosis and Management of Patients with Stable Ischemic Heart Disease (SIHD) states that a majority of patients with SIHD have clinical features indicating that revascularization is unlikely to improve life expectancy or the risk of subsequent myocardial infarction. For such patients,

antianginal therapy and intensive treatment for risk factors are recommended before considering percutaneous coronary intervention (PCI) or coronary artery bypass graft (CABG) to relieve symptoms. A broad range of highly effective drugs is available, including beta blockers, calcium channel blockers, long-acting nitrates, and new agents such as ranolazine. Comparative trials among these medications are relatively few and for the most part small. Based on available data, however, all the agents appear to be relatively similar in antianginal efficacy, and all have very acceptable profiles of safety and tolerability.[4]

Beta blockers have been shown to improve survival in patients after acute myocardial infarction and in patients with hypertension; they provide 24 hour coverage and have a long history of clinical use. For these reasons, the guideline recommends these agents as first-line drugs for treating angina.[4]

In patients who do not tolerate or adequately respond to beta blockers, calcium channel blockers and/or long-acting nitrates may be substituted or added. Calcium channel blockers or long-acting nitrates, in combination with beta blockers, should be prescribed for relief of symptoms when initial treatment with beta blockers is unsuccessful. Calcium channel blockers or long-acting nitrates should be prescribed for relief of symptoms when beta blockers are contraindicated or cause unacceptable side effects.[4]

Ranolazine has been approved by the U.S. Food and Drug Administration (FDA) for first-line use in patients with chronic angina; however, the guideline recommends that ranolazine be considered in circumstances in which beta blockers, calcium channel blockers, and long-acting nitrates are contraindicated, not adequately effective, or are not tolerated. The guideline states that although ranolazine has been well studied in SIHD, the agent was not administered in the COURAGE (Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation) study, and further clinical evaluation is needed, especially of ranolazine as an element of intensive interventions for multiple risk factors.[4] Therefore, coverage will be considered for patients who have experienced an inadequate treatment response, intolerance, or have a contraindication to a beta blocker used in combination with either a calcium channel blocker or long-acting nitrate.

For immediate or acute relief of angina episodes, the guideline also recommends all patients with SIHD be prescribed sublingual nitroglycerin or nitroglycerin spray.[4] Therefore, it is not included in the initial step therapy.

REFERENCES

1. Ranexa [package insert]. Foster City, CA: Gilead Sciences, Inc.; October 2019.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2022; Accessed March 22, 2022.
3. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed March 22, 2022.
4. Fihn SD, Gardin J, Abrams J, et al. American College of Cardiology Foundation/American Heart Association Task Force. 2012 ACCF/AHA/ACP/AATS/PCNA/SCAI/STS Guideline for the Diagnosis and Management of Patients with Stable Ischemic Heart Disease. *J Am Coll Cardiol*. 2012;60(24):e44-e164.

Written by:	UM Development (CT)
Date written:	06/2011
Revised:	10/2011; (PL) 10/2012; CF 09/2013, 05/2014; (CT) 04/2015; (CF) 04/2016 (no clinical changes); (CT) 04/2017 (no clinical changes); (KM) 04/2018; (MAC) 04/2019, 04/2020 (no clinical changes), (DFW) 04/2021 (no clinical changes); (RZ) 04/2022 (no clinical changes)
Reviewed:	Medical Affairs (KP) 06/2011, 10/2011; (LMS) 10/2012; (DNC) 09/2013; (LMS) 05/2014; (LMS) 04/2015; (EPA) 04/2018; (AN) 4/2019, (CHART) 04/30/20, (CHART) 04/22/2021, (CHART) 04/28/2022 External Review: 08/2011, 12/2011, 12/2012, 12/2013, 08/2014, 08/2015, 08/2016, 08/2017, 08/2018, 08/2019, 08/2020, 08/2021, 08/2022

CRITERIA FOR APPROVAL

1	Is the requested drug being prescribed for the treatment of chronic angina? [If no, then no further questions.]	Yes	No
2	Has the patient experienced an inadequate treatment response, intolerance, or does the patient have a contraindication to a beta blocker used in combination with either a calcium channel blocker or long-acting nitrate?	Yes	No

Mapping Instructions			
	Yes	**No**	**DENIAL REASONS – DO NOT USE FOR MEDICARE PART D**
1.	Go to 2	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you are taking it to treat chronic angina. Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]
2.	Approve, 36 months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have tried a beta blocker in combination with either a calcium channel blocker or a long-acting nitrate and they either did not work for you or you cannot use them. Your request has been denied based on the information we have. [Short Description: No inadequate treatment response, intolerance, or contraindication to a beta blocker used in combination with a calcium channel blocker or long-acting nitrate]

Reference number(s)
2018-A

SPECIALTY GUIDELINE MANAGEMENT

RASUVO (methotrexate injection)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

1. Rheumatoid Arthritis including Polyarticular Juvenile Idiopathic Arthritis
   Rasuvo is indicated in the management of selected adults with severe, active rheumatoid arthritis (RA) or children with active polyarticular juvenile idiopathic arthritis, who have had an insufficient therapeutic response to, or are intolerant of, an adequate trial of first-line therapy including full dose non-steroidal anti-inflammatory agents (NSAIDs).
2. Psoriasis
   Rasuvo is indicated in adults for the symptomatic control of severe, recalcitrant, disabling psoriasis that is not adequately responsive to other forms of therapy, but only when the diagnosis has been established, as by biopsy and/or after dermatologic consultation. It is important to ensure that a psoriasis “flare” is not due to an undiagnosed concomitant disease affecting immune responses.

Limitations of use: *Rasuvo is not indicated for the treatment of neoplastic diseases*

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

A. Chart notes, medical record documentation, or claims history supporting previous use of generic oral methotrexate and inadequate response or intolerance to therapy.
B. Chart notes or medical record documentation of member’s inability to prepare and administer generic injectable methotrexate.

III. CRITERIA FOR INITIAL APPROVAL

Authorization of 12 months may be granted for treatment of rheumatoid arthritis (RA), polyarticular juvenile idiopathic arthritis (pJIA), or psoriasis when BOTH of the following criteria are met:

A. Member has tried and had an inadequate response or intolerance to generic oral methotrexate.
B. Member has inability to prepare and administer generic injectable methotrexate.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for all members (including new members) who meet ALL initial authorization criteria and achieve or maintain positive clinical response after at least 3 months of therapy with Rasuvo as evidenced by low disease activity or improvement in signs and symptoms of the condition.

V. REFERENCES

1. Rasuvo [package insert]. Chicago, IL: Medexus Pharma Inc.; March 2020.
2. Fraenkel L, Bathon JM, England BR, et al. 2021 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. *Arthritis Care Res (Hoboken).* 2021;73(7):924-939.
3. Smolen JS, Landewé R, Billsma J, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2019 update. *Ann Rheum Dis.* 2020;*79*:685-699.
4. Ringold, S, Angeles-Han, S, Beukelman, T, et al. 2019 American College of Rheumatology recommendations for the treatment of juvenile idiopathic arthritis: Therapeutic approaches for non-systemic polyarthritis, sacroilitis, and enthesitis. *Arthritis Care Res*. 2019;71(6):717-734.
5. Menter A, Korman NJ, Elmets CA, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis. Section 4: Guidelines of care for the management and treatment of psoriasis with traditional systemic agents. *J Am Acad Dermatol.* 2009;61:451-485.

Reference number(s)
2123-A

SPECIALTY GUIDELINE MANAGEMENT

RAVICTI (glycerol phenylbutyrate)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Ravicti is indicated for the chronic management of patients with urea cycle disorders (UCDs) who cannot be managed by dietary protein restriction and/or amino acid supplementation alone. Ravicti must be used with dietary protein restriction and, in some cases, dietary supplements.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

A. Initial Requests:
   1. Enzyme assay, biochemical, or genetic testing results supporting diagnosis; and
   2. Lab results documenting baseline plasma ammonia levels.
B. Continuation of therapy requests: lab results documenting a reduction in plasma ammonia levels from baseline.

III. CRITERIA FOR INITIAL APPROVAL

Urea cycle disorder (UCD)
Authorization of 12 months may be granted for chronic management of a UCD when both of the following criteria are met:
1. The diagnosis is confirmed by enzymatic, biochemical, or genetic testing.
2. The member has elevated plasma ammonia levels at baseline.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for chronic management of a urea cycle disorder (UCD), who are experiencing benefit from therapy as evidenced by a reduction in plasma ammonia levels from baseline.

V. REFERENCES

1. Ravicti [package insert]. Lake Forest, IL: Horizon Pharma USA, Inc.; September 2021.
2. Mew NA, Lanpher BC. Urea Cycle Disorders Overview. In: Pagon RA, Adam MP, Ardinger HH, et. al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2017 [updated April 9, 2015]. Available at: https://www.ncbi.nlm.nih.gov/books/NBK1217/?report=printable.
3. Häberle J, Boddaert N, Burlina A, et al. Suggested guidelines for the diagnosis and management of urea cycle disorders. *J Inherit Metab Dis*. 2019;42(6):1192-1230.

4. Diaz GA, Krivitzky LS, Mokhtarani M, et al. Ammonia control and neurocognitive outcome among urea cycle disorder patients treated with glycerol phenylbutyrate. *Hepatology*. 2013;57(6):2171-2179.
5. Smith W, Diaz GA, Lichter-Konecki U, et al. Ammonia control in children ages 2 months through 5 years with urea cycle disorders: comparison of sodium phenylbutyrate and glycerol phenylbutyrate. *J Pediatr*. 2013;162(6):1228-1234.

Reference number(s)
1839-A

SPECIALTY GUIDELINE MANAGEMENT

REBIF (interferon beta-1a)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Rebif is indicated for the treatment of patients with relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.

All other indications are considered experimental/investigational and are not medically necessary.

II. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with a neurologist.

III. CRITERIA FOR INITIAL APPROVAL

A. Relapsing forms of multiple sclerosis
Authorization of 12 months may be granted to members who have been diagnosed with a relapsing form of multiple sclerosis (including relapsing-remitting and secondary progressive disease for those who continue to experience relapse).

B. Clinically isolated syndrome[1]
Authorization of 12 months may be granted to members for the treatment of clinically isolated syndrome of multiple sclerosis.

IV. CONTINUATION OF THERAPY

For all indications: Authorization of 12 months may be granted for members who are experiencing disease stability or improvement while receiving Rebif.

V. OTHER

Members will not use Rebif concomitantly with other disease modifying multiple sclerosis agents (Note: Ampyra and Nuedexta are not disease modifying).

VI. REFERENCES

Reference number(s)
1839-A

1. Rebif [package insert]. Rockland, MA; EMD Serono Inc.; November 2021.

Reference number(s)
3499-A

SPECIALTY GUIDELINE MANAGEMENT

REDITREX (methotrexate injection)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

A. Rheumatoid Arthritis (RA) including Polyarticular Juvenile Idiopathic Arthritis (pJIA)
RediTrex is indicated in the management of selected adults with severe, active rheumatoid arthritis (RA) or children with active polyarticular juvenile idiopathic arthritis (pJIA), who have had an insufficient therapeutic response to, or are intolerant of, an adequate trial of first-line therapy including full dose non-steroidal anti-inflammatory agents (NSAIDs).

B. Psoriasis
RediTrex is indicated in adults for the symptomatic control of severe, recalcitrant, disabling psoriasis that is not adequately responsive to other forms of therapy, but only when the diagnosis has been established, as by biopsy and/or after dermatologic consultations. It is important to ensure that a psoriasis "flare" is not due to an undiagnosed concomitant disease affecting immune responses.

Limitations of use:
RediTrex is not indicated for the treatment of neoplastic diseases

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

A. Chart notes, medical record documentation, or claims history supporting previous use of generic oral methotrexate and inadequate response or intolerance to therapy.
B. Chart notes or medical record documentation of member's inability to prepare and administer generic injectable methotrexate.

III. CRITERIA FOR INITIAL APPROVAL

Authorization of 12 months may be granted for treatment of rheumatoid arthritis (RA), polyarticular juvenile idiopathic arthritis (pJIA), or psoriasis when BOTH of the following criteria are met:

A. Member has tried and had an inadequate response or intolerance to generic oral methotrexate.
B. Member has inability to prepare and administer generic injectable methotrexate.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for all members (including new members) who meet ALL initial authorization criteria and achieve or maintain positive clinical response after at least 3 months of therapy with RediTrex as evidenced by low disease activity or improvement in signs and symptoms of the condition.

V. REFERENCES

1. RediTrex [package insert]. Nashville, TN: Cumberland Pharmaceuticals, Inc; August 2020.
2. Fraenkel L, Bathon JM, England BR, et al. 2021 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. *Arthritis* Care Res (Hoboken). 2021;73(7):924-939.
3. Smolen JS, Landewé R, Billsma J, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2019 update. *Ann Rheum Dis.* 2020*;79*:685-699.
4. Ringold, S, Angeles-Han, S, Beukelman, T, et al. 2019 American College of Rheumatology recommendations for the treatment of juvenile idiopathic arthritis: Therapeutic approaches for non-systemic polyarthritis, sacroilitis, and enthesitis. *Arthritis Care Res*. 2019;71(6):717-734.
5. Menter A, Korman NJ, Elmets CA, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis. Section 4: Guidelines of care for the management and treatment of psoriasis with traditional systemic agents. *J Am Acad Dermatol.* 2009;61:451-485.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME
(generic)

REGRANEX (all topical)
(becaplermin)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization with Quantity Limit

POLICY

FDA-APPROVED INDICATIONS

Regranex is indicated for the treatment of lower extremity diabetic neuropathic ulcers that extend into the subcutaneous tissue or beyond and have an adequate blood supply, when used as an adjunct to, and not a substitute for, good ulcer care practices including initial sharp debridement, pressure relief and infection control.

Limitations of Use:
The efficacy of Regranex has not been established for the treatment of pressure ulcers and venous stasis ulcers and has not been evaluated for the treatment of diabetic neuropathic ulcers that do not extend through the dermis into subcutaneous tissue [Stage I or II, International Association of Enterostomal Therapy (IAET) staging classification] or ischemic diabetic ulcers.

The effects of becaplermin on exposed joints, tendons, ligaments, and bone have not been established in humans.

Regranex is not intended to be used in wounds that close by primary intention.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for the treatment of a lower extremity diabetic neuropathic ulcer that extends into the subcutaneous tissue or beyond and has an adequate blood supply
  AND
- Good ulcer care practices including initial sharp debridement, pressure relief, and infection control will be performed
  AND
- If additional quantities are being requested, then the requested drug is being prescribed to treat an ulcer greater than 2.5 square inches in size or multiple ulcers

Quantity Limits apply.
30 grams/25 days*
For multiple ulcers or an ulcer greater than 2.5 square inches in size: 60 grams/25 days*
** The duration of 25 days is used for a 30-day fill period to allow time for refill processing.*
***** This drug is for short-term acute use; therefore, the mail limit will be the same as the retail limit. The intent is for prescriptions of the requested drug to be filled one month at a time, even if filled at mail order; there should be no 3 month supplies filled.***

REFERENCES

1. Regranex [package insert]. Fort Worth, TX: Smith & Nephew Inc.; August 2019.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2022; Accessed January 30, 2023.

3. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed January 30, 2023.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME*
(generic)

RELISTOR
(methylnaltrexone bromide)

Status: CVS Caremark Criteria ***REG***
Type: Initial Prior Authorization ***Ref # 505-A***

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Relistor tablets and Relistor injection are indicated for the treatment of opioid-induced constipation (OIC) in adult patients with chronic non-cancer pain, including patients with chronic pain related to prior cancer or its treatment who do not require frequent (e.g., weekly) opioid dosage escalation.

Relistor injection is indicated for the treatment of opioid-induced constipation (OIC) in adult patients with advanced illness or pain caused by active cancer who require opioid dosage escalation for palliative care.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for opioid-induced constipation in an adult patient with chronic non-cancer pain, including patients with chronic pain related to prior cancer or its treatment who do not require frequent (e.g., weekly) opioid dosage escalation

OR

- The requested drug is being prescribed for opioid-induced constipation in an adult patient with advanced illness or pain caused by active cancer who requires opioid dosage escalation for palliative care
  AND
- The request is for Relistor injection

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Relistor tablet and Relistor injection are indicated for the treatment of opioid-induced constipation (OIC) in adult patients with chronic non-cancer pain, including patients with chronic pain related to prior cancer or its treatment who do not require frequent (e.g., weekly) opioid dosage escalation. Relistor injection is also indicated for the treatment of opioid-induced constipation in adult patients with advanced illness or pain caused by active cancer who require opioid dosage escalation for palliative care.[1-3] Use of Relistor beyond 4 months has not been studied in the advanced illness population.[3]

Constipation is by far the most common and debilitating gastrointestinal effect of opioids, and some degree of constipation is near universal in patients taking opioid medications. Lifestyle modifications are an appropriate first step for all those with constipation, and include increasing one's fluid intake, regular moderate exercise as tolerated, and toileting as soon as possible in response to the urge to defecate. The American Gastroenterological Association (AGA) presents a strong recommendation that laxatives be used as first-line agents in this disorder. If an adequate trial of laxatives results in incomplete relief of OIC symptoms, other agents might be needed.[9] If the nonspecific regimens do not provide satisfactory relief from the gastrointestinal manifestations of opioid-induced constipation, as evidenced by a bowel function index (BFI) score of more than 30 points, then specific treatment options with peripherally restricted opioid receptor antagonists such as methylnaltrexone bromide may be more efficacious for treatment of opioid-induced constipation and may thereby improve bowel function.[5,6] The AGA suggests methylnaltrexone over no treatment in patients with laxative refractory OIC.[9]

CVS caremark

The National Comprehensive Cancer Network (NCCN) Adult Cancer Pain guidelines recommend a prophylactic bowel regimen with a stimulant laxative with or without a stool softener or polyethylene glycol (PEG) and to increase the dose of the laxative when increasing the dose of opioids. When response to laxative therapy has not been sufficient for opioid induced constipation in patients with advanced illness, methylnaltrexone can be used.[4]

Most studies regarding the safety and efficacy of Relistor have not exceeded 4 months in duration.[5-7] The use of methylnaltrexone beyond 4 months has not been studied in the advanced illness population.[3] The long-term effects of methylnaltrexone (i.e., > 12 weeks) have not been often evaluated.[8] One phase 3, open-label trial studied the effects of injectable methylnaltrexone for 48 weeks in patients 18 years of age or older with opioid-induced constipation (OIC) with chronic non-cancer pain. The study excluded patients with a history of chronic constipation prior to opioid treatment, patients with significant gastrointestinal (GI) disorder, patients with cardiovascular conditions, and patients with unstable hepatic, renal, pulmonary, psychiatric, or other medical conditions. The study showed overall safety and efficacy with chronic use of injectable methylnaltrexone but had several limitations and suggested further research was needed. Additional studies are needed to assess the effects of methylnaltrexone on diverse patient populations.[8] Due to the lack of information regarding extended use, Relistor will be approved for 4 months if conditions are met.

REFERENCES

1. Relistor [package insert]. Bridgewater, NJ: Salix Pharmaceuticals.; April 2020.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2021; Accessed August 16, 2021
3. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed August 16, 2021.
4. Swarm R, Youngwerth J, Anghelescu D, et al. National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology: Adult Cancer Pain version 2.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/pain.pdf. Accessed August 17, 2021.
5. Clemens KE and Klaschik E. Managing opioid-induced constipation in advanced illness: focus on methylnaltrexone bromide. *Therapeutics and Clinical Risk Management* 2010;6:77–82.
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7. Waldemar S and Becker G. Methylnaltrexone for opioid-induced constipation: review and meta-analysis for objective plus subjective efficacy and safety outcomes. *Therapeutics and Clinical Risk Management* 2016;12:401-412.
8. Webster LR, Michna E, Khan A, et al. Long-term safety and efficacy of subcutaneous methylnaltrexone in patients with opioid-induced constipation and chronic noncancer pain: a phase 3, open-label trial. *Pain Medicine* 2017;18:1496-1504.
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Written by:	UM Development (SE)
Date written:	12/2009
Revised:	UM Development: (CY/KD/SE) 10/2010 (CAS Adapted); (CT) 10/2011; (TM) 10/2012; (CT) 10/2013, 10/2014 (added new indication), 10/2014, 02/2015, (JH) 09/2015, (SE) 06/2016 (created separate Med D); (JH) 08/2016 (added Relistor tablets); 09/2016 (removed safety question); (DS) 08/2017 (no clinical changes), 01/2018 (update to indication); (KC) 09/2018 (no clinical changes), 09/2019 (no clinical changes), 09/2020 (no clinical changes); (DRS) 10/2021 (no clinical changes), 01/2022 (updated document title to add REG designation)
Reviewed:	Medical Affairs (WLF) 12/2009; (KP) 10/2010, 10/2011; (LS) 10/2012; (LMS) 10/2013; (DNC) 10/2014; (DHR) 02/2015; (GAD) 09/2015; (LCB) 08/2016; (ME) 09/2016, 09/2017; (AN) 01/2018; (CHART) 09/26/19, 09/24/20, 09/2021 External Review: 02/2010, 12/2010, 02/2012, 12/2012, 12/2013, 12/2014, 04/2015, 12/2015, 08/2016, 12/2016, 12/2017, 12/2018, 12/2019, 12/2020, 12/2021

CRITERIA FOR APPROVAL

1	Is the requested drug being prescribed for opioid-induced constipation in an adult patient with chronic non-cancer pain, including chronic pain related to prior cancer or its treatment who does not require frequent (e.g., weekly) opioid dosage escalation?	Yes	No

	[If yes, then no further questions.]		
2	Is the requested drug being prescribed for opioid-induced constipation in an adult patient with advanced illness or pain caused by active cancer who requires opioid dosage escalation for palliative care? [If no, then no further questions.]	Yes	No
3	Is this a request for Relistor injection?	Yes	No

Mapping Instructions			
	Yes	**No**	**DENIAL REASONS – DO NOT USE FOR MEDICARE PART D**
1.	Approve, 4 months	Go to 2	
2.	Go to 3	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have one of these conditions: - You are an adult with chronic non-cancer pain, including chronic pain related to prior cancer or its treatment who does not require frequent (e.g., weekly) opioid dosage escalation and you are requesting Relistor to treat opioid-induced constipation - You are an adult with advanced illness or pain caused by active cancer who requires increases in opioid dosage for palliative care and you are requesting Relistor injection to treat opioid-induced constipation Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]
3.	Approve, 4 Months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have the following condition: - You are an adult with chronic non-cancer pain, including chronic pain related to prior cancer or its treatment who does not require frequent (e.g., weekly) opioid dosage escalation and you are requesting Relistor tablets to treat opioid-induced constipation Your request has been denied based on the information we have. [Short Description: No approvable diagnosis for Relistor tablets]

PRIOR AUTHORIZATION CRITERIA

BRAND NAME
(generic)

RELTONE
(ursodiol capsules)

Status: CVS Caremark® Criteria
Type: Initial Prior Authorization

POLICY

FDA-APPROVED INDICATIONS

1. Reltone is indicated for patients with radiolucent, noncalcified gallbladder stones < 20 mm in greatest diameter in whom elective cholecystectomy would be undertaken except for the presence of increased surgical risk due to systemic disease, advanced age, idiosyncratic reaction to general anesthesia, or for those patients who refuse surgery. Safety of use of Reltone beyond 24 months is not established.

2. Reltone is indicated for the prevention of gallstone formation in obese patients experiencing rapid weight loss.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has radiolucent, noncalcified gallbladder stones less than 20 millimeters in greatest diameter
  AND
  - The request is for a patient in whom elective cholecystectomy would be undertaken except for the presence of any of the following: A) Increased surgical risk due to systemic disease, advanced age, or idiosyncratic reaction to general anesthesia, B) Patient refuses surgery
  AND
  - The patient cannot use generic ursodiol 300 mg capsules

OR

- The requested drug is being prescribed for the prevention of gallstone formation in an obese patient experiencing rapid weight loss
  AND
  - The patient has experienced an intolerance to generic ursodiol 300 mg capsules due to an adverse event (examples: rash, nausea, vomiting, anaphylaxis) that is thought to be due to an inactive ingredient

REFERENCES

1. Reltone [package insert]. Las Vegas, Nevada: Intra-Sana Laboratories LLC; November 2020.
2. Ursodiol Capsules [package insert]. Franklin, Kentucky: PuraCap Laboratories, LLC; October 2021.
3. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Waltham, MA: UpToDate, Inc.; 2023. https://online.lexi.com. Accessed March 3, 2023.
4. Micromedex (electronic version). Merative, Ann Arbor, Michigan, USA. Available at: https://www.micromedexsolutions.com/ (cited: 03-03-2023).

Reference number(s)
2494-A

ENHANCED SPECIALTY GUIDELINE MANAGEMENT

REPATHA (evolocumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

A. Repatha is indicated in adults with established cardiovascular disease to reduce the risk of myocardial infarction, stroke, and coronary revascularization.
B. Repatha is indicated as an adjunct to diet, alone or in combination with other low-density lipoprotein cholesterol (LDL-C)-lowering therapies, in adults with primary hyperlipidemia, including heterozygous familial hypercholesterolemia (HeFH), to reduce LDL-C.
C. Repatha is indicated as an adjunct to diet and other LDL-C-lowering therapies in pediatric patients aged 10 years and older with HeFH, to reduce LDL-C.
D. Repatha is indicated as an adjunct to other LDL-C-lowering therapies in adults and pediatric patients aged 10 years and older with homozygous familial hypercholesterolemia (HoFH), to reduce LDL-C.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

A. Current LDL-C level for both initial requests and continuation requests. The level must be dated within the six months preceding the authorization request.
B. Untreated (before any lipid lowering therapy) LDL-C level if requesting Repatha to treat primary hyperlipidemia, heterozygous or homozygous familial hypercholesterolemia.
C. Chart notes confirming clinical atherosclerotic cardiovascular disease (ASCVD) if requesting Repatha to treat clinical ASCVD. (See Appendix A).
D. If member has contraindication or intolerance to statins, chart notes confirming the contraindication or intolerance. (See Appendix B and C).

III. CRITERIA FOR INITIAL APPROVAL

A. Clinical atherosclerotic cardiovascular disease (ASCVD)
Authorization of 6 months may be granted for treatment of clinical atherosclerotic cardiovascular disease when both of the following criteria are met:

1. Member has a history of clinical ASCVD (See Appendix A).
2. Member meets at least one of the following criteria:
   a. Member has a current LDL-C level ≥ 70 mg/dL after at least three months of treatment with a high-intensity statin dose in combination with ezetimibe. If the member is unable to tolerate a high-intensity statin dose, a moderate-intensity statin dose may be used.

b. Member has a current LDL-C level ≥ 70 mg/dL with contraindication or intolerance to statins (See Appendix B and C).

B. Primary hyperlipidemia

Authorization of 6 months may be granted for treatment of primary hyperlipidemia when both of the following criteria are met:

1. Member had an untreated (before any lipid lowering therapy) LDL-C level ≥ 190 mg/dL in the absence of a secondary cause.
2. Member meets at least one of the following criteria:
   a. Member has a current LDL-C level ≥ 100 mg/dL after at least three months of treatment with a high-intensity statin dose in combination with ezetimibe. If the member is unable to tolerate a high-intensity statin dose, a moderate-intensity statin dose may be used.
   b. Member has a current LDL-C level ≥ 100 mg/dL with a contraindication or intolerance to statins (See Appendix B and C).

C. Heterozygous familial hypercholesterolemia (HeFH)

Authorization of 6 months may be granted for treatment of heterozygous familial hypercholesterolemia when both of the following criteria are met:

1. Member meets either of the following criteria:
   a. Member is 18 years of age or older and had an untreated (before any lipid lowering therapy) LDL-C level ≥ 190 mg/dL in the absence of a secondary cause.
   b. Member is less than 18 years of age and had an untreated (before any lipid lowering therapy) LDL-C level ≥ 160 mg/dL in the absence of a secondary cause.
2. Member meets at least one of the following criteria:
   a. Member has a current LDL-C level ≥ 100 mg/dL after at least three months of treatment with a high-intensity statin dose in combination with ezetimibe. If the member is unable to tolerate a high-intensity statin dose, a moderate-intensity statin dose may be used.
   b. Member has a current LDL-C level ≥ 100 mg/dL with a contraindication or intolerance to statins (See Appendix B and C).

D. Homozygous familial hypercholesterolemia (HoFH)

Authorization of 6 months may be granted for treatment of homozygous familial hypercholesterolemia when both of the following criteria are met:

1. Member meets either of the following criteria:
   a. Member is 18 years of age or older and had an untreated (before any lipid lowering therapy) LDL-C level ≥ 190 mg/dL in the absence of a secondary cause.
   b. Member is less than 18 years of age and had an untreated (before any lipid lowering therapy) LDL-C level ≥ 160 mg/dL in the absence of a secondary cause.
2. Member meets at least one of the following criteria:
   a. Member has a current LDL-C level ≥ 100 mg/dL after at least three months of treatment with a high-intensity statin dose in combination with ezetimibe. If the member is unable to tolerate a high-intensity statin dose, a moderate-intensity statin dose may be used.
   b. Member has a current LDL-C level ≥ 100 mg/dL with a contraindication or intolerance to statins (See Appendix B and C).

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III who achieve or maintain an LDL-C reduction (e.g., LDL-C is now at goal, robust lowering of LDL-C).

V. APPENDICES

APPENDIX A. Clinical ASCVD

- Acute coronary syndromes
- Myocardial infarction
- Stable or unstable angina
- Coronary or other arterial revascularization procedure (e.g., percutaneous coronary intervention [PCI], coronary artery bypass graft [CABG] surgery)
- Stroke of presumed atherosclerotic origin
- Transient ischemic attack (TIA)
- Non-cardiac peripheral arterial disease of presumed atherosclerotic origin (e.g., carotid artery stenosis, lower extremity PAD)
- Obstructive coronary artery disease (defined as fifty percent or greater stenosis on cardiac computed tomography angiogram or catheterization)
- Coronary Artery Calcium (CAC) Score ≥ 1000

APPENDIX B. Statin-associated muscle symptoms (SAMS) and statin re-challenge

- Score of 7 or higher on the Statin-Associated Muscle Symptom Clinical Index (SAMS-CI)
- Statin-associated elevation in creatine kinase (CK) level ≥ 10 times upper limit of normal (ULN)
  NOTE: Statin re-challenge is NOT required for members who have experienced an elevation of CK level ≥10 times ULN after receiving lipid-lowering therapy (LLT) with a statin.

APPENDIX C. Contraindications to statins

- Active liver disease, including unexplained persistent elevations in hepatic transaminase levels (e.g., alanine transaminase (ALT) level ≥ 3 times ULN)
- Pregnancy or planned pregnancy
- Breastfeeding

VI. REFERENCES

1. Repatha [package insert]. Thousand Oaks, CA: Amgen, Inc.; September 2021.
2. Lloyd-Jones DM, Morris PB, Ballantybe CM, et al. 2017 Focused Update of the 2016 ACC expert consensus decision pathway on the role of non-statin therapies for LDL-cholesterol lowering in the management of atherosclerotic cardiovascular disease risk: a report of the American College of Cardiology Task Force on Clinical Expert Consensus Documents. *J Am Coll Cardiol*. 2017;70:1785-822.
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4. Jacobson TA, Ito MK, Maki KC, et al. National Lipid Association recommendations for patient-centered management of dyslipidemia: part 1 — full report. *J Clin Lipidol*. 2015;9:129–169.
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13. Pandor A, Ara RM, Tumur I, et al. Ezetimibe monotherapy for cholesterol lowering in 2,722 people: systematic review and meta-analysis of randomized controlled trials. *J Intern Med*. 2009 May;265(5):568-80.
14. Grundy SM, Stone NJ, Bailey AL, et al. 2018 AHA/ACC guideline on the management of blood cholesterol: report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *J Am Coll Cardiol* 2018.
15. Beavers CJ, Kelly MS. Dyslipidemia.In: Murphy Je, Lee MW,eds. Pharmacotherapy Self-Assessment Program, 2019 Book 1. Cardiology. Lenexa, KS: American College of Clinical Pharmacy, 2019:41-42.
16. McGowan MP, Hosseini Dehkordi SH, Moriarty PM, et al. Diagnosis and Treatment of Heterozygous Familial Hypercholesterolemia. *J Am Heart Assoc*. 2019; 8:e013225. DOI: 10.1161/JAHA119.013225.

Reference number(s)
3874-A

SPECIALTY GUIDELINE MANAGEMENT

RETEVMO (selpercatinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
1. Adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with a rearranged during transfection *(RET)* gene fusion
2. Adult and pediatric patients 12 years of age and older with advanced or metastatic medullary thyroid cancer (MTC) with a *RET mutation* who require systemic therapy.
3. Adult and pediatric patients 12 years of age and older with advanced or metastatic thyroid cancer with a *RET gene* fusion who require systemic therapy and who are radioactive iodine-refractory (if radioactive iodine is appropriate).
4. Adult patients with locally advanced or metastatic solid tumors with a *RET gene* fusion that have progressed on or following prior systemic treatment or who have no satisfactory alternative treatment options.

B. Compendial Uses
1. Recurrent, advanced or metastatic NSCLC with *RET rearrangement*-positive tumors
2. Brain metastases from *RET fusion* positive NSCLC
3. Histiocytic Neoplasms with *RET gene fusion*:
   a. Erdheim-Chester Disease (ECD)
   b. Langerhans Cell Histiocytosis (LCH)
   c. Rosai-Dorfman Disease
4. Occult primary cancer with *RET gene fusion*
5. Solid tumors with *RET-gene fusion* for recurrent, persistent, progressive, unresectable disease
6. Thyroid cancer with *RET gene fusion:*
   a. Locoregional or metastatic anaplastic thyroid carcinoma
   b. Unresectable or recurrent medullary thyroid cancer
   c. Progressive/symptomatic thyroid cancer

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: Documentation of the presence of a *RET* gene fusion or specific *RET* gene mutation in tumor specimens or plasma (where applicable).

III. CRITERIA FOR INITIAL APPROVAL

A. Non-Small Cell Lung Cancer
Authorization of 12 months may be granted as a single agent for treatment of recurrent, advanced, or metastatic non-small cell lung cancer (including brain metastases from NSCLC) when the tumors have a *RET* gene fusion.

B. Thyroid Cancer
Authorization of 12 months may be granted for treatment of thyroid cancer with a *RET gene* mutation when any of the following criteria are met:
1. Member has locoregional or metastatic anaplastic thyroid cancer and the requested medication will be used as a single agent
2. Member has unresectable, recurrent, advanced, or metastatic medullary thyroid cancer
3. Member has progressive/symptomatic, advanced, or metastatic follicular, Hürthle cell, or papillary thyroid carcinoma that is not amenable to radioactive iodine therapy

C. Solid Tumors
Authorization of 12 months may be granted for treatment of solid tumors when all of the following criteria are met:
1. The disease is recurrent, persistent, progressive, unresectable, advanced or metastatic
2. The tumor has a *RET gene fusion*
3. Member has not responded to preoperative therapy, has progressed on or following prior systemic treatment, or has no satisfactory alternative treatment options
4. The medication will be used as a single agent for the following solid tumors:
    a. Epithelial ovarian cancer, fallopian tube cancer, primary peritoneal cancer
    b. Pancreatic adenocarcinoma
    c. Cervical cancer
    d. Small bowel adenocarcinoma
    e. Colorectal cancer, including appendiceal adenocarcinoma and anal adenocarcinoma
    f. Hepatocellular carcinoma
    g. Hepatobiliary carcinoma, including intrahepatic and extrahepatic cholangiocarcinoma and gallbladder cancer
    h. Breast cancer
    i. Salivary gland tumors
    j. Esophageal and esophagogastric junction cancers
    k. Gastric cancer
    l. Soft tissue sarcoma of the extremity/body wall, head/neck, retroperitoneal/intra-abdominal sarcoma

D. Histiocytic Neoplasms
Authorization of 12 months may be granted for the treatment of any of the following histiocytic neoplasm subtypes as a single agent in members with a *RET* gene fusion:
1. Symptomatic or relapsed/refractory Erdheim-Chester Disease (ECD)
2. Symptomatic or relapsed/refractory Rosai-Dorfman Disease
3. Langerhans Cell Histiocytosis (LCH)

E. Occult Primary Cancer
Authorization of 12 months may be granted for treatment of occult primary cancer with a *RET gene fusion* that has progressed on or following systemic treatment, or who have no satisfactory alternative treatment options, when used as a single agent.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

V. REFERENCES

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STEP THERAPY CRITERIA

BRAND NAME
(generic)

REYVOW
(lasmiditan)

Status: CVS Caremark® Criteria
Type: Initial Step Therapy with Quantity Limit;
Post Step Therapy Prior Authorization with Quantity Limit

POLICY

FDA-APPROVED INDICATIONS
Reyvow is indicated for the acute treatment of migraine with or without aura in adults.

Limitations of Use
Reyvow is not indicated for the preventive treatment of migraine.

INITIAL STEP THERAPY with QUANTITY LIMIT*
Include Rx and OTC products unless otherwise stated.

If the patient has filled a prescription for at least a 30-day supply of TWO triptan 5-HT1 agonists (include combinations) within the past 180 days under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit.** If the patient does not meet the initial step therapy criteria, then the claim will reject with a message indicating that a prior authorization (PA) is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

**If the patient meets the initial step therapy criteria, then the initial limit criteria will apply. If the patient is requesting more than the initial quantity limit the claim will reject with a message indicating that a PA is required.

INITIAL LIMIT CRITERIA
Limits do not accumulate together, patient is allowed the maximum limit for each drug and strength.
PLEASE NOTE: Since manufacturer package sizes may vary, it is the discretion of the dispensing pharmacy to fill quantities per package size up to these quantity limits. In such cases the filling limit and day supply may be less than what is indicated.

Drug	1 Month Limit*	3 Month Limit*
Reyvow 50 mg	4 tablets / 25 days	12 tablets / 75 days
Reyvow 100 mg	8 tablets / 25 days	24 tablets / 75 days

**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*

COVERAGE CRITERIA
The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for the acute treatment of migraine with or without aura in an adult patient

AND

- The patient has experienced an inadequate treatment response or an intolerance to TWO triptan 5-HT1agonists

OR

- The patient has a contraindication that would prohibit a trial of triptan 5-HT1 agonists

AND

- If additional quantities are being requested, medication overuse headache has been considered and ruled out
  AND
  - The patient is currently using migraine prophylactic therapy
    [Note: Examples of prophylactic therapy are divalproex sodium, topiramate, valproate sodium, metoprolol, propranolol, timolol, atenolol, nadolol, amitriptyline, venlafaxine.]
    OR
  - The patient is unable to take migraine prophylactic therapy due to an inadequate treatment response, intolerance, or contraindication
    [Note: Examples of prophylactic therapy are divalproex sodium, topiramate, valproate sodium, metoprolol, propranolol, timolol, atenolol, nadolol, amitriptyline, venlafaxine.]

Quantity Limits apply.
Reyvow 50 mg: 4 tablets per 25 days*, 12 tablets per 75 days*,
Reyvow 100 mg: 8 tablets per 25 days*, 24 tablets per 75 days*

Post Limit, If additional quantities are being requested,
Reyvow 50 mg: 8 tablets per 25 days*, 24 tablets per 75 days*,
Reyvow 100 mg: 16 tablets per 25 days*, 48 tablets per 75 days*
**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*

Duration of Approval (DOA):

- 3373-E: DOA: 12 months

REFERENCES

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Reference number(s)
5688-A

SPECIALTY GUIDELINE MANAGEMENT

REZLIDHIA (olutasidenib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Relapsed or Refractory Acute Myeloid Leukemia
Rezlidhia is indicated for the treatment of adult patients with relapsed or refractory acute myeloid leukemia (AML) with a susceptible isocitrate dehydrogenase-1 (IDH1) mutation as detected by an FDA-approved test.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: medical record documentation of isocitrate dehydrogenase-1 (IDH1) mutation

III. CRITERIA FOR INITIAL APPROVAL

Acute Myeloid Leukemia (AML)
Authorization of 12 months may be granted for treatment as a single agent in members with relapsed or refractory AML with a susceptible IDH1 mutation.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

V. REFERENCES

1. Rezlidhia [package insert]. South San Francisco, CA: Rigel Pharmaceuticals, Inc.; December 2022.
2. The NCCN Drugs & Biologics Compendium®. © 2023 National Comprehensive Cancer Network, Inc. Available at: https://www.nccn.org. Accessed January 17, 2023.

Reference number(s)
2140-A

SPECIALTY GUIDELINE MANAGEMENT

RIBAVIRIN PRODUCTS
(COPEGUS, MODERIBA, REBETOL, RIBASPHERE, RIBASPHERE RIBAPAK, RIBATAB, ribavirin capsules and tablets)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Copegus
Copegus is indicated for the treatment of chronic hepatitis C (CHC) virus infection in combination with Pegasys in patients 5 years of age and older with compensated liver disease not previously treated with interferon alpha, and in adult CHC patients coinfected with HIV.

Moderiba
Moderiba is indicated for the treatment of chronic hepatitis C (CHC) virus infection in combination with peginterferon alfa-2a in patients 5 years of age and older with compensated liver disease not previously treated with interferon alpha, and in adult CHC patients coinfected with HIV.

Rebetol
Rebetol is indicated in combination with interferon alfa-2b (pegylated and nonpegylated) for the treatment of chronic hepatitis C (CHC) in patients 3 years of age and older with compensated liver disease.

Ribasphere/RibaPak
Ribasphere is indicated for the treatment of chronic hepatitis C (CHC) virus infection in combination with peginterferon alfa-2a in patients 5 years of age and older with compensated liver disease not previously treated with interferon alpha, and in adult CHC patients coinfected with HIV.

All other indications are considered experimental/investigational and not medically necessary.

II. EXCLUSIONS

Exclusions to other antiviral drugs being used in combination with the requested drug apply. Refer to the SGM policy for each drug in the treatment regimen for applicable exclusions.

III. CRITERIA FOR APPROVAL

Hepatitis C virus (HCV) infection
Refer to the SGM of requested regimen for the specific criteria for approval and approval durations.

IV. REFERENCES

1. Copegus [package insert]. South San Francisco, CA: Genentech USA, Inc.; August 2015.
2. Moderiba [package insert]. North Chicago, IL: AbbVie Inc.; December 2017.
3. Rebetol [package insert]. Whitehouse Station, NJ: Merck & Co., Inc.; January 2020.
4. Ribasphere/Ribapak [package insert]. Warrendale, PA: Kadmon Pharmaceuticals, LLC; September 2017.
5. AASLD/IDSA/IAS–USA. Recommendations for testing, managing, and treating hepatitis C. https://www.hcvguidelines.org. Last changes made on September 29, 2021. Accessed October 15, 2021.
6. Sovaldi [package insert]. Foster City, CA: Gilead Sciences, Inc.; March 2020.
7. Viekira Pak [package insert]. North Chicago, IL: AbbVie Inc.; December 2019.
8. Zepatier [package insert]. Whitehouse Station, NJ: Merck & Co., Inc.; December 2019.
9. Epclusa [package insert]. Foster City, CA: Gilead Sciences, Inc.; June 2021.
10. Vosevi [package insert]. Foster City, CA: Gilead Sciences, Inc.; November 2019.

Reference number(s)
3173-A

SPECIALTY GUIDELINE MANAGEMENT

RINVOQ (upadacitinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Rinvoq is indicated for:

A. Treatment of adults with moderately to severely active rheumatoid arthritis who have had an inadequate response or intolerance to one or more tumor necrosis factor (TNF) blockers.
B. Treatment of adults with active psoriatic arthritis who have had an inadequate response or intolerance to one or more TNF blockers.
C. Treatment of adults and pediatric patients 12 years of age and older with refractory, moderate to severe atopic dermatitis whose disease is not adequately controlled with other systemic drug products, including biologics, or when use of those therapies are inadvisable.
D. Treatment of adult patients with moderately to severely active ulcerative colitis who have had an inadequate response or intolerance to one or more TNF blockers.
E. Treatment of adults with active ankylosing spondylitis who have had an inadequate response or intolerance to one or more TNF blockers.
F. Treatment of adults with active non-radiographic axial spondyloarthritis with objective signs of inflammation who have had an inadequate response or intolerance to TNF blocker therapy.
G. Treatment of adult patients with moderately to severely active Crohn's disease who have had an inadequate response or intolerance to one or more TNF blockers.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

A. Rheumatoid arthritis (RA), psoriatic arthritis (PsA), ankylosing spondylitis (AS), and non-radiographic axial spondyloarthritis (nr-axSpA)
    1. Initial requests: Chart notes, medical record documentation, or claims history supporting previous medications tried, including response to therapy (if applicable).
    2. Continuation requests: Chart notes or medical record documentation supporting positive clinical response.

B. Atopic dermatitis
    1. Initial requests:
        i. Chart notes or medical records showing affected area(s) and affected body surface area (where applicable).

ii. Chart notes, medical record documentation, or claims history of prerequisite therapies, including response to therapy. If prerequisite therapies are not advisable, documentation of why therapies are not advisable for the member.

2. Continuation requests: Documentation (e.g., chart notes) that the member has experienced a positive clinical response to therapy as evidenced by low disease activity or improvement in signs or symptoms of atopic dermatitis.

C. Ulcerative colitis (UC)
1. Initial Requests: Chart notes, medical record documentation, or claims history supporting previous medications tried, including response to therapy.
2. Continuation requests: Chart notes or medical record documentation supporting positive clinical response to therapy or remission.

D. Crohn's disease (CD)
1. Initial requests: Chart notes, medical record documentation, or claims history supporting previous medications tried, including response to therapy.
2. Continuation requests: Chart notes or medical record documentation supporting positive clinical response to therapy or remission.

III. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with one of the following:
A. Rheumatoid arthritis, ankylosing spondylitis, and non-radiographic axial spondyloarthritis: rheumatologist
B. Psoriatic arthritis: rheumatologist or dermatologist
C. Atopic dermatitis: dermatologist or allergist/immunologist
D. Ulcerative colitis and Crohn's disease: gastroenterologist

IV. CRITERIA FOR INITIAL APPROVAL

A. Rheumatoid arthritis (RA)

1. Authorization of 12 months may be granted for adult members for treatment of moderately to severely active rheumatoid arthritis (RA) when the member has experienced an inadequate response or intolerance to at least one tumor necrosis factor (TNF) inhibitor.

2. Authorization of 12 months may be granted for adult members who have previously received a biologic (other than a TNF inhibitor) or targeted synthetic drug (e.g., Xeljanz, Olumiant) indicated for moderately to severely active RA.

B. Psoriatic arthritis (PsA)

1. Authorization of 12 months may be granted for adult members for treatment of active psoriatic arthritis when the member has experienced an inadequate response or intolerance to at least one TNF inhibitor.

2. Authorization of 12 months may be granted for adult members who have previously received a biologic (other than a TNF inhibitor) or targeted synthetic drug (e.g., Xeljanz, Otezla) indicated for active psoriatic arthritis.

C. Atopic dermatitis

Authorization of 4 months may be granted for treatment of moderate-to-severe atopic dermatitis in members 12 years of age or older when all of the following criteria are met:

1. Affected body surface is greater than or equal to 10% body surface area OR crucial body areas (e.g., hands, feet, face, neck, scalp, genitals/groin, intertriginous areas) are affected.
2. Member meets one of the following:
   i. Member has had an inadequate treatment response with one of the following in the past year:
      a. A medium potency to super-high potency topical corticosteroid (see Appendix)
      b. A topical calcineurin inhibitor
   ii. The use of medium potency to super-high potency topical corticosteroid and topical calcineurin inhibitor are not advisable for the member (e.g., due to contraindications, prior intolerances).
3. Member has had an inadequate response to treatment with a systemic drug product (e.g., oral cyclosporine, azathioprine, methotrexate, mycophenolate mofetil) or a biologic (e.g., Dupixent, Adbry) indicated for the treatment of atopic dermatitis, or use of these therapies are not advisable for the member.

D. Ulcerative colitis (UC)

1. Authorization of 12 months may be granted for adult members for treatment of moderately to severely active UC when the member has had an inadequate response or intolerance to at least one TNF inhibitor.

2. Authorization of 12 months may be granted for adult members who have previously received a biologic (other than a TNF inhibitor) or targeted synthetic drug (e.g., Xeljanz) indicated for moderately to severely active ulcerative colitis.

E. Ankylosing spondylitis (AS) and non-radiographic axial spondyloarthritis (nr-axSpA)

1. Authorization of 12 months may be granted for adult members for treatment of active ankylosing spondylitis or active non-radiographic axial spondyloarthritis when the member has experienced an inadequate response or intolerance to at least one TNF inhibitor.

2. Authorization of 12 months may be granted for adult members who have previously received a biologic (other than a TNF inhibitor) or targeted synthetic drug (e.g., Xeljanz) indicated for active ankylosing spondylitis or active non-radiographic axial spondyloarthritis.

F. Crohn's disease (CD)

1. Authorization of 12 months may be granted for adult members for treatment of moderately to severely active CD when the member has had an inadequate response or intolerance to at least one TNF inhibitor.

2. Authorization of 12 months may be granted for adult members who have previously received a biologic (other than a TNF inhibitor) indicated for moderately to severely active Crohn's disease.

V. CONTINUATION OF THERAPY

A. Rheumatoid arthritis (RA)

Authorization of 12 months may be granted for all adult members (including new members) who are using the requested medication for moderately to severely active rheumatoid arthritis and who achieve or maintain a positive clinical response as evidenced by disease activity improvement of at least 20% from baseline in tender joint count, swollen joint count, pain, or disability.

B. Psoriatic arthritis

Authorization of 12 months may be granted for all adult members (including new members) who are using the requested medication for psoriatic arthritis and who achieve or maintain a positive clinical response as

evidenced by low disease activity or improvement in signs and symptoms of the condition when there is improvement in any of the following from baseline:

1. Number of swollen joints
2. Number of tender joints
3. Dactylitis
4. Enthesitis
5. Axial disease
6. Skin and/or nail involvement

C. Atopic dermatitis

Authorization of 12 months may be granted for members 12 years of age or older (including new members) who are using the requested medication for moderate-to-severe atopic dermatitis when the member has achieved or maintained a positive clinical response as evidenced by low disease activity (i.e., clear or almost clear skin), or improvement in signs and symptoms of atopic dermatitis (e.g., redness, itching, oozing/crusting).

D. Ulcerative colitis (UC)

1. Authorization of 12 months may be granted for all adult members (including new members) who are using the requested medication for moderately to severely active ulcerative colitis and who achieve or maintain remission.

2. Authorization of 12 months may be granted for all adult members (including new members) who are using the requested medication for moderately to severely active ulcerative colitis and who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition when there is improvement in any of the following from baseline:
   i. Stool frequency
   ii. Rectal bleeding
   iii. Urgency of defecation
   iv. C-reactive protein (CRP)
   v. Fecal calprotectin (FC)
   vi. Appearance of the mucosa on endoscopy, computed tomography enterography (CTE), magnetic resonance enterography (MRE), or intestinal ultrasound
   vii. Improvement on a disease activity scoring tool (e.g., Ulcerative Colitis Endoscopic Index of Severity [UCEIS], Mayo score)

E. Ankylosing spondylitis (AS) and non-radiographic axial spondyloarthritis (nr-axSpA)

Authorization of 12 months may be granted for all adult members (including new members) who are using the requested medication for active ankylosing spondylitis or active non-radiographic axial spondyloarthritis and who achieve or maintain a positive clinical response with the requested medication as evidenced by low disease activity or improvement in signs and symptoms of the condition when there is improvement in any of the following from baseline:

1. Functional status
2. Total spinal pain
3. Inflammation (e.g., morning stiffness)

F. Crohn's disease (CD)

1. Authorization of 12 months may be granted for all adult members (including new members) who are using the requested medication for moderately to severely active Crohn's disease and who achieve or maintain remission.

2. Authorization of 12 months may be granted for all adult members (including new members) who are using the requested medication for moderately to severely active Crohn's disease and who achieve or

maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition when there is improvement in any of the following from baseline:

i. Abdominal pain or tenderness
ii. Diarrhea
iii. Body weight
iv. Abdominal mass
v. Hematocrit
vi. Appearance of the mucosa on endoscopy, computed tomography enterography (CTE), magnetic resonance enterography (MRE), or intestinal ultrasound
vii. Improvement on a disease activity scoring tool (e.g., Crohn's Disease Activity Index [CDAI] score)

VI. OTHER

For all indications: Member has had a documented negative tuberculosis (TB) test (which can include a tuberculosis skin test [PPD], an interferon-release assay [IGRA], or a chest x-ray)* within 6 months of initiating therapy for persons who are naïve to biologic drugs or targeted synthetic drugs associated with an increased risk of TB.

* If the screening testing for TB is positive, there must be further testing to confirm there is no active disease. Do not administer the requested medication to members with active TB infection. If there is latent disease, TB treatment must be started before initiation of the requested medication.

For all indications: Member cannot use the requested medication concomitantly with any other biologic drug, targeted synthetic drug, or potent immunosuppressant such as azathioprine or cyclosporine.

VII. DOSAGE AND ADMINISTRATION

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

VIII. APPENDIX

Table. Relative potency of select topical corticosteroid products

Potency	Drug	Dosage form	Strength
I. Super-high potency (group 1)	Augmented betamethasone dipropionate	Ointment, Lotion, Gel	0.05%
	Clobetasol propionate	Cream, Gel, Ointment, Solution, Cream (emollient), Lotion, Shampoo, Foam, Spray	0.05%
	Fluocinonide	Cream	0.1%
	Flurandrenolide	Tape	4 mcg/cm^2
	Halobetasol propionate	Cream, Lotion, Ointment, Foam	0.05%
II. High potency (group 2)	Amcinonide	Ointment	0.1%
	Augmented betamethasone dipropionate	Cream	0.05%
	Betamethasone dipropionate	Ointment	0.05%
	Clobetasol propionate	Cream	0.025%
	Desoximetasone	Cream, Ointment, Spray	0.25%
		Gel	0.05%

Potency	Drug	Dosage form	Strength
	Diflorasone diacetate	Ointment, Cream (emollient)	0.05%
	Fluocinonide	Cream, Ointment, Gel, Solution	0.05%
	Halcinonide	Cream, Ointment	0.1%
	Halobetasol propionate	Lotion	0.01%
Potency	**Drug**	**Dosage form**	**Strength**
III. High potency (group 3)	Amcinonide	Cream, Lotion	0.1%
	Betamethasone dipropionate	Cream, hydrophilic emollient	0.05%
	Betamethasone valerate	Ointment	0.1%
		Foam	0.12%
	Desoximetasone	Cream, Ointment	0.05%
	Diflorasone diacetate	Cream	0.05%
	Fluocinonide	Cream, aqueous emollient	0.05%
	Fluticasone propionate	Ointment	0.005%
	Mometasone furoate	Ointment	0.1%
	Triamcinolone acetonide	Cream, Ointment	0.5%
IV. Medium potency (group 4)	Betamethasone dipropionate	Spray	0.05%
	Clocortolone pivalate	Cream	0.1%
	Fluocinolone acetonide	Ointment	0.025%
	Flurandrenolide	Ointment	0.05%
	Hydrocortisone valerate	Ointment	0.2%
	Mometasone furoate	Cream, Lotion, Solution	0.1%
	Triamcinolone acetonide	Cream	0.1%
		Ointment	0.05% and 0.1%
		Aerosol Spray	0.2 mg per 2-second spray
V. Lower-mid potency (group 5)	Betamethasone dipropionate	Lotion	0.05%
	Betamethasone valerate	Cream	0.1%
	Desonide	Ointment, Gel	0.05%
	Fluocinolone acetonide	Cream	0.025%
	Flurandrenolide	Cream, Lotion	0.05%
	Fluticasone propionate	Cream, Lotion	0.05%
	Hydrocortisone butyrate	Cream, Lotion, Ointment, Solution	0.1%
	Hydrocortisone probutate	Cream	0.1%
	Hydrocortisone valerate	Cream	0.2%
	Prednicarbate	Cream (emollient), Ointment	0.1%
	Triamcinolone acetonide	Lotion	0.1%
		Ointment	0.025%
VI. Low potency (group 6)	Alclometasone dipropionate	Cream, Ointment	0.05%
	Betamethasone valerate	Lotion	0.1%
	Desonide	Cream, Lotion, Foam	0.05%
	Fluocinolone acetonide	Cream, Solution, Shampoo, Oil	0.01%
	Triamcinolone acetonide	Cream, lotion	0.025%
		Cream, Ointment, Solution	2.5%

Potency	Drug	Dosage form	Strength
VII. Least potent (group 7)	Hydrocortisone (base, greater than or equal to 2%)	Lotion	2%
	Hydrocortisone (base, less than 2%)	Cream, Ointment, Gel, Lotion, Spray, Solution	1%
		Cream, Ointment	0.5%
	Hydrocortisone acetate	Cream	2.5%
		Lotion	2%
		Cream	1%

IX. REFERENCES

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Reference number(s)
1641-A

SPECIALTY GUIDELINE MANAGEMENT

Adempas (riociguat)
riociguat (generic)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

A. Pulmonary Arterial Hypertension (PAH)
Adempas is indicated for the treatment of adults with pulmonary arterial hypertension (PAH), (World Health Organization [WHO] Group 1), to improve exercise capacity, WHO functional class and to delay clinical worsening. Efficacy was shown in patients on Adempas monotherapy or in combination with endothelin receptor antagonists or prostanoids. Studies establishing effectiveness included predominately patients with WHO functional class II-III and etiologies of idiopathic or heritable PAH or PAH associated with connective tissue diseases.

B. Chronic Thromboembolic Pulmonary Hypertension (CTEPH)
Adempas is indicated for the treatment of adults with persistent/recurrent chronic thromboembolic pulmonary hypertension (CTEPH) (WHO Group 4) after surgical treatment or inoperable CTEPH to improve exercise capacity and WHO functional class.

All other indications are considered experimental/investigational and not medically necessary.

II. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with a pulmonologist or cardiologist.

III. CRITERIA FOR INITIAL APPROVAL

A. Pulmonary Arterial Hypertension (PAH)
Authorization of 12 months may be granted for treatment of PAH when ALL of the following criteria are met:
1. Member has PAH defined as WHO Group 1 class of pulmonary hypertension (Refer to Appendix)
2. PAH was confirmed by right heart catheterization with all of the following pretreatment results:
   i. mPAP > 20 mmHg
   ii. PCWP ≤ 15 mmHg
   iii. PVR ≥ 3 Wood units

B. Chronic Thromboembolic Pulmonary Hypertension (CTEPH)
Authorization of 12 months may be granted for treatment of CTEPH when ALL of the following criteria are met:

1. Member has CTEPH defined as WHO Group 4 class of pulmonary hypertension (Refer to Appendix)
2. Member meets either criterion (i) or criterion (ii) below:
   i. Recurrent or persistent CTEPH after pulmonary endarterectomy (PEA)
   ii. Inoperable CTEPH with diagnosis confirmed by BOTH of the following (a. and b.):
      a. Computed tomography (CT)/magnetic resonance imaging (MRI) angiography or pulmonary angiography
      b. Pretreatment right heart catheterization with all of the following results:
         1. mPAP > 20 mmHg
         2. PCWP ≤ 15 mmHg
         3. PVR ≥ 3 Wood units

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for members with an indication listed in Section III who are currently receiving the requested medication through a paid pharmacy or medical benefit, and who are experiencing benefit from therapy as evidenced by disease stability or disease improvement.

V. APPENDIX

WHO Classification of Pulmonary Hypertension

1 PAH

1.1 Idiopathic (PAH)
1.2 Heritable PAH
1.3 Drug- and toxin-induced PAH
1.4. PAH associated with:
   1.4.1 Connective tissue diseases
   1.4.2 HIV infection
   1.4.3 Portal hypertension
   1.4.4 Congenital heart diseases
   1.4.5 Schistosomiasis
1.5 PAH long-term responders to calcium channel blockers
1.6 PAH with overt features of venous/capillaries (PVOD/PCH) involvement
1.7 Persistent PH of the newborn syndrome

2 PH due to left heart disease

2.1 PH due to heart failure with preserved LVEF
2.2 PH due to heart failure with reduced LVEF
2.3 Valvular heart disease
2.4 Congenital/acquired cardiovascular conditions leading to post-capillary PH

3 PH due to lung diseases and/or hypoxia

3.1 Obstructive lung disease
3.2 Restrictive lung disease
3.3 Other lung disease with mixed restrictive/obstructive pattern
3.4 Hypoxia without lung disease
3.5 Developmental lung disorders

4 PH due to pulmonary artery obstruction

4.1 Chronic thromboembolic PH
4.2 Other pulmonary artery obstructions
   4.2.1 Sarcoma (high or intermediate grade) or angiosarcoma

4.2.2 Other malignant tumors
Renal carcinoma
Uterine carcinoma
Germ cell tumours of the testis
Other tumours
4.2.3 Non-malignant tumours
Uterine leiomyoma
4.2.4 Arteritis without connective tissue disease
4.2.5 Congenital pulmonary artery stenosis
4.2.6 Parasites
Hydatidosis

5 PH with unclear and/or multifactorial mechanisms

5.1 Hematologic disorders: Chronic hemolytic anemia, myeloproliferative disorders
5.2 Systemic and metabolic disorders: Pulmonary Langerhans cell histiocytosis, Gaucher disease, glycogen storage disease, neurofibromatosis, sarcoidosis
5.3 Others: chronic renal failure with or without hemodialysis, fibrosing mediastinitis
5.4 Complex congenital heart disease

VI. REFERENCES

1. Adempas [package insert]. Whippany, NJ: Bayer HealthCare Pharmaceuticals, Inc.; September 2021.
2. Riociguat [package insert]. Telangana, India: MSN Laboratories Private Limited: September 2022.
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PRIOR AUTHORIZATION CRITERIA

DRUG CLASS	**ROSACEA PRODUCTS**
BRAND NAME* (generic)	
	FINACEA (azelaic acid)
	MIRVASO (brimonidine)
	NORITATE (metronidazole)
	RHOFADE (oxymetazoline)
	SOOLANTRA (ivermectin)

Status: CVS Caremark Criteria ***Ref # BOG 4915-A***
Type: Initial Prior Authorization ***Ref # 1486-A***

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Finacea Gel

Finacea Gel, 15% is indicated for topical treatment of the inflammatory papules and pustules of mild to moderate rosacea.

Limitations of Use

Although some reduction of erythema which was present in patients with papules and pustules of rosacea occurred in clinical studies, efficacy for treatment of erythema in rosacea in the absence of papules and pustules has not been evaluated.

Finacea Foam

Finacea Foam, 15% is indicated for topical treatment of the inflammatory papules and pustules of mild to moderate rosacea.

Mirvaso

Mirvaso (brimonidine) topical gel, 0.33% is an alpha adrenergic agonist indicated for the topical treatment of persistent (non-transient) erythema of rosacea in adults 18 years of age or older.

Noritate

Noritate is indicated for the topical treatment of inflammatory lesions and erythema of rosacea.

Rhofade

Rhofade (oxymetazoline hydrochloride) cream, 1% is indicated for the topical treatment of persistent facial erythema associated with rosacea in adults.

Soolantra
Soolantra cream is indicated for the treatment of inflammatory lesions of rosacea.

COVERAGE CRITERIA
The requested drug will be covered with prior authorization when the following criteria are met:
- The patient has a diagnosis of rosacea

RATIONALE
The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Finacea (azelaic acid) is indicated for topical treatment of the inflammatory papules and pustules of mild to moderate rosacea. Mirvaso (brimonidine) is indicated for the topical treatment of persistent (non-transient) facial erythema of rosacea in adults 18 years of age or older. Noritate is indicated for the topical treatment of inflammatory lesions and erythema of rosacea. Rhofade (oxymetazoline hydrochloride) is indicated for the topical treatment of persistent facial erythema associated with rosacea in adults. Soolantra (ivermectin) is indicated for the treatment of inflammatory lesions of rosacea.[1-6]

REFERENCES

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2. Finacea Foam [package insert]. Madison, NJ: LEO Pharma Inc.; December 2020.
3. Mirvaso [package insert]. Fort Worth, TX: Galderma Laboratories, L.P.; August 2021.
4. Noritate [package insert]. Bridgewater, NJ: Bausch Health US, LLC; June 2020.
5. Rhofade [package insert]. Charleston, SC: EPI Health, LLC; November 2019.
6. Soolantra [package insert]. Fort Worth, TX: Galderma Laboratories, L.P.; July 2018.
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Written by:	UM Development (SF)
Date Written:	06/2016
Revised:	09/2016 (added target drugs); MS) 02/2017(added Rhofade), (SF) 06/2017 (no clinical changes), (ME) 06/2018 (no clinical changes), 06/2019 (no clinical changes), 07/2020 (no clinical changes); (PM) 08/2021 (no clinical changes), 09/2021 (added BOG 4915-A); (DRS) 07/2022 (no clinical changes)
Reviewed:	Medical Affairs (LMS) 06/2016, (JG) 02/2017, (CHART) 07/30/20, 08/05/21, 09/16/21, 07/28/2022 External Review: 09/2016, 02/2016, 04/2017, 10/2017, 10/2018, 10/2019, 10/2020, 10/2021, 10/2022

CRITERIA FOR APPROVAL

1	Does the patient have a diagnosis of rosacea? [No further questions]	Yes	No

Mapping Instructions			
	Yes	**No**	**DENIAL REASONS**
1.	Approve, 36 Months, Note for Ref # BOG 4915-A only: If the request is for	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have rosacea. Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]

	Soolantra approve Brand name Soolantra		

Reference number(s)
3165-A

SPECIALTY GUIDELINE MANAGEMENT

ROZLYTREK (entrectinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. Solid tumors
      Rozlytrek is indicated for the treatment of adult and pediatric patients 12 years and older with solid tumors that:
      a. have a neurotrophic tyrosine receptor kinase (NTRK) gene fusion without a known acquired resistance mutation,
      b. are metastatic or where surgical resection is likely to result in severe morbidity, and
      c. have either progressed following treatment or have no satisfactory alternative therapy.

   2. Non-small cell lung cancer
      Rozlytrek is indicated for the treatment of adult patients with metastatic non-small cell lung cancer (NSCLC) whose tumors are ROS1-positive.

B. Compendial Use
   1. Cutaneous Melanoma

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: NTRK gene fusion status or ROS1 status (where applicable).

III. CRITERIA FOR INITIAL APPROVAL

A. Solid tumors
Authorization of 12 months may be granted for treatment of solid tumors when the tumors have a NTRK gene fusion without a known acquired resistance mutation, as demonstrated by laboratory testing (e.g., next-generation sequencing [NGS] or fluorescence in situ hybridization [FISH]).

B. Non-small cell lung cancer (NSCLC)
Authorization of 12 months may be granted for treatment of recurrent, advanced, or metastatic NTRK gene fusion-positive or ROS1-positive NSCLC as a single agent.

C. Cutaneous Melanoma

Authorization of 12 months may be granted for treatment of metastatic or unresectable NTRK gene fusion-positive or ROS1-positive cutaneous melanoma as second-line or subsequent therapy for disease progression, intolerance, and/or projected risk of progression with BRAF-targeted therapy.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication in Section III when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

V. REFERENCES

1. Rozlytrek [package insert]. South San Francisco, CA: Genentech, Inc. November 2021.
2. The NCCN Drugs & Biologics Compendium® © 2023 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed January 25, 2023.

Reference number(s)
2256-A

SPECIALTY GUIDELINE MANAGEMENT

RUBRACA (rucaparib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. Ovarian Cancer
      Maintenance treatment of adult patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to platinum-based chemotherapy.
   2. Prostate Cancer
      Treatment of adult patients with a deleterious *BRCA* mutation (germline and/or somatic)-associated metastatic castration-resistant prostate cancer (mCRPC) who have been treated with androgen receptor-directed therapy and a taxane-based chemotherapy. Select patients for therapy based on an FDA-approved companion diagnostic test for Rubraca.

B. Compendial Uses
   1. Prostate Cancer
   2. Uterine Leiomyosarcoma (uLMS)
   3. Pancreatic Adenocarcinoma

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
A. Documentation of laboratory report confirming BRCA mutation status, where applicable
B. Documentation of laboratory report confirming PALB2 mutation status, where applicable

III. CRITERIA FOR INITIAL APPROVAL

A. Epithelial ovarian, fallopian tube, or primary peritoneal cancer
Authorization of 12 months may be granted for the maintenance treatment of recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer as a single agent when all of the following criteria are met:
1. Member is in complete or partial response to platinum-based chemotherapy
2. Member has received at least two prior platinum-containing regimens

B. Prostate cancer
Authorization of 12 months may be granted for treatment of metastatic castration-resistant prostate cancer when all of the following criteria are met:

1. Tumor has a deleterious BRCA mutation (germline, somatic, or both)
2. Member has been treated with androgen receptor-directed therapy
3. Member has been treated with a taxane-based chemotherapy or is not fit for chemotherapy
4. Member is receiving therapy concurrently with a gonadotropin-releasing hormone (GnRH) analog or has had a bilateral orchiectomy
5. The requested medication will be used as a single agent (concurrent use with a GnRH analog is allowed)

C. Uterine Leiomyosarcoma

Authorization of 12 months may be granted for treatment of BRCA altered uterine leiomyosarcoma (uLMS) as second-line therapy when used as a single agent.

D. Pancreatic Adenocarcinoma

Authorization of 12 months may be granted for the maintenance treatment of metastatic pancreatic adenocarcinoma when all of the following criteria are met:

1. Tumor has BRCA-mutations (germline or somatic) or PALB2-mutations
2. Disease has not progressed on at least 16 weeks of a platinum-based chemotherapy
3. The requested medication will be used as a single agent

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

V. REFERENCES

1. Rubraca [package insert]. Boulder, CO: Clovis Oncology, Inc.; June 2022.
2. The NCCN Drugs & Biologics Compendium® © 2022 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed July 19, 2022.

Reference number(s)
1612-A

SPECIALTY GUIDELINE MANAGEMENT

RUCONEST (C1 esterase inhibitor [recombinant])

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Ruconest is indicated for the treatment of acute attacks in adult and adolescent patients with hereditary angioedema (HAE).

Limitation of Use
Effectiveness was not established in HAE patients with laryngeal attacks.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
A. For initial authorization, the following should be documented:
   1. C1 inhibitor functional and antigenic protein levels
   2. F12, angiopoietin-1, plasminogen, kininogen-1 (KNG1), heparan sulfate-glucosamine 3-O-sulfotransferase 6 (HS3ST6), or myoferlin (MYOF) gene mutation testing, if applicable
   3. Chart notes confirming family history of angioedema and the angioedema was refractory to a trial of high-dose antihistamine therapy, if applicable
B. For continuation of therapy, chart notes demonstrating a reduction in severity and/or duration of attacks

III. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with a prescriber who specializes in the management of HAE.

IV. CRITERIA FOR INITIAL APPROVAL

Hereditary angioedema (HAE)
Authorization of 6 months may be granted for treatment of acute HAE attacks when the requested medication will not be used in combination with any other medication used for the treatment of acute HAE attacks and either of the following criteria is met at the time of diagnosis:
A. Member has C1 inhibitor deficiency or dysfunction as confirmed by laboratory testing and meets one of the following criteria.
   1. C1 inhibitor (C1-INH) antigenic level below the lower limit of normal as defined by the laboratory performing the test; or

2. Normal C1-INH antigenic level and a low C1-INH functional level (functional C1-INH less than 50% or C1-INH functional level below the lower limit of normal as defined by the laboratory performing the test)

B. Member has normal C1 inhibitor as confirmed by laboratory testing and meets one of the following criteria:
   1. Member has an F12, angiopoietin-1, plasminogen, kininogen-1 (KNG1), heparan sulfate-glucosamine 3-O-sulfotransferase 6 (HS3ST6), or myoferlin (MYOF) gene mutation as confirmed by genetic testing, or
   2. Member has a documented family history of angioedema and the angioedema was refractory to a trial of high-dose antihistamine therapy (i.e., cetirizine at 40 mg per day or the equivalent) for at least one month.

V. CONTINUATION OF THERAPY

Authorization of 6 months may be granted for continuation of therapy when all of the following criteria are met:
A. Member meets the criteria for initial approval.
B. Member has experienced a reduction in severity and/or duration of acute attacks.
C. Prophylaxis should be considered based on the attack frequency, attack severity, comorbid conditions, and member's quality of life.

VI. REFERENCES

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2. Bowen T, Cicardi M, Farkas H, et al. 2010 International consensus algorithm for the diagnosis, therapy, and management of hereditary angioedema. *Allergy Asthma Clin Immunol*. 2010;6(1):24.
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Reference number
1817-A

SPECIALTY GUIDELINE MANAGEMENT

RYDAPT (midostaurin)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Rydapt is indicated, in combination with standard cytarabine and daunorubicin induction and cytarabine consolidation chemotherapy, for the treatment of adult patients with newly diagnosed acute myeloid leukemia (AML) who are FLT3 mutation-positive, as detected by an FDA approved test.

   Limitations of Use: Rydapt is not indicated as a single-agent induction therapy for the treatment of patients with AML.

2. Rydapt is indicated for the treatment of adult patients with aggressive systemic mastocytosis (ASM), systemic mastocytosis with associated hematological neoplasm (SM-AHN), or mast cell leukemia (MCL).

B. Compendial Uses

1. AML: Relapsed/refractory disease, post-induction therapy, re-induction of residual disease
2. Myeloid/lymphoid neoplasms with eosinophilia and FGFR1 or FLT3 rearrangements in chronic phase
3. Myeloid, lymphoid, or mixed lineage neoplasms with eosinophilia and FGFR1 or FLT3 rearrangements in blast phase

All other indications are considered experimental/investigational and are not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: Medical record documentation of FLT3 mutation or FGFR1 rearrangement (where applicable)

III. CRITERIA FOR INITIAL APPROVAL

A. Acute myeloid leukemia (AML)
Authorization of 12 months may be granted for the treatment of FLT3 mutation-positive AML when it is not used as a single-agent for induction therapy.

B. Aggressive systemic mastocytosis (ASM), systemic mastocytosis with associated hematological neoplasm (SM-AHN), and mast cell leukemia (MCL)

Authorization of 12 months may be granted for the treatment of ASM, SM-AHN, or MCL as a single agent.

C. Myeloid/Lymphoid Neoplasms with eosinophilia
Authorization of 12 months may be granted for the treatment of myeloid and/or lymphoid neoplasms with eosinophilia with a FGFR1 or FLT3 rearrangement in the chronic phase or blast phase.

IV. CONTINUATION OF THERAPY

A. Acute myeloid leukemia (AML)
Authorization of 12 months may be granted for continued treatment in members requesting reauthorization when there is no evidence of unacceptable toxicity.

B. Aggressive systemic mastocytosis (ASM), systemic mastocytosis with associated hematological neoplasm (SM-AHN), mast cell leukemia (MCL), myeloid/lymphoid neoplasms with eosinophilia
Authorization of 12 months may be granted for continued treatment in members requesting reauthorization when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

V. REFERENCES

1. Rydapt [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; November 2021.
2. The NCCN Drugs & Biologics Compendium®. © 2022 National Comprehensive Cancer Network, Inc. Available at: https://www.nccn.org. Accessed January 10, 2022.

Reference number(s)
2012-A

SPECIALTY GUIDELINE MANAGEMENT

KUVAN (sapropterin dihydrochloride)
sapropterin dihydrochloride (generic)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication
Kuvan is indicated to reduce blood phenylalanine (Phe) levels in adult and pediatric patients one month of age and older with hyperphenylalaninemia (HPA) due to tetrahydrobiopterin- (BH4-) responsive phenylketonuria (PKU). Kuvan is to be used in conjunction with a Phe-restricted diet.

B. Compendial Uses
1. Autosomal dominant guanine triphosphate cyclohydrolase deficiency (Segawa disease)
2. Autosomal recessive guanine (GTP) cyclohydrolase deficiency
3. 6-pyruvoyl-tetrahydropterin synthase (6-PTS) deficiency
4. Sepiapterin reductase deficiency
5. Dihydropteridine reductase (DHPR) deficiency
6. Pterin-4a-carbinolamine dehydratase deficiency (also called primapterinuria)

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: enzyme assay, genetic testing, or phenylalanine level results supporting diagnosis.

III. CRITERIA FOR INITIAL APPROVAL

A. Phenylketonuria (PKU)
Authorization of 60 days may be granted for members with a diagnosis of phenylketonuria who have a baseline phenylalanine level greater than or equal to 360 micromol/L (6mg/dL) with dietary interventions alone.

Note: If Kuvan is initiated in a member currently receiving Palynziq for phenylketonuria (PKU), then Palynziq will be discontinued after an appropriate period of overlap.

B. Biopterin Metabolic Defects
Authorization of 6 months may be granted for members who have any of the following biopterin metabolic defects:
1. Autosomal dominant guanine triphosphate cyclohydrolase deficiency (Segawa disease)
2. Autosomal recessive guanine (GTP) cyclohydrolase deficiency

3. 6-pyruvoyl-tetrahydropterin synthase (6-PTS) deficiency
4. Sepiapterin reductase deficiency
5. Dihydropteridine reductase (DHPR) deficiency
6. Pterin-4a-carbinolamine dehydratase deficiency (also called primapterinuria)

IV. CONTINUATION OF THERAPY

A. Phenylketonuria (PKU)

Authorization of 6 months may be granted for continued treatment in members requesting reauthorization for phenylketonuria (PKU) who meet any of the following criteria:

1. Achieve or maintain a 30% decrease in phenylalanine levels from baseline; or
2. Phenylalanine levels are in an acceptable range (less than 360 micromol/L or 6mg/dL); or
3. Demonstrate an improvement in neuropsychiatric symptoms.

Note: Kuvan should not be used concomitantly with Palynziq for phenylketonuria (PKU).

B. Biopterin Metabolic Defects

Authorization of 6 months may be granted for continued treatment in members requesting reauthorization for any biopterin metabolic defect listed in Section III who are experiencing benefit from therapy as evidenced by disease stability or disease improvement.

V. REFERENCES

1. Kuvan [package insert]. Novato, CA: BioMarin Pharmaceutical Inc.; March 2020.
2. Vockley J, Andersson HC, Antshel KM, et al. Phenylalanine hydroxylase deficiency: diagnosis and management guideline. *Genet Med.* 2014;16(2):188-200.
3. Singh RH, Rohr F, Frazier D, et al. Recommendations for the nutrition management of phenylalanine hydroxylase deficiency. *Genet Med.* 2014;16(2):121-131.
4. Sapropterin dihydrochloride [package insert]. Chestnut Ridge, NY: Par Pharmaceutical; April 2020.

PRIOR AUTHORIZATION CRITERIA

DRUG CLASS	**WEIGHT LOSS MANAGEMENT**
BRAND NAME (generic)	**SAXENDA (liraglutide injection)**

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

POLICY

FDA-APPROVED INDICATIONS
Saxenda is indicated as an adjunct to a reduced-calorie diet and increased physical activity for chronic weight management in:

Adult patients with an initial body mass index (BMI) of:
- 30 kg/m^2 or greater (obese), or
- 27 kg/m^2 or greater (overweight) in the presence of at least one weight-related comorbid condition (e.g., hypertension, type 2 diabetes mellitus, or dyslipidemia)

Pediatric patients aged 12 years and older with:
- body weight above 60 kg and
- an initial BMI corresponding to 30 kg/m^2 or greater for adults (obese) by international cut-offs (Cole Criteria)

Limitations of Use
- Saxenda contains liraglutide and should not be coadministered with other liraglutide-containing products or with any other GLP-1 receptor agonist.
- The safety and effectiveness of Saxenda in pediatric patients with type 2 diabetes have not been established.
- The safety and effectiveness of Saxenda in combination with other products intended for weight loss, including prescription drugs, over-the-counter drugs, and herbal preparations, have not been established.

COVERAGE CRITERIA
The requested drug will be covered with prior authorization when the following criteria are met:
- The patient is 18 years of age or older
  AND
  - The patient has completed at least 16 weeks of therapy with the requested drug
    AND
    - The patient lost at least 4 percent of baseline body weight OR the patient has continued to maintain their initial 4 percent weight loss. [Documentation is required for approval.]

  OR
  - The requested drug will be used with a reduced calorie diet and increased physical activity for chronic weight management in an adult
    AND
  - The patient has participated in a comprehensive weight management program that encourages behavioral modification, reduced calorie diet and increased physical activity with continuing follow-up for at least 6 months prior to using drug therapy
    AND
    - The patient has a body mass index (BMI) greater than or equal to 30 kilogram per square meter
      OR

- The patient has a body mass index (BMI) greater than or equal to 27 kilogram per square meter AND has at least one weight related comorbid condition (e.g., hypertension, type 2 diabetes mellitus or dyslipidemia)

OR

- The patient is 12 to 17 years of age

  AND

  - The patient has completed at least 12 weeks of therapy on the maintenance dose of therapy with the requested drug

    AND

    - The patient has at least 1 percent reduction in body mass index (BMI) from baseline OR the patient has continued to maintain their initial 1 percent reduction in BMI from baseline. [Documentation is required for approval.]

  OR

  - The requested drug will be used with a reduced calorie diet and increased physical activity for chronic weight management

    AND

  - The patient has participated in a comprehensive weight management program that encourages behavioral modification, reduced calorie diet and increased physical activity with continuing follow-up for at least 6 months prior to using drug therapy

    AND

  - The patient has a body weight above 60 kilograms

    AND

  - The patient has an initial body mass index (BMI) corresponding to 30 kilogram per square meter or greater for adults by international cut-off points based on the Cole Criteria

REFERENCES

1. Saxenda [package insert]. Plainsboro, NJ: Novo Nordisk Inc; June 2022.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, Ohio: UpToDate, Inc.; 2022; Accessed May 18, 2022.
3. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com/. Accessed May 18, 2022.
4. Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents. National Heart, Lung, and Blood Institute. NIH Publication No. 12-7486. October 2012. http://www.nhlbi.nih.gov/guidelines/cvd_ped/peds_guidelines_full.pdf. 141-159. Accessed May 17, 2022.
5. Pharmacological Management of Obesity: An Endocrine Society Clinical Practice Guideline. The Journal of Clinical Endocrinology & Metabolism, Volume 100, Issue 2, 1 February 2015, Pages 342–362. https://academic.oup.com/jcem/article/100/2/342/2813109. Accessed May 17, 2022.
6. Jensen MD, et al. 2013 AHA/ACC/TOS guideline for the management of overweight and obesity in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and The Obesity Society. *Circulation.* 2013; 129:S102–S138.

STEP THERAPY CRITERIA

DRUG CLASS	**PAIN MANAGEMENT**
BRAND NAME (generic)	**SAVELLA (milnacipran)**

Status: CVS Caremark Criteria
Type: Initial Step Therapy; Post Step Therapy Prior Authorization

POLICY

FDA-APPROVED INDICATIONS
Savella is indicated for the management of fibromyalgia.
Savella is not approved for use in pediatric patients.

INITIAL STEP THERAPY
If the patient has filled a prescription for at least a 30 day supply of immediate-release pregabalin or duloxetine within the past 120 days under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit. If the patient does not meet the initial step therapy criteria, then the claim will reject with a message indicating that a prior authorization (PA) is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

COVERAGE CRITERIA
The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for the treatment of fibromyalgia in a patient 18 years of age or older
  AND
- The patient has experienced an inadequate treatment response to duloxetine
  OR
- The patient has experienced an intolerance to duloxetine
  OR
- The patient has a contraindication that would prohibit a trial of duloxetine

REFERENCES

1. Savella [package insert]. Irvine, CA: Allergan USA, Inc; February 2022.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, Ohio: UpToDate, Inc.; 2022; Accessed April 11, 2022.
3. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed April 12, 2022.
4. Sommer, C. Fibromyalgia: A Clinical Update. *Pain: Clinical Updates* 2010;18(4):1-4.

PRIOR AUTHORIZATION CRITERIA

DRUG CLASS	**SELF INJECTABLES**
BRAND NAME (generic)	
	(cyanocobalamin b12 injection)
	(estradiol cypionate in oil)
	(estradiol valerate in oil)
	(estrogens conjugated 25 mg)
	(heparin injection)
	(medroxyprogesterone acetate suspension 400 mg/ml)
	SOLU-CORTEF (hydrocortisone sodium succinate)
	(testosterone cypionate injection)
	(testosterone enanthate injection)

Status: Client Requested Criteria
Type: Initial Prior Authorization ***Ref # C6947-A***

CRITERIA FOR APPROVAL

1.	Is the requested drug being administered in a physician's office? [If yes, then no further questions.]	Yes	No
2.	Is the requested drug being administered by the patient, or care provider outside of the physician's office? [If no, then no further questions.]	Yes	No
3.	Has the patient and/or caregiver been trained to self administer the medication? [If no, then no further questions.]	Yes	No
4.	Has this training been documented in the patient chart?	Yes	No

REFERENCES

1. CareFirst Medical Policy.

CVS caremark™

Written by:	UM Development (MS)
Date Written:	04/2015
Revised:	(ME) 07/2018 (added testosterone enanthate), 10/2019 (added estrogen products), 09/2020 (Solu-Cortef)
Reviewed:	05/2015, (AM) 07/2018, (LMS) 11/2019, (TP) 09/2020

Reference number(s)
5042-A

SPECIALTY GUIDELINE MANAGEMENT

SCEMBLIX (asciminib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. Adult patients with Philadelphia chromosome-positive chronic myeloid leukemia in chronic phase (Ph+ CML-CP), previously treated with two or more tyrosine kinase inhibitors (TKIs)
   2. Adult patients with Philadelphia chromosome-positive chronic myeloid leukemia in chronic phase (Ph+ CML-CP) with the T315I mutation

B. Compendial Use
   Myeloid/lymphoid neoplasms with eosinophilia and ABL1 rearrangement in chronic or blast phase

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

The following information is necessary to initiate the prior authorization review:
A. Prior to initiation of therapy for treatment of CML: results of cytogenetic and/or molecular testing for detection of the Ph chromosome or the BCR::ABL gene
B. For members requesting initiation of therapy with the requested medication for treatment of T315I-positive CML: results of BCR::ABL1 mutation testing for T315I, A337T and P465S mutations
C. For members requesting initiation of therapy with the requested medication for treatment of myeloid and/or lymphoid neoplasms with eosinophilia: results of testing or analysis confirming ABL1 rearrangement

III. CRITERIA FOR INITIAL APPROVAL

A. Chronic Myeloid Leukemia (CML)
Authorization of 12 months may be granted for treatment of Philadelphia chromosome positive (Ph+) CML in chronic phase (CP) when either of the following criteria are met:
1. Member has T315I mutation positive CML and results of BCR::ABL1 mutation testing are negative for the following: A337T, P465S, or
2. Member has been previously treated with at least two kinase inhibitors (e.g., bosutinib, dasatinib, imatinib, nilotinib) and has not tested positive for the following mutations: A337T, P465S

B. Myeloid/Lymphoid Neoplasms with Eosinophilia
Authorization of 12 months may be granted for treatment of myeloid and/or lymphoid neoplasms with eosinophilia and ABL1 rearrangement in the chronic phase or blast phase.

Reference number(s)
5042-A

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

V. REFERENCES

1. Scemblix [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; October 2022.
2. The NCCN Drugs & Biologics Compendium® © 2023 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed May 24, 2023.

Reference number
1870-A

SPECIALTY GUIDELINE MANAGEMENT

SEROSTIM (somatropin)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Serostim is indicated for the treatment of human immunodeficiency virus (HIV) patients with wasting or cachexia to increase lean body mass and body weight, and improve physical endurance. Concomitant antiretroviral therapy is necessary.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Treatment of HIV patients with wasting or cachexia to increase lean body mass and body weight, and improve physical endurance
Authorization of 12 weeks may be granted for treatment of HIV-associated wasting/cachexia when all of the following criteria are met:
A. Member is currently on antiretroviral therapy
B. Trial with suboptimal response to alternative therapies (See Appendix A) or contraindication or intolerance to alternative therapies
C. Body mass index (BMI) was less than 18.5 kg/m^2 prior to initiating therapy with Serostim (See Appendix B)

III. CONTINUATION OF THERAPY

Treatment of HIV patients with wasting or cachexia to increase lean body mass and body weight, and improve physical endurance
Authorization of 12 weeks may be granted for continued treatment in members requesting reauthorization for treatment of HIV-associated wasting/cachexia when all of the following criteria are met:
A. Member is currently on antiretroviral therapy
B. Member is currently receiving treatment with Serostim excluding obtainment as samples or via manufacturer's patient assistance programs
C. Current BMI is less than 27 kg/m^2 (See Appendix B)

IV. APPENDICES

Appendix A – Alternative therapies for HIV Wasting
- Cyproheptadine
- Marinol (dronabinol)
- Megace (megestrol acetate)
- Testosterone therapy if hypogonadal

Appendix B – Calculation of BMI

$$BMI = \frac{\text{Weight (pounds)} \times 703}{[\text{Height (inches)}]^2} \quad \text{OR} \quad \frac{\text{Weight (kg)}}{[\text{Height (m)}]^2}$$

BMI classification:		
	Underweight	< 18.5 kg/m^2
	Normal weight	18.5 – 24.9 kg/m^2
	Overweight	25 – 29.9 kg/m^2
	Obesity (class 1)	30 – 34.9 kg/m^2
	Obesity (class 2)	35 – 39.9 kg/m^2
	Extreme obesity (class 3)	≥ 40 kg/m^2

V. REFERENCES

1. Serostim [package insert]. Rockland, MA: EMD Serono, Inc.; June 2019.
2. Mangili A, Murman H, Zampini AM, et al. Nutrition and HIV infection: review of weight loss and wasting in the era of highly active antiretroviral therapy from the nutrition for healthy living cohort. *Clin Infect Dis*. 2006;42:836-42.
3. Grinspoon S, Mulligan K for the Department of Health and Human Services Working Group on the Prevention and Treatment of Wasting and Weight Loss. Weight loss and wasting in patients infected with human immunodeficiency virus. *Clin Infect Dis*. 2003;36(Suppl 2):S69-78.
4. Polsky B, Kotler D, Steinhart C. HIV-associated wasting in the HAART era: guidelines for assessment, diagnosis, and treatment. *AIDS Patient Care STDS*. 2001;15(8):411-23.
5. Schambelan M, Mulligan K, Grunfeld C, et al. Recombinant human growth hormone in patients with HIV-associated wasting: a randomized placebo-controlled trial. *Ann Intern Med*. 1996;125:873-882.
6. Evans WJ, Kotler DP, Staszewski S, et al. Effect of recombinant human growth hormone on exercise capacity in patients with HIV-associated wasting on HAART. *AIDS Read*. 2005;15:301-314.
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8. National Heart, Lung, and Blood Institute. Obesity Education Initiative: The practical guide: identification, evaluation, and treatment of overweight and obesity in adults. Bethesda, MD: US Department of Health and Human Services, National Heart, Lung, and Blood Institute; 2000. NIH Publication No. 00-4084.

Reference number
2096-A

SPECIALTY GUIDELINE MANAGEMENT

SIGNIFOR LAR (pasireotide injectable suspension)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

A. Treatment of patients with acromegaly who have had an inadequate response to surgery and/or for whom surgery is not an option
B. Treatment of patients with Cushing's disease for whom pituitary surgery is not an option or has not been curative

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

A. For acromegaly:
   1. For initial approval: Laboratory report indicating high pretreatment insulin-like growth factor-1 (IGF-1) level and chart notes indicating an inadequate or partial response to surgery or a clinical reason for not having surgery.
   2. For continuation: Laboratory report indicating normal current IGF-1 levels or chart notes indicating that the member's IGF-1 level has decreased or normalized since initiation of therapy.
B. Cushing's disease:
   1. For initial requests, pretreatment cortisol level as measured by one of the following tests:
      a. Urinary free cortisol (UFC) level
      b. Late-night salivary cortisol
      c. 1 mg overnight dexamethasone suppression test (DST)
      d. Longer, low dose DST (2mg per day for 48 hours)
   2. For continuation of therapy (if applicable), laboratory report indicating current cortisol level has decreased from baseline as measured by one of the following tests:
      a. Urinary free cortisol (UFC) level
      b. Late-night salivary cortisol
      c. 1 mg overnight dexamethasone suppression test (DST)
      d. Longer, low dose DST (2mg per day for 48 hours)

III. CRITERIA FOR INITIAL APPROVAL

A. Acromegaly

Authorization of 12 months may be granted for the treatment of acromegaly when all of the following criteria are met:

1. Member has a high pretreatment IGF-1 level for age and/or gender based on the laboratory reference range.
2. Member had an inadequate or partial response to surgery OR there is a clinical reason why the member has not had surgery.

B. Cushing's disease
Authorization of 12 months may be granted for the treatment of Cushing's disease when the member has had surgery that was not curative OR the member is not a candidate for surgery.

IV. CONTINUATION OF THERAPY

A. Acromegaly
Authorization of 12 months may be granted for continuation of therapy for acromegaly when the member's IGF-1 level has decreased or normalized since initiation of therapy.

B. Cushing's disease
Authorization of 12 months for continuation of therapy may be granted for members that meet one of the following criteria:
1. Lower cortisol levels since the start of therapy per one of the following tests:
   a. Urinary free cortisol (UFC)
   b. Late-night salivary cortisol
   c. 1 mg overnight dexamethasone suppression test (DST)
   d. Longer, low dose DST (2mg per day for 48 hours)
2. Improvement in signs and symptoms of the disease

V. REFERENCES

1. Signifor LAR [package insert]. Lebanon, NJ: Recordati Rare Diseases Inc.; June 2020.
2. Katznelson L, Laws ER Jr, Melmed S, et al. Acromegaly: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab.* 2014;99:3933-3951.
3. American Association of Clinical Endocrinologists Acromegaly Guidelines Task Force. Medical guidelines for clinical practice for the diagnosis and treatment of acromegaly – 2011 update. *Endocr Pract*. 2011;17(suppl 4):1-44.
4. Gadelha MR, Bronstein MD, Brue T, et al. Pasireotide versus continued treatment with octreotide or lanreotide in patients with inadequately controlled acromegaly (PAOLA): a randomized, phase 3 trial. *Lancet Diabetes Endocrinol*. 2014;2:875-84.
5. Colao A, Bronstein MD, Freda P, et al. Pasireotide versus octreotide in acromegaly: a head-to-head superiority study. *J Clin Endocrinol Metab.* 2014;99:791–799.
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Reference number(s)
1651-A

SPECIALTY GUIDELINE MANAGEMENT

REVATIO (sildenafil)
LIQREV (sildenafil)
sildenafil

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
1. Revatio/Liqrev/sildenafil is indicated for the treatment of pulmonary arterial hypertension (PAH) (World Health Organization [WHO] Group 1) in adults to improve exercise ability and delay clinical worsening.
2. Revatio/sildenafil is indicated in pediatric patients 1 to 17 years old for the treatment of pulmonary arterial hypertension (PAH) (WHO Group I) to improve exercise ability and, in pediatric patients too young to perform standardized exercise testing, pulmonary hemodynamics thought to underly improvements in exercise.

B. Compendial Uses
1. Secondary Raynaud's phenomenon
2. Pulmonary arterial hypertension (PAH) (WHO Group I) in pediatric members less than 1 year of age

All other indications are considered experimental/investigational and not medically necessary.

II. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with a pulmonologist or cardiologist for the diagnosis of pulmonary arterial hypertension (PAH).

III. CRITERIA FOR INITIAL APPROVAL

A. Pulmonary Arterial Hypertension (PAH)
Authorization of 12 months may be granted for treatment of PAH when ALL of the following criteria are met:
1. Member has PAH defined as WHO Group 1 class of pulmonary hypertension (refer to Appendix).
2. PAH was confirmed by either criterion (i) or criterion (ii) below:
   i. Pretreatment right heart catheterization with all of the following results:
      a. Mean pulmonary arterial pressure (mPAP) > 20 mmHg
      b. Pulmonary capillary wedge pressure (PCWP) ≤ 15 mmHg
      c. Pulmonary vascular resistance (PVR) ≥ 3 Wood units in adult patients or pulmonary vascular resistance index (PVRI) ≥ 3 Wood units x m^2 in pediatric patients

ii. For infants less than one year of age, PAH was confirmed by Doppler echocardiogram if right heart catheterization cannot be performed.

B. Secondary Raynaud's Phenomenon

Authorization of 12 months may be granted for treatment of secondary Raynaud's phenomenon when the member has had an inadequate response to one of the following medications:

1. Calcium channel blockers
2. Angiotensin II receptor blockers
3. Selective serotonin reuptake inhibitors
4. Alpha blockers
5. Topical nitrates

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for members with an indication listed in Section III who are currently receiving the requested medication through a paid pharmacy or medical benefit, and who are experiencing benefit from therapy as evidenced by disease stability or disease improvement.

V. APPENDIX

WHO Classification of Pulmonary Hypertension (PH)

1 PAH

1.1 Idiopathic (PAH)
1.2 Heritable PAH
1.3 Drug- and toxin-induced PAH
1.4. PAH associated with:
  1.4.1 Connective tissue diseases
  1.4.2 Human Immunodeficiency Virus (HIV) infection
  1.4.3 Portal hypertension
  1.4.4 Congenital heart diseases
  1.4.5 Schistosomiasis
1.5 PAH long-term responders to calcium channel blockers
1.6 PAH with overt features of venous/capillaries (PVOD/PCH) involvement
1.7 Persistent PH of the newborn syndrome

2 PH due to left heart disease

2.1 PH due to heart failure with preserved left ventricular ejection fraction (LVEF)
2.2 PH due to heart failure with reduced LVEF
2.3 Valvular heart disease
2.4 Congenital/acquired cardiovascular conditions leading to post-capillary PH

3 PH due to lung diseases and/or hypoxia

3.1 Obstructive lung disease
3.2 Restrictive lung disease
3.3 Other lung disease with mixed restrictive/obstructive pattern
3.4 Hypoxia without lung disease
3.5 Developmental lung disorders

4 PH due to pulmonary artery obstruction

4.1 Chronic thromboembolic PH

4.2 Other pulmonary artery obstructions
- 4.2.1 Sarcoma (high or intermediate grade) or angiosarcoma
- 4.2.2 Other malignant tumors
  - Renal carcinoma
  - Uterine carcinoma
  - Germ cell tumours of the testis
  - Other tumours
- 4.2.3 Non-malignant tumours
  - Uterine leiomyoma
- 4.2.4 Arteritis without connective tissue disease
- 4.2.5 Congenital pulmonary artery stenosis
- 4.2.6 Parasites
  - Hydatidosis

5 PH with unclear and/or multifactorial mechanisms

5.1 Hematologic disorders: Chronic hemolytic anemia, myeloproliferative disorders

5.2 Systemic and metabolic disorders: Pulmonary Langerhans cell histiocytosis, Gaucher disease, glycogen storage disease, neurofibromatosis, sarcoidosis

5.3 Others: chronic renal failure with or without hemodialysis, fibrosing mediastinitis

5.4 Complex congenital heart disease

VI. REFERENCES

1. Revatio [package insert]. Morgantown, WV; Viatris Specialty LLC; January 2023.
2. Sildenafil [package insert]. Morgantown, WV: Mylan Pharmaceuticals Inc.; February 2018.
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Reference number
1731-A

SPECIALTY GUIDELINE MANAGEMENT

SILIQ (brodalumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Treatment of moderate to severe plaque psoriasis in adult patients who are candidates for systemic therapy or phototherapy and have failed to respond or have lost response to other systemic therapies

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

A. Initial requests:
   1. Chart notes or medical record documentation of affected area(s) and body surface area (BSA) affected.
   2. Chart notes, medical record documentation, or claims history supporting previous medications tried (if applicable), including response to therapy. If therapy is not advisable, documentation of clinical reason to avoid therapy.

B. Continuation requests: Chart notes or medical record documentation of decreased body surface area (BSA) affected and/or improvement in signs and symptoms.

III. CRITERIA FOR INITIAL APPROVAL

Moderate to severe plaque psoriasis (PsO)

A. Authorization of 12 months may be granted for members who have previously received Otezla or a biologic indicated for the treatment of moderate to severe plaque psoriasis.

B. Authorization of 12 months may be granted for treatment of moderate to severe plaque psoriasis in members when any of the following criteria is met:
   1. Crucial body areas (e.g., hands, feet, face, neck, scalp, genitals/groin, intertriginous areas) are affected.
   2. At least 10% of the body surface area (BSA) is affected.
   3. At least 3% of body surface area (BSA) is affected and the member meets any of the following criteria:
      i. Member has had an inadequate response or intolerance to either phototherapy (e.g., UVB, PUVA) or pharmacologic treatment with methotrexate, cyclosporine or acitretin.
      ii. Member has a clinical reason to avoid pharmacologic treatment with methotrexate, cyclosporine and acitretin (see Appendix).

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for all members (including new members) who are using the requested medication for moderate to severe plaque psoriasis and who achieve or maintain positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition when any of the following is met:

A. Reduction in body surface area (BSA) affected from baseline.
B. Improvement in signs and symptoms from baseline (e.g., itching, redness, flaking, scaling, burning, cracking, pain).

V. OTHER

For all indications: Member has had a documented negative TB test (which can include a tuberculosis skin test [PPD], an interferon-release assay [IGRA], or a chest x-ray)* within 6 months of initiating therapy for persons who are naïve to biologic DMARDs or targeted synthetic DMARDs associated with an increased risk of TB.

* If the screening testing for TB is positive, there must be further testing to confirm there is no active disease. Do not administer the requested medication to members with active TB infection. If there is latent disease, TB treatment must be started before initiation of the requested medication.

For all indications: Member cannot use the requested medication concomitantly with any other biologic DMARD or targeted synthetic DMARD.

VI. DOSAGE AND ADMINISTRATION

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

VII. APPENDIX

Examples of Clinical Reasons to Avoid Pharmacologic Treatment with Methotrexate, Cyclosporine or Acitretin

1. Clinical diagnosis of alcohol use disorder, alcoholic liver disease or other chronic liver disease
2. Breastfeeding
3. Drug interaction
4. Cannot be used due to risk of treatment-related toxicity
5. Pregnancy or currently planning pregnancy
6. Significant comorbidity prohibits use of systemic agents (examples include liver or kidney disease, blood dyscrasias, uncontrolled hypertension)

VIII. REFERENCES

1. Siliq [package insert]. Bridgewater, NJ: Bausch Health US, LLC; April 2020.
2. Lebwohl M, Strober B, Menter A, et al. Phase 3 studies comparing brodalumab with ustekinumab in psoriasis. *N Engl J Med*. 2015;373(14):1318-1328.

3. Menter A, Korman NJ, Elmets CA, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis. Section 6: Guidelines of care for the treatment of psoriasis and psoriatic arthritis: case-based presentations and evidence-based conclusions. *J Am Acad Dermatol*. 2011;65(1):137-174.
4. Menter A, Strober BE, Kaplan DH, et al. Joint AAD-NPF guidelines of care for the management and treatment of psoriasis with biologics. J Am Acad Dermatol. 2019;80(4):1029-1072.
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Reference number(s)
2014-A

SPECIALTY GUIDELINE MANAGEMENT

SIMPONI (golimumab for subcutaneous injection)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. Moderately to severely active rheumatoid arthritis (RA) in adults, in combination with methotrexate.
   2. Active psoriatic arthritis (PsA) in adults, alone or in combination with methotrexate.
   3. Active ankylosing spondylitis (AS) in adults.
   4. Moderately to severely active ulcerative colitis (UC) in adults who have demonstrated corticosteroid dependance or who have had an inadequate response to or failed to tolerate oral aminosalicylates, oral corticosteroids, azathioprine, or 6-mercaptopurine.

B. Compendial Use
   Non-radiographic axial spondyloarthritis

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

A. Rheumatoid arthritis (RA)
   1. Initial requests:
      i. Chart notes, medical record documentation, or claims history supporting previous medications tried (if applicable), including response to therapy. If therapy is not advisable, documentation of clinical reason to avoid therapy.
      ii. Laboratory results, chart notes, or medical record documentation of biomarker testing (i.e., rheumatoid factor [RF], anti-cyclic citrullinated peptide [anti-CCP], and C-reactive protein [CRP] and/or erythrocyte sedimentation rate [ESR]) (if applicable).
   2. Continuation requests: Chart notes or medical record documentation supporting positive clinical response.

B. Ankylosing spondylitis (AS), non-radiographic axial spondyloarthritis (nr-axSpA), and psoriatic arthritis (PsA)
   1. Initial requests: Chart notes, medical record documentation, or claims history supporting previous medications tried (if applicable), including response to therapy. If therapy is not advisable, documentation of clinical reason to avoid therapy.
   2. Continuation requests: Chart notes or medical record documentation supporting positive clinical response.

C. Ulcerative colitis (UC)
Continuation requests: Chart notes or medical record documentation supporting positive clinical response to therapy or remission.

III. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with one of the following:
A. Rheumatoid arthritis, ankylosing spondylitis, and non-radiographic axial spondyloarthritis: rheumatologist
B. Psoriatic arthritis: rheumatologist or dermatologist
C. Ulcerative colitis: gastroenterologist

IV. CRITERIA FOR INITIAL APPROVAL

A. Rheumatoid arthritis (RA)

1. Authorization of 12 months may be granted for adult members who have previously received a biologic or targeted synthetic drug (e.g., Rinvoq, Xeljanz) indicated for moderately to severely active rheumatoid arthritis. The requested medication must be prescribed in combination with methotrexate or leflunomide unless the member has a clinical reason not to use methotrexate or leflunomide (see Appendix).

2. Authorization of 12 months may be granted for adult members for treatment of moderately to severely active RA when all of the following criteria are met:
   i. Member meets either of the following criteria:
      a. Member has been tested for either of the following biomarkers and the test was positive:
         1. Rheumatoid factor (RF)
         2. Anti-cyclic citrullinated peptide (anti-CCP)
      b. Member has been tested for ALL of the following biomarkers:
         1. RF
         2. Anti-CCP
         3. C-reactive protein (CRP) and/or erythrocyte sedimentation rate (ESR)
   ii. Member is prescribed the requested medication in combination with methotrexate or leflunomide or has a clinical reason not to use methotrexate or leflunomide (see Appendix).
   iii. Member meets either of the following criteria:
      a. Member has experienced an inadequate response to at least a 3-month trial of methotrexate despite adequate dosing (i.e., titrated to at least 15 mg/week).
      b. Member has an intolerance or contraindication to methotrexate (see Appendix).

B. Psoriatic arthritis (PsA)

1. Authorization of 12 months may be granted for adult members who have previously received a biologic or targeted synthetic drug (e.g., Rinvoq, Otezla) indicated for active psoriatic arthritis.

2. Authorization of 12 months may be granted for adult members for treatment of active psoriatic arthritis when either of the following criteria is met:
   i. Member has mild to moderate disease and meets one of the following criteria:
      a. Member has had an inadequate response to methotrexate, leflunomide, or another conventional synthetic drug (e.g., sulfasalazine) administered at an adequate dose and duration.
      b. Member has an intolerance or contraindication to methotrexate or leflunomide (see Appendix), or another conventional synthetic drug (e.g., sulfasalazine).

c. Member has enthesitis or predominantly axial disease.
ii. Member has severe disease.

C. Ankylosing spondylitis (AS) and non-radiographic axial spondyloarthritis (nr-axSpA)

1. Authorization of 12 months may be granted for adult members who have previously received a biologic or targeted synthetic drug (e.g., Rinvoq, Xeljanz) indicated for active ankylosing spondylitis or active non-radiographic axial spondyloarthritis.

2. Authorization of 12 months may be granted for adult members for treatment of active ankylosing spondylitis or active non-radiographic axial spondyloarthritis when either of the following criteria is met:
   i. Member has experienced an inadequate response to at least two non-steroidal anti-inflammatory drugs (NSAIDs).
   ii. Member has an intolerance or contraindication to two or more NSAIDs.

D. Ulcerative colitis (UC)

Authorization of 12 months may be granted for adult members for treatment of moderately to severely active ulcerative colitis.

V. CONTINUATION OF THERAPY

A. Rheumatoid arthritis (RA)

Authorization of 12 months may be granted for all adult members (including new members) who are using the requested medication for moderately to severely active rheumatoid arthritis and who achieve or maintain a positive clinical response as evidenced by disease activity improvement of at least 20% from baseline in tender joint count, swollen joint count, pain, or disability.

B. Psoriatic arthritis (PsA)

Authorization of 12 months may be granted for all adult members (including new members) who are using the requested medication for psoriatic arthritis and who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition when there is improvement in any of the following from baseline:

1. Number of swollen joints
2. Number of tender joints
3. Dactylitis
4. Enthesitis
5. Axial disease
6. Skin and/or nail involvement

C. Ankylosing spondylitis (AS) and non-radiographic axial spondyloarthritis (nr-axSpA)

Authorization of 12 months may be granted for all adult members (including new members) who are using the requested medication for active ankylosing spondylitis or active non-radiographic axial spondyloarthritis and who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition when there is improvement in any of the following from baseline:

1. Functional status
2. Total spinal pain
3. Inflammation (e.g., morning stiffness)

D. Ulcerative colitis (UC)

1. Authorization of 12 months may be granted for all adult members (including new members) who are using the requested medication for moderately to severely active ulcerative colitis and who achieve or maintain remission.

2. Authorization of 12 months may be granted for all adult members (including new members) who are using the requested medication for moderately to severely active ulcerative colitis and who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition when there is improvement in any of the following from baseline:
   i. Stool frequency
   ii. Rectal bleeding
   iii. Urgency of defecation
   iv. C-reactive protein (CRP)
   v. Fecal calprotectin (FC)
   vi. Appearance of the mucosa on endoscopy, computed tomography enterography (CTE), magnetic resonance enterography (MRE), or intestinal ultrasound
   vii. Improvement on a disease activity scoring tool (e.g., Ulcerative Colitis Endoscopic Index of Severity [UCEIS], Mayo score)

VI. OTHER

For all indications: Member has had a documented negative tuberculosis (TB) test (which can include a tuberculosis skin test [PPD], an interferon-release assay [IGRA], or a chest x-ray)* within 6 months of initiating therapy for persons who are naïve to biologic drugs or targeted synthetic drugs associated with an increased risk of TB.

* If the screening testing for TB is positive, there must be further testing to confirm there is no active disease. Do not administer the requested medication to members with active TB infection. If there is latent disease, TB treatment must be started before initiation of the requested medication.

For all indications: Member cannot use the requested medication concomitantly with any other biologic drug or targeted synthetic drug.

VII. DOSAGE AND ADMINISTRATION

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

VIII. APPENDIX

Examples of Clinical Reasons to Avoid Pharmacologic Treatment with Methotrexate or Leflunomide

1. Clinical diagnosis of alcohol use disorder, alcoholic liver disease, or other chronic liver disease
2. Drug interaction
3. Risk of treatment-related toxicity
4. Pregnancy or currently planning pregnancy
5. Breastfeeding
6. Significant comorbidity prohibits use of systemic agents (e.g., liver or kidney disease, blood dyscrasias, uncontrolled hypertension)
7. Hypersensitivity
8. History of intolerance or adverse event

IX. REFERENCES

1. Simponi [package insert]. Horsham, PA: Janssen Biotech, Inc.; September 2019.
2. van der Heijde D, Ramiro S, Landewe R, et al. 2016 Update of the international ASAS-EULAR management recommendations for axial spondyloarthritis. *Ann Rheum Dis.* 2017;76(6):978-991.
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11. Ward MM, Deodhar A, Gensler LS, et al. 2019 Update of the American College of Rheumatology/Spondylitis Association of America/Spondyloarthritis Research and Treatment Network Recommendations for the Treatment of Ankylosing Spondylitis and Nonradiographic Axial Spondyloarthritis. *Arthritis Rheumatol.* 2019;71(10):1599-1613. doi:10.1002/art.41042.
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15. Feuerstein JD, Isaacs KL, Schneider Y, et al. AGA Clinical Practice Guidelines on the Management of Moderate to Severe Ulcerative Colitis. *Gastroenterology*. 2020;158:1450.
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17. Rubin DT, Ananthakrishnan AN, et al. 2019 ACG Clinical Guideline: Ulcerative Colitis in Adults. *Am J Gastroenterol.* 2019;114:384-413.
18. Smolen JS, Aletaha D. Assessment of rheumatoid arthritis activity in clinical trials and clinical practice. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. Available with subscription. URL: www.uptodate.com. Accessed March 19, 2021.
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20. Menter A, Gelfand JM, Connor C, et al. Joint AAD-NPF guidelines of care for the management of psoriasis with systemic nonbiologic therapies. *J Am Acad Dermatol.* 2020;82(6): 1445-86.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME
(generic)

SIRTURO
(bedaquiline)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

POLICY

FDA-APPROVED INDICATIONS

Sirturo is a diarylquinoline antimycobacterial drug indicated as part of combination therapy in the treatment of adult and pediatric patients (5 years and older and weighing at least 15 kg) with pulmonary multi-drug resistant tuberculosis (MDR-TB). Reserve Sirturo for use when an effective treatment regimen cannot otherwise be provided.
This indication is approved under accelerated approval based on time to sputum culture conversion. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

Limitations of Use:

- Do not use Sirturo for the treatment of:
  - Latent infection due to *Mycobacterium tuberculosis*
  - Drug-sensitive tuberculosis
  - Extra-pulmonary tuberculosis
  - Infections caused by non-tuberculous mycobacteria
- The safety and efficacy of Sirturo in the treatment of HIV infected patients with MDR-TB have not been established as clinical data are limited

Compendial Uses

Combination regimen with Pretomanid and linezolid for the treatment of adults with pulmonary tuberculosis (TB) resistant to isoniazid, rifamycins, a fluoroquinolone and a second line injectable antibacterial drug OR adults with pulmonary TB resistant to isoniazid and rifampin, who are treatment-intolerant or nonresponsive to standard therapy.[2,4-6]

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed as part of combination therapy in a patient with pulmonary multi-drug resistant tuberculosis (MDR-TB)

  AND
- Another effective treatment regimen cannot be used instead of Sirturo (bedaquiline)

OR

- The requested drug is being prescribed for pulmonary tuberculosis (TB) resistant to isoniazid, rifamycins, a fluoroquinolone and a second line injectable antibacterial drug OR TB resistant to isoniazid and rifampin, that is treatment-intolerant or nonresponsive to standard therapy

  AND
- The requested drug is being prescribed as part of a combination regimen with Pretomanid and Zyvox (linezolid)

REFERENCES

1. Sirturo [package insert]. Titusville, New Jersey: Janssen Therapeutics; September 2021.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2022; Accessed January 29, 2023.
3. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed January 29, 2023.

4. Pretomanid [package insert]. Morgantown, West Virginia: Mylan Specialty L.P.; December 2022.
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Reference number(s)
5803-A

SPECIALTY GUIDELINE MANAGEMENT

SKYCLARYS (omaveloxolone)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Skyclarys is indicated for the treatment of Friedreich's ataxia in adults and adolescents aged 16 years and older.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
A. For initial requests:
   1. Testing or analysis confirming a mutation of the *FXN* gene
   2. Medical record documentation confirming the member demonstrates clinical manifestations of disease (e.g., muscle weakness, decline in coordination, frequent falling)

III. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with a physician who specializes in the treatment of Friedreich's ataxia.

IV. CRITERIA FOR INITIAL APPROVAL

Friedreich's Ataxia
Authorization of 12 months may be granted for treatment of Friedreich's ataxia when all of the following criteria are met:
A. The diagnosis is confirmed by detection of a mutation of the *FXN* gene.
B. Member exhibits clinical manifestations of disease (e.g., muscle weakness, decline in coordination, frequent falling).
C. Member is 16 years of age or older.

V. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment of Friedreich's ataxia when the disease has improved or stabilized (e.g., improvement in speech or swallowing, upper/lower limb coordination, upright stability).

VI. REFERENCES

1. Skyclarys [package insert]. Plano, TX: Reata Pharmaceuticals, Inc.; February 2023.
2. Bidichandani SI, Duncan CG. Friedreich's ataxia - symptoms, causes, treatment: NORD. National Organization for Rare Disorders. https://rarediseases.org/rare-diseases/friedreichs-ataxia/. Published January 25, 2023. Accessed March 9, 2023.

Reference number(s)
3677-A

SPECIALTY GUIDELINE MANAGEMENT

XYREM (sodium oxybate)
LUMRYZ (sodium oxybate)
sodium oxybate

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

A. Xyrem/sodium oxybate is indicated for the treatment of cataplexy or excessive daytime sleepiness (EDS) in patients 7 years of age and older with narcolepsy.
B. Lumryz is indicated for the treatment of cataplexy or excessive daytime sleepiness (EDS) in adults with narcolepsy.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

A. For initial requests, all of the following (if applicable):
    1. Documentation of a sleep lab evaluation.
    2. Chart notes, medical record documentation, or claims history supporting previous medications tried (if applicable), including response to therapy. If therapy is not advisable, documentation of clinical reason to avoid therapy.
B. For continuation requests, chart notes or medical record documentation supporting a beneficial response to therapy (e.g., decrease in daytime sleepiness, decrease in cataplexy episodes from baseline).

III. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with a sleep specialist (e.g., neurologist experienced with sleep disorders, physician certified in sleep medicine).

IV. CRITERIA FOR INITIAL APPROVAL

A. Excessive Daytime Sleepiness with Narcolepsy

Authorization of 12 months may be granted for treatment of excessive daytime sleepiness when all of the following criteria are met:

1. The diagnosis of narcolepsy is confirmed by a sleep lab evaluation.
2. Member meets one of the following:
    a. Member is 7 years of age or older and less than 18 years of age and meets one of the following:

i. The member has experienced an inadequate treatment response or intolerance to at least one central nervous system (CNS) stimulant drug (e.g., amphetamine, dextroamphetamine, or methylphenidate).
ii. The member has a contraindication to at least one central nervous system (CNS) stimulant drug (e.g., amphetamine, dextroamphetamine, or methylphenidate).

b. Member is 18 years of age or older and meets one of the following:
i. The member has experienced an inadequate treatment response or intolerance to modafinil or armodafinil.
ii. The member has a contraindication to both modafinil and armodafinil.

B. Cataplexy with Narcolepsy
Authorization of 12 months may be granted for treatment of cataplexy with narcolepsy when all of the following criteria are met:
1. The member is 7 years of age or older.
2. The diagnosis of narcolepsy is confirmed by a sleep lab evaluation.
3. The member has a baseline history of at least 14 cataplexy attacks in a typical 2-week period.

V. CONTINUATION OF THERAPY

A. Excessive Daytime Sleepiness with Narcolepsy
Authorization of 12 months may be granted for continued treatment of excessive daytime sleepiness (EDS) with narcolepsy when the member has demonstrated beneficial response to treatment as defined by a decrease in daytime sleepiness with narcolepsy from baseline.

B. Cataplexy with Narcolepsy
Authorization of 12 months may be granted for continued treatment of cataplexy with narcolepsy when the member has demonstrated beneficial response to treatment as defined by a decrease in cataplexy episodes from baseline.

VI. REFERENCES

1. Xyrem [package insert]. Palo Alto, CA: Jazz Pharmaceuticals, Inc.; April 2023.
2. Sodium oxybate [package insert]. Berkeley Heights, NJ: Hikma Pharmaceuticals USA Inc.; April 2023.
3. Lumryz [package insert]. Chesterfield, MO: Avadel CNS Pharmaceuticals, LLC; May 2023.
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Reference number
3047-A

SPECIALTY GUIDELINE MANAGEMENT

SKYRIZI (risankizumab-rzaa)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

A. Treatment of moderate-to-severe plaque psoriasis (PsO) in adults who are candidates for systemic therapy or phototherapy
B. Treatment of active psoriatic arthritis (PsA) in adults
C. Treatment of moderately to severely active Crohn's disease (CD) in adults

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

A. Plaque psoriasis (PsO)
   1. Initial requests:
      i. Chart notes or medical record documentation of affected area(s) and body surface area (BSA) affected (if applicable).
      ii. Chart notes, medical record documentation, or claims history supporting previous medications tried (if applicable), including response to therapy. If therapy is not advisable, documentation of clinical reason to avoid therapy.
   2. Continuation requests: Chart notes or medical record documentation of decreased body surface area (BSA) affected and/or improvement in signs and symptoms.

B. Psoriatic arthritis (PsA)
   1. Initial requests: Chart notes, medical record documentation, or claims history supporting previous medications tried (if applicable), including response to therapy. If therapy is not advisable, documentation of clinical reason to avoid therapy.
   2. Continuation requests: Chart notes or medical record documentation supporting positive clinical response.

C. Crohn's disease (CD)
   Continuation requests: Chart notes or medical record documentation supporting positive clinical response to therapy or remission.

III. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with one of the following:
A. Plaque psoriasis: dermatologist

Reference number(s)
3677-A

SPECIALTY GUIDELINE MANAGEMENT

XYREM (sodium oxybate)
LUMRYZ (sodium oxybate)
sodium oxybate

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

1. Xyrem/sodium oxybate is indicated for the treatment of cataplexy or excessive daytime sleepiness (EDS) in patients 7 years of age and older with narcolepsy.
2. Lumryz is indicated for the treatment of cataplexy or excessive daytime sleepiness (EDS) in adults with narcolepsy.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

A. For initial requests, all of the following (if applicable):
   1. Documentation of a sleep lab evaluation
   2. Chart notes, medical record documentation, or claims history supporting previous medications tried (if applicable), including response to therapy. If therapy is not advisable, documentation of clinical reason to avoid therapy

B. For continuation requests, chart notes or medical record documentation supporting a beneficial response to therapy (e.g., decrease in daytime sleepiness, decrease in cataplexy episodes from baseline)

III. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with a sleep specialist.

IV. CRITERIA FOR INITIAL APPROVAL

A. Excessive Daytime Sleepiness with Narcolepsy

Authorization of 12 months may be granted for treatment of excessive daytime sleepiness when all of the following criteria are met:

1. The diagnosis of narcolepsy is confirmed by a sleep lab evaluation
2. Member meets one of the following:
   a. Member is 7 years of age or older and less than 18 years of age and meets one of the following:

i. The member has experienced an inadequate treatment response or intolerance to at least one central nervous system (CNS) stimulant drug (e.g., amphetamine, dextroamphetamine, or methylphenidate)
ii. The member has a contraindication to at least one central nervous system (CNS) stimulant drug (e.g., amphetamine, dextroamphetamine, or methylphenidate)

b. Member is 18 years of age or older and meets one of the following:
i. The member has experienced an inadequate treatment response or intolerance to modafinil or armodafinil
ii. The member has a contraindication to both modafinil and armodafinil

B. Cataplexy with Narcolepsy

Authorization of 12 months may be granted for treatment of cataplexy with narcolepsy when all of the following criteria are met:

1. The member is 7 years of age or older
2. The diagnosis of narcolepsy is confirmed by a sleep lab evaluation
3. The member has a baseline history of at least 14 cataplexy attacks in a typical 2-week period

V. CONTINUATION OF THERAPY

A. Excessive Daytime Sleepiness with Narcolepsy

Authorization of 12 months may be granted for continued treatment of excessive daytime sleepiness (EDS) with narcolepsy when the member has demonstrated beneficial response to treatment as defined by a decrease in daytime sleepiness with narcolepsy from baseline.

B. Cataplexy with Narcolepsy

Authorization of 12 months may be granted for continued treatment of cataplexy with narcolepsy when the member has demonstrated beneficial response to treatment as defined by a decrease in cataplexy episodes from baseline.

VI. REFERENCES

1. Xyrem [package insert]. Palo Alto, CA: Jazz Pharmaceuticals, Inc.; April 2023.
2. Sodium oxybate [package insert]. Berkeley Heights, NJ: Hikma Pharmaceuticals USA Inc.; April 2023.
3. Lumryz [package insert]. Chesterfield, MO: Avadel CNS Pharmaceuticals, LLC; May 2023.
4. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. http://www.micromedexsolutions.com/. Accessed March 1, 2023.
5. Morgenthaler TI, Vishesh KK, Brown T, et al. Practice Parameters for the Treatment of Narcolepsy and Other Hypersomnias of Central Origin. *Sleep* 2007; 30(12):1705-11.
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7. Krahn, L, Hershner S, et al. Quality Measures for the Care of Patients with Narcolepsy; *Journal of Clinical Sleep Medicine*; 2015; 11(3): 335-55.
8. Nuvigil [package insert]. Parsippany, NJ: Teva Pharmaceuticals USA, Inc.; December 2023.
9. Provigil [package insert]. Parsippany, NJ: Teva Pharmaceuticals USA, Inc.; December 2023.
10. Maski K, Trotti LM, Kotagal S, Auger RR, et al. Treatment of central disorders of hypersomnolence: an American Academy of Sleep Medicine clinical practice guideline. *J Clin Sleep Med.* Published online September 1, 2021.

B. Psoriatic arthritis: rheumatologist or dermatologist
C. Crohn's disease: gastroenterologist

IV. CRITERIA FOR INITIAL APPROVAL

A. Plaque psoriasis (PsO)

1. Authorization of 12 months may be granted for adult members who have previously received a biologic or targeted synthetic drug (e.g., Sotyktu, Otezla) indicated for the treatment of moderate to severe plaque psoriasis.

2. Authorization of 12 months may be granted for adult members for treatment of moderate to severe plaque psoriasis when any of the following criteria is met:
   i. Crucial body areas (e.g., hands, feet, face, neck, scalp, genitals/groin, intertriginous areas) are affected.
   ii. At least 10% of body surface area (BSA) is affected.
   iii. At least 3% of body surface area (BSA) is affected and the member meets either of the following criteria:
      a. Member has had an inadequate response or intolerance to either phototherapy (e.g., UVB, PUVA) or pharmacologic treatment with methotrexate, cyclosporine, or acitretin.
      b. Member has a clinical reason to avoid pharmacologic treatment with methotrexate, cyclosporine, and acitretin (see Appendix).

B. Psoriatic arthritis (PsA)

1. Authorization of 12 months may be granted for adult members who have previously received a biologic or targeted synthetic drug (e.g., Rinvoq, Otezla) indicated for active psoriatic arthritis.

2. Authorization of 12 months may be granted for adult members for treatment of active psoriatic arthritis when either of the following criteria is met:
   i. Member has mild to moderate disease and meets one of the following criteria:
      a. Member has had an inadequate response to methotrexate, leflunomide, or another conventional synthetic drug (e.g., sulfasalazine) administered at an adequate dose and duration.
      b. Member has an intolerance or contraindication to methotrexate or leflunomide (see Appendix), or another conventional synthetic drug (e.g., sulfasalazine).
      c. Member has enthesitis or predominantly axial disease.
   ii. Member has severe disease.

C. Crohn's disease (CD)

Authorization of 12 months may be granted for adult members for the treatment of moderately to severely active Crohn's disease.

V. CONTINUATION OF THERAPY

A. Plaque psoriasis (PsO)

Authorization of 12 months may be granted for all adult members (including new members) who are using the requested medication for moderate to severe plaque psoriasis and who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition when either of the following is met:

1. Reduction in body surface area (BSA) affected from baseline

2. Improvement in signs and symptoms from baseline (e.g., itching, redness, flaking, scaling, burning, cracking, pain)

B. Psoriatic arthritis (PsA)

Authorization of 12 months may be granted for all adult members (including new members) who are using the requested medication for psoriatic arthritis and who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition when there is improvement in any of the following from baseline:

1. Number of swollen joints
2. Number of tender joints
3. Dactylitis
4. Enthesitis
5. Axial disease
6. Skin and/or nail involvement

C. Crohn's Disease (CD)

1. Authorization of 12 months may be granted for all adult members (including new members) who are using the requested medication for moderately to severely active Crohn's disease and who achieve or maintain remission.

2. Authorization of 12 months may be granted for all adult members (including new members) who are using the requested medication for moderately to severely active Crohn's disease and who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition when there is improvement in any of the following from baseline:
   i. Abdominal pain or tenderness
   ii. Diarrhea
   iii. Body weight
   iv. Abdominal mass
   v. Hematocrit
   vi. Appearance of the mucosa on endoscopy, computed tomography enterography (CTE), magnetic resonance enterography (MRE), or intestinal ultrasound
   vii. Improvement on a disease activity scoring tool (e.g., Crohn's Disease Activity Index [CDAI] score)

VI. OTHER

For all indications: Member has had a documented negative tuberculosis (TB) test (which can include a tuberculosis skin test [PPD], an interferon-release assay [IGRA], or a chest x-ray)* within 6 months of initiating therapy for persons who are naïve to biologic drugs or targeted synthetic drugs associated with an increased risk of TB.

* If the screening testing for TB is positive, there must be further testing to confirm there is no active disease. Do not administer the requested medication to members with active TB infection. If there is latent disease, TB treatment must be started before initiation of the requested medication.

For all indications: Member cannot use the requested medication concomitantly with any other biologic drug or targeted synthetic drug.

VII. DOSAGE AND ADMINISTRATION

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

VIII. APPENDIX

Examples of Clinical Reasons to Avoid Pharmacologic Treatment with Methotrexate, Cyclosporine, Acitretin, or Leflunomide

1. Clinical diagnosis of alcohol use disorder, alcoholic liver disease or other chronic liver disease
2. Drug interaction
3. Risk of treatment-related toxicity
4. Pregnancy or currently planning pregnancy
5. Breastfeeding
6. Significant comorbidity prohibits use of systemic agents (e.g., liver or kidney disease, blood dyscrasias, uncontrolled hypertension)
7. Hypersensitivity
8. History of intolerance or adverse event

IX. REFERENCES

1. Skyrizi [package insert]. North Chicago, IL: AbbVie Inc.; December 2022.
2. Menter A, Korman NJ, Elmets CA, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis. Section 4: Guidelines of care for the management and treatment of psoriasis with traditional systemic agents. *J Am Acad Dermatol.* 2009;61(3):451-485.
3. Menter A, Korman NJ, Elmets CA, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis. Section 6: Guidelines of care for the treatment of psoriasis and psoriatic arthritis: case-based presentations and evidence-based conclusions. *J Am Acad Dermatol*. 2011;65(1):137-174.
4. Gordon KB, Strober B, Lebwohl M, et al. Efficacy and safety of risankizumab in moderate-to-severe plaque psoriasis (UltIMMa-1 and UltIMMa-2): results from two double-blind, randomised, placebo-controlled and ustekinumab-controlled phase 3 trials. *Lancet*. 2018;392(10148):650-661.
5. Menter A, Strober BE, Kaplan DH, et al. Joint AAD-NPF guidelines of care for the management and treatment of psoriasis with biologics. *J Am Acad Dermatol*. 2019;80(4):1029-1072.
6. Testing for TB Infection. Centers for Disease Control and Prevention. Retrieved on January 11, 2023 from: https://www.cdc.gov/tb/topic/testing/tbtesttypes.htm.
7. Singh JA, Guyatt G, Ogdie A, et al. 2018 American College of Rheumatology/National Psoriasis Foundation Guideline for the Treatment of Psoriatic Arthritis. *Arthritis Rheum.* 2018;71:5-32.
8. Gossec L, Baraliakos X, Kerschbaumer A, et al. European League Against Rheumatism (EULAR) recommendations for the management of psoriatic arthritis with pharmacological therapies: 2019 update. *Ann Rheum Dis*. 2020;79(6):700-712.
9. D'Haens G, Panaccione R, Baert F, et al. Risankizumab as induction therapy for Crohn's disease: results from the phase 3 ADVANCE and MOTIVATE induction trials. *Lancet.* 2022;399(10340):2015-2030.
10. Lichtenstein GR, Loftus Jr EV, Isaacs KI, et al. ACG Clinical Guideline: Management of Crohn's Disease in Adults. Am J Gastroenterol. 2018;113:481-517.
11. Coates LC, Soriano ER, Corp N, et al. Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA): updated treatment recommendations for psoriatic arthritis 2021. *Nat Rev Rheumatol.* 2022;18(8):465-479.
13. Menter A, Gelfand JM, Connor C, et al. Joint American Academy of Dermatology-National Psoriasis Foundation guidelines of care for the management of psoriasis with systemic nonbiologic therapies. *J Am Acad Dermatol*. 2020;82(6):1445-1486.

QUANTITY LIMIT CRITERIA

BRAND NAME*
(generic)

(carisoprodol/aspirin)

(carisoprodol/aspirin/codeine phosphate)

SOMA
(carisoprodol)

Status: CVS Caremark Criteria
Type: Quantity Limit ***Ref # 206-H***

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Carisoprodol/aspirin, Soma
Carisoprodol/aspirin and Soma are indicated for the relief of discomfort associated with acute, painful musculoskeletal conditions in adults.

Limitations of Use
Carisoprodol/aspirin and Soma should only be used for short periods (up to two or three weeks) because adequate evidence of effectiveness for more prolonged use has not been established and because acute, painful musculoskeletal conditions are generally of short duration.

Carisoprodol/aspirin/codeine phosphate
Carisoprodol/aspirin/codeine phosphate tablets are indicated for the relief of discomfort associated with acute, painful musculoskeletal conditions in adults.

Limitations of Use
Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, reserve carisoprodol/aspirin/codeine phosphate tablets for use in patients for whom alternative treatment options (e.g., non-opioid analgesics):

- Have not been tolerated, or are not expected to be tolerated,
- Have not provided adequate analgesia, or are not expected to provide adequate analgesia

Carisoprodol/aspirin/codeine phosphate tablets should only be used for short periods (up to two or three weeks) because adequate evidence of effectiveness for more prolonged use has not been established and because acute, painful musculoskeletal conditions are generally of short duration.

RATIONALE

Carisoprodol/aspirin, carisoprodol/aspirin/codeine phosphate, and Soma are indicated for the relief of discomfort associated with acute, painful musculoskeletal conditions in adults. Carisoprodol/aspirin, carisoprodol/aspirin/codeine phosphate, and Soma should only be used for short periods (up to two or three weeks) because adequate evidence of effectiveness for more prolonged use has not been established and because acute, painful musculoskeletal conditions are generally of short duration.[1-5]

The recommended dose of Soma is 250 mg to 350 mg three times a day and at bedtime. The recommended maximum duration of Soma use is up to two or three weeks. Because Soma tablets are only indicated for short-term use (up to two or three weeks), the limit is 84 tablets per month, and 3 month limits will not apply.[1,4,5]

The recommended dose of carisoprodol/aspirin or carisoprodol/aspirin/codeine phosphate is one or two tablets four times daily in adults. The recommended maximum duration of carisoprodol/aspirin or carisoprodol/aspirin/codeine phosphate use is up to two or three weeks. Because carisoprodol/aspirin and carisoprodol/aspirin/codeine phosphate tablets are only indicated for short-term use (up to two or three weeks), the limit is 168 tablets per month, and 3 month limits will not apply.[2-5]

If the patient is requesting more than the initial quantity limit, then the claim will reject with a message indicating that quantity limits are exceeded.

There is no clinical documentation supporting quantities greater than the recommended dosage, therefore post limit prior authorization will not be available.

REFERENCES

1. Soma [package insert]. Somerset, NJ: Meda Pharmaceuticals Inc.; March 2019.
2. Carisoprodol and aspirin [package insert]. Eatontown, NJ: Heritage Pharmaceuticals Inc; December 2019.
3. Carisoprodol, aspirin, and codeine [package insert]. Orlando, FL: Ingenus Pharmaceuticals, LLC; April 2021.
4. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2021; Accessed August 2021.
5. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed August 2021.

Written by:	UM Development (JG)
Date Written:	03/2003
Revised:	(MB) 08/2004; (NG) 08/2005; (CT) 08/2006, 07/2007; (MS) 07/2008; (CT) 08/2009, 12/2009, 06/2011, 03/2012, 03/2013; (CF) 01/2014; (CT) 01/2015; (MS) 01/2016 (no clinical changes); (SF) 01/2017 (no clinical changes); (CF) 09/2017 (no clinical changes); (DS) 09/2018 (no clinical changes); (CF) 09/2019 (no clinical changes); (CM) 09/2020 (removed brand Soma Compound and brand Soma Compound with Codeine from target box; no clinical changes); (DS) 09/2021 (no clinical changes)
Reviewed:	CRC 03/2003; CDPR/Medical Affairs (MM) 08/2004, 08/2005, 08/2006; (WF) 07/2007, 08/2008, 08/2009, 12/2009; (KP) 06/2011, 03/2012; (KP) 03/2013, 01/2014; (LCB) 01/2015; (CHART) 9/26/2019, 09/24/20, 09/30/2021 External Review: 12/2004; 12/2006, 02/2008, 12/2008, 10/2009, 10/2010, 10/2011, 08/2012, 06/2013, 03/2014, 06/2014, 04/2015, 04/2016, 04/2017, 02/2018, 02/2019, 02/2020, 12/2020, 12/2021

LIMIT CRITERIA

Limits should accumulate across all drugs and strengths up to highest quantity listed depending on the order the claims are processed. Accumulation does not apply if limit is coded for daily dose.

Drug	1 Month Limit*	3 Month Limit
Carisoprodol/aspirin	168 tablets / 25 days	Does Not Apply**
Carisoprodol/aspirin/codeine phosphate	168 tablets / 25 days	Does Not Apply**
Soma (carisoprodol)	84 tablets / 25 days	Does Not Apply**

** The duration of 25 days is used for a 30-day fill period to allow time for refill processing.*

***** These drugs are for short-term acute use; therefore, the mail limit will be the same as the retail limit. The intent is for prescriptions of the requested drug to be filled one month at a time, even if filled at mail order; there should be no 3 month supplies filled.***

Reference number
2097-A

SPECIALTY GUIDELINE MANAGEMENT

SOMAVERT (pegvisomant)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Somavert is indicated for the treatment of acromegaly in patients who have had an inadequate response to surgery or radiation therapy, or for whom these therapies are not appropriate.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

A. For initial approval: Laboratory report indicating high pretreatment insulin-like growth factor-1 (IGF-1) level and chart notes indicating an inadequate or partial response to surgery or radiotherapy or a clinical reason for not having surgery or radiotherapy
B. For continuation: Laboratory report indicating normal current IGF-1 levels or chart notes indicating that the member's IGF-1 level has decreased or normalized since initiation of therapy

III. CRITERIA FOR INITIAL APPROVAL

Acromegaly
Authorization of 12 months may be granted for the treatment of acromegaly when all of the following criteria are met:

A. Member has a high pretreatment IGF-1 level for age and/or gender based on the laboratory reference range.
B. Member had an inadequate or partial response to surgery or radiotherapy OR there is a clinical reason why the member has not had surgery or radiotherapy.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continuation of therapy for acromegaly when the member's IGF-1 level has decreased or normalized since initiation of therapy.

V. REFERENCES

1. Somavert [package insert]. New York, NY: Pharmacia & Upjohn Company LLC; August 2021.
2. Katznelson L, Laws ER, Melmed S, et al. Acromegaly: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2014; 99:3933-3951.

3. American Association of Clinical Endocrinologists Acromegaly Guidelines Task Force. Medical guidelines for clinical practice for the diagnosis and treatment of acromegaly – 2011 update. Endocr Pract. 2011;17(suppl 4):1-44.

Reference number(s)
4210-A

SPECIALTY GUIDELINE MANAGEMENT

SOGROYA (somapacitan-beco)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

A. Sogroya is indicated for the replacement of endogenous growth hormone (GH) in adults with growth hormone deficiency (GHD).
B. Sogroya is indicated for the treatment of pediatric patients aged 2.5 years and older who have growth failure due to inadequate secretion of endogenous growth hormone (GH).

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review for both initial and continuation or therapy requests (where applicable):

A. Medical records supporting the diagnosis of neonatal GH deficiency
B. Pretreatment growth hormone provocative test result(s) (laboratory report or medical record documentation)
C. Growth chart
D. Pretreatment and/or current IGF-1 level (laboratory report or medical record documentation)*
E. The following information must be provided for all continuation of therapy requests:
    1. Total duration of treatment (approximate duration is acceptable)
    2. Date of last dose administered
    3. Approving health plan/pharmacy benefit manager
    4. Date of prior authorization/approval
    5. Prior authorization approval letter

* IGF-1 levels vary based on the laboratory performing the analysis. Laboratory-specific values must be provided to determine whether the value is within the normal range.

III. CRITERIA FOR INITIAL APPROVAL

A. **Pediatric Growth Hormone (GH) Deficiency**
Authorization of 12 months may be granted to members with pediatric GH deficiency 2.5 years of age or older when EITHER criteria 1. or 2. below is met:
    1. Member was diagnosed with GH deficiency as a neonate. Medical records must be available to support the diagnosis of neonatal GH deficiency (e.g., hypoglycemia with random GH level, evidence of multiple pituitary hormone deficiency, chart notes, or magnetic resonance imaging [MRI] results).
    2. Member meets ALL of the following:

i. Member has EITHER:
   a. Two pretreatment pharmacologic provocative GH tests with both results demonstrating a peak GH level < 10 ng/mL, OR
   b. A documented pituitary or CNS disorder (refer to Appendix A) and a pretreatment IGF-1 level > 2 standard deviations (SD) below the mean
ii. Member meets one of the following:
   a. Pretreatment height is > 2 SD below the mean and 1-year height velocity is > 1 SD below the mean, OR
   b. Pretreatment 1-year height velocity is > 2 SD below the mean
iii. Epiphyses are open

B. **Adult Growth Hormone Deficiency**
Authorization of 12 months may be granted to members with adult GH deficiency when ANY of the following criteria is met:
1. Member meets both of the following:
   i. Member has had 2 pretreatment pharmacologic provocative GH tests and both results demonstrated deficient GH responses defined as the following:
      a. Insulin tolerance test (ITT) with a peak GH level ≤ 5 ng/mL
      b. Macrilen with a peak GH level of less than 2.8 ng/mL
      c. Glucagon stimulation test with a peak GH level ≤ 3.0 ng/mL in patients with a body mass index (BMI) ≤ 30 kg/m^2 and a high pretest probability of GHD (e.g., acquired structural abnormalities) OR a BMI < 25 kg/m^2
      d. Glucagon stimulation test with a peak GH level ≤ 1.0 ng/mL in patients with a BMI of ≥ 25 kg/m^2 and a low pretest probability of GHD (e.g., acquired structural abnormalities) OR a BMI > 30 kg/m^2
   ii. Member has a low pretreatment IGF-1 (between 0 to 2 SD below the mean for age and gender)
2. Member meets both of the following:
   i. Member has had 1 pretreatment pharmacologic provocative GH test that demonstrated deficient GH responses defined as one of the following:
      a. Insulin tolerance test (ITT) with a peak GH level ≤ 5 ng/mL
      b. Macrilen with a peak GH level of less than 2.8 ng/mL
      c. Glucagon stimulation test with a peak GH level ≤ 3.0 ng/mL in patients with a body mass index (BMI) ≤ 30 kg/m^2 and a high pretest probability of GHD (e.g., acquired structural abnormalities) OR a BMI < 25 kg/m^2
      d. Glucagon stimulation test with a peak GH level ≤ 1.0 ng/mL in patients with a BMI of ≥ 25 kg/m^2 and a low pretest probability of GHD (e.g., acquired structural abnormalities) OR a BMI > 30 kg/m^2
   ii. Member has a pretreatment IGF-1 level that is more than 2 SD below the mean for age and gender
3. Member has organic hypothalamic-pituitary disease (e.g., suprasellar mass with previous surgery and cranial irradiation) with ≥ 3 documented pituitary hormone deficiencies (refer to Appendix B) and a low pretreatment IGF-1 more than 2 standard deviations below the mean for age and gender
4. Member has genetic or structural hypothalamic-pituitary defects (refer to Appendix C)
5. Member has childhood-onset GH deficiency and a congenital abnormality of the CNS, hypothalamus or pituitary (refer to Appendix C)

IV. CONTINUATION OF THERAPY

A. Pediatric Growth Hormone Deficiency

Authorization of 12 months may be granted for continuation of therapy when ALL of the following criteria are met:

1. Epiphyses are open (confirmed by X-ray or X-ray is not available)
2. Member's growth rate is > 2 cm/year unless there is a documented clinical reason for lack of efficacy (e.g., on treatment less than 1 year, nearing final adult height/late stages of puberty)

B. Adult Growth Hormone Deficiency

Authorization of 12 months may be granted for continuation of therapy when ANY of the following criteria is met:

1. Member meets all of the following:
   i. Member has had 2 pretreatment pharmacologic provocative GH tests and both results demonstrated deficient GH responses defined as the following:
      a. Insulin tolerance test (ITT) or another provocative GH test with a peak GH level ≤ 5 ng/mL
      b. Macrilen with a peak GH level of less than 2.8 ng/ml
      c. Glucagon stimulation test with a peak GH level ≤ 3.0 ng/mL in patients with a body mass index (BMI) ≤ 30 kg/m^2 and a high pretest probability of GHD (e.g., acquired structural abnormalities) OR a BMI < 25 kg/m^2
      d. Glucagon stimulation test with a peak GH level ≤ 1.0 ng/mL in patients with a BMI of ≥ 25 kg/m^2 and a low pretest probability of GHD (e.g., acquired structural abnormalities) OR a BMI > 30 kg/m^2
   ii. Member has a low pretreatment IGF-1 (between 0 to 2 SD below the mean for age and gender)
   iii. Current IGF-1 level is not elevated for age and gender
2. Member meets all of the following:
   i. Member has had 1 pretreatment pharmacologic provocative GH test that demonstrated deficient GH responses defined as one of the following:
      a. Insulin tolerance test (ITT) or another provocative GH test with a peak GH level ≤ 5 ng/mL
      b. Macrilen with a peak GH level of less than 2.8 ng/mL
      c. Glucagon stimulation test with a peak GH level ≤ 3.0 ng/mL in patients with a body mass index (BMI) ≤ 30 kg/m^2 and a high pretest probability of GHD (e.g., acquired structural abnormalities) OR a BMI < 25 kg/m^2
      d. Glucagon stimulation test with a peak GH level ≤ 1.0 ng/mL in patients with a BMI of ≥ 25 kg/m^2 and a low pretest probability of GHD (e.g., acquired structural abnormalities) OR a BMI > 30 kg/m^2
   ii. Member has a pretreatment IGF-1 level that is more than 2 SD below the mean for age and gender
   iii. Current IGF-1 level is not elevated for age and gender
3. Member meets both of the following:
   i. Member has organic hypothalamic-pituitary disease (e.g., suprasellar mass with previous surgery and cranial irradiation) with ≥ 3 documented pituitary hormone deficiencies (refer to Appendix B) and a low pretreatment IGF-1 more than 2 standard deviations below the mean for age and gender
   ii. Current IGF-1 level is not elevated for age and gender
4. Member has genetic or structural hypothalamic-pituitary defects (refer to Appendix C) and current IGF-1 level is not elevated for age and gender
5. Member has childhood-onset GH deficiency and a congenital abnormality of the CNS, hypothalamus or pituitary (refer to Appendix C) and current IGF-1 level is not elevated for age and gender

V. APPENDICES

A. Appendix A: Examples of Hypothalamic/Pituitary/CNS Disorders

1. Congenital genetic abnormalities
   a. Transcription factor defects (PIT-1, PROP-1, LHX3/4, HESX-1, PITX-2)
   b. Growth hormone releasing hormone (GHRH) receptor gene defects

   c. GH secretagogue receptor gene defects
   d. GH gene defects
   e. GH receptor/post receptor defects
2. Congenital structural abnormalities
   a. Optic nerve hypoplasia/septo-optic dysplasia
   b. Agenesis of corpus callosum
   c. Empty sella syndrome
   d. Ectopic posterior pituitary
   e. Pituitary aplasia/hypoplasia
   f. Pituitary stalk defect
   g. Holoprosencephaly
   h. Encephalocele
   i. Hydrocephalus
   j. Anencephaly or prosencephaly
   k. Arachnoid cyst
   l. Other mid-line facial defects (e.g., single central incisor, cleft lip/palate)
   m. Vascular malformations
3. Acquired structural abnormalities (or causes of hypothalamic/pituitary damage)
   a. CNS tumors/neoplasms (e.g., craniopharyngioma, glioma/astrocytoma, pituitary adenoma, germinoma)
   b. Cysts (Rathke cleft cyst or arachnoid cleft cyst)
   c. Surgery
   d. Radiation
   e. Chemotherapy
   f. CNS infections
   g. CNS infarction (e.g., Sheehan's syndrome)
   h. Inflammatory processes (e.g., autoimmune hypophysitis)
   i. Infiltrative processes (e.g., sarcoidosis, histiocytosis, hemochromatosis)
   j. Head trauma/traumatic brain injury
   k. Aneurysmal subarachnoid hemorrhage
   l. Perinatal or postnatal trauma
   m. Surgery of the pituitary or hypothalamus

B. Appendix B: Pituitary Hormones (Other than Growth Hormone)

1. Adrenocorticotropic hormone (ACTH)
2. Antidiuretic hormone (ADH)
3. Follicle stimulating hormone (FSH)
4. Luteinizing hormone (LH)
5. Thyroid stimulating hormone (TSH)
6. Prolactin

C. Appendix C: Requirements for GH-Stimulation Testing in Adults

1. Testing for adult GHD is not required
   a. Three or more pituitary hormone deficiencies and low IGF-1
   b. Congenital structural abnormalities
      i. Transcription factor defects (PIT-1, PROP-1, LHX3/4, HESX-1, PITX-2)
      ii. GHRH receptor-gene defects
      iii. GH-receptor/post-receptor defects
      iv. GH-gene defects associated with brain structural defects
      v. Single central incisor
      vi. Cleft lip/palate
   c. Acquired causes such as perinatal insults

2. Testing for adult GHD is required
   a. Acquired
      i. Skull-base lesions
      ii. Pituitary adenoma
      iii. Craniopharyngioma
      iv. Rathke's cleft cyst
      v. Meningioma
      vi. Glioma/astrocytoma
      vii. Neoplastic sellar and parasellar lesions
      viii. Chordoma
      ix. Hamartoma
      x. Lymphoma
      xi. Metastases
      xii. Other brain injury
      xiii. Traumatic brain injury
      xiv. Sports-related head trauma
      xv. Blast injury
      xvi. Infiltrative/granulomatous disease
      xvii. Langerhans cell histiocytosis
      xviii. Autoimmune hypophysitis (primary or secondary)
      xix. Sarcoidosis
      xx. Tuberculosis
      xxi. Amyloidosis
   b. Surgery to the sella, suprasellar, and parasellar region
   c. Cranial irradiation
   d. Central nervous system infections (bacteria, viruses, fungi, parasites)
   e. Infarction/hemorrhage (e.g., apoplexy, Sheehan's syndrome, subarachnoid hemorrhage, ischemic stroke, snake bite)
   f. Empty sella
   g. Hydrocephalus
   h. Idiopathic

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Reference number(s)
2141-A, 2680-A

SPECIALTY GUIDELINE MANAGEMENT

SOVALDI (sofosbuvir)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
Sovaldi is indicated for the treatment of:
1. Adult patients with chronic hepatitis C virus (HCV) infection as a component of a combination antiviral treatment regimen
   a. genotype 1 or 4 infection without cirrhosis or with compensated cirrhosis for use in combination with pegylated interferon and ribavirin
   b. genotype 2 or 3 infection without cirrhosis or with compensated cirrhosis for use in combination with ribavirin.
2. Chronic HCV genotype 2 or 3 infection in pediatric patients 3 years of age and older without cirrhosis or with compensated cirrhosis for use in combination with ribavirin.

B. Compendial Uses
Hepatitis C genotype 5 or 6 infection (refer to Mavyret SGM)

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Hepatitis C virus infection, in combination with peginterferon alfa (PEG-IFN) and ribavirin (RBV)

1. Genotype 1 infection
Authorization of up to 12 weeks total may be granted for members who are treatment-naïve.

2. Genotype 4 infection
Authorization of up to 12 weeks total may be granted for members who are treatment-naïve.

B. Hepatitis C virus infection, in combination with ribavirin

1. Genotype 1 infection
Authorization of up to 24 weeks total may be granted for members who have documented interferon (IFN) ineligibility (see Section IV).

2. Genotype 2 infection
Authorization of up to 12 weeks total may be granted for members who are treatment-naïve or failed prior treatment with PEG-IFN and RBV.

3. Genotype 3 infection
Authorization of up to 24 weeks total may be granted for members who are treatment-naïve or failed prior treatment with PEG-IFN and RBV.

4. Members with hepatocellular carcinoma awaiting liver transplantation

Authorization of up to 48 weeks total or until liver transplantation, whichever occurs first, may be granted for members with genotype 1, 2, 3, or 4 infection and hepatocellular carcinoma who meet the MILAN criteria, defined as the following:

i. Tumor size 5 cm or less in diameter with single hepatocellular carcinomas OR 3 tumor nodules or less, each 3 cm or less in diameter with multiple tumors AND
ii. No extrahepatic manifestations of the cancer or evidence of vascular invasion of tumor

C. Hepatitis C virus infection, in combination with Mavyret (with ribavirin)

Authorization of up to 24 weeks total (as applicable) may be granted for members prescribed Sovaldi in combination with Mavyret (with ribavirin) who meet the criteria for approval for the requested regimen. Refer to the Mavyret SGM for the specific criteria for approval and approval durations.

D. HCV and HIV coinfection

Authorization may be granted for members with HCV and HIV coinfection when the criteria for approval of the requested regimen in Section A, B, or C above are met.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. APPENDIX: INTERFERON INELIGIBLITY

IFN ineligible is defined as one or more of the below:

- Intolerance to IFN
- Autoimmune hepatitis and other autoimmune disorders
- Hypersensitivity to PEG-IFN or any of its components
- Major uncontrolled depressive illness
- A baseline neutrophil count < 1,500/mcL
- A baseline platelet count < 90,000/mcL
- A baseline hemoglobin < 10 g/dL
- History of pre-existing cardiac disease

V. REFERENCES

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Reference number(s)
2889-A

SPECIALTY GUIDELINE MANAGEMENT

SPRAVATO (esketamine) nasal spray

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Spravato is indicated, in conjunction with an oral antidepressant, for the treatment of:

1. Treatment-resistant depression (TRD) in adults
2. Depressive symptoms in adults with major depressive disorder (MDD) with acute suicidal ideation or behavior

Limitations of Use:
The effectiveness of Spravato in preventing suicide or in reducing suicidal ideation or behavior has not been demonstrated. Use of Spravato does not preclude the need for hospitalization if clinically warranted, even if patients experience improvement after an initial dose of Spravato.

Spravato is not approved as an anesthetic agent. The safety and effectiveness of Spravato as an anesthetic agent have not been established.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

A. For initial requests:
   1. Pretreatment depression severity score(s) from standardized rating scale(s) that reliably measure depressive symptoms (e.g., Beck Depression Inventory [BDI], Hamilton Depression Rating Scale [HDRS], Montgomery-Asberg Depression Rating Scale [MADRS], etc.)
   2. Medical records documenting inadequate response with antidepressant and augmentation agents for the current depressive episode (if applicable)

B. For continuation of therapy:
   Current depression severity score(s) from standardized rating scale(s) that reliably measure depressive symptoms (if applicable)

III. EXCLUSION

Coverage will not be provided for members with moderate or severe substance or alcohol use disorder that is not currently being treated or medically managed.

IV. CRITERIA FOR INITIAL APPROVAL

A. Treatment-resistant depression (TRD)/Major Depressive Disorder (MDD) with acute suicidal ideation or behavior

Authorization of 1 month may be granted for treatment of TRD or MDD with acute suicidal ideation or behavior when all of the following criteria are met:

1. Member has a confirmed diagnosis of severe major depressive disorder (single or recurrent episode), documented by standardized rating scales that reliably measure depressive symptoms (e.g., Beck Depression Inventory [BDI], Hamilton Depression Rating Scale [HDRS], Montgomery-Asberg Depression Rating Scale [MADRS]).
2. The requested medication will be prescribed by or in consultation with a psychiatrist.
3. Member is 18 years of age or older.
4. Requested drug will be administered under the direct supervision of a healthcare provider.
5. Member will be monitored by a health care provider for at least 2 hours after administration.
6. Requested drug will be used in combination with an oral antidepressant (e.g., duloxetine, escitalopram, sertraline, venlafaxine).
7. Member meets either of the following criteria:
   i. Member must meet both of the following:
      a. Member has experienced inadequate response during the current depressive episode with two antidepressants (e.g., selective serotonin reuptake inhibitor [SSRI], serotonin-norepinephrine reuptake inhibitor [SNRI], tricyclic antidepressant [TCA], bupropion, mirtazapine) from at least two different classes (different mechanisms of action) at the maximally tolerated labeled dose, each used for at least 8 weeks;
         - Aminoketone (Wellbutrin/SR/XL [bupropion])
         - Monoamine oxidase inhibitors (MAOIs) (e.g., Marplan, Nardil, Parnate, phenelzine, tranylcypromine)
         - Noradrenaline and specific serotoninergic antidepressants (NASSAs) (e.g., amoxapine, maprotiline, mirtazapine/ODT, Oleptro ER, Remeron/Solutab, trazodone)
         - Selective serotonin reuptake inhibitors (SSRIs) (e.g., Celexa, citalopram, escitalopram, fluoxetine, fluvoxamine, Lexapro, Luvox/CR, paroxetine, Paxil/CR, Pexeva, Prozac/Weekly, sertraline, Zoloft)
         - Serotonin-norepinephrine reuptake inhibitors (SNRIs) (e.g., Cymbalta, desvenlafaxine/ER, duloxetine, Effexor/XR, Fetzima, Irenka, Khedezla, Pristiq, venlafaxine/ER)
         - Tricyclic antidepressants (TCAs) (e.g., amitriptyline, desipramine, doxepin, Elavil, imipramine, Norpramin, nortriptyline, Pamelor, Surmontil, Tofranil, trimipramine)
      b. Member has experienced an inadequate response with an adequate trial of augmentation therapy OR evidenced based psychotherapy (e.g., cognitive behavioral therapy) during the current depressive episode
         - Augmentation therapy is defined as:
           - Two antidepressants with different mechanisms of action used concomitantly
           - An antidepressant and a second-generation antipsychotic used concomitantly
           - An antidepressant and lithium used concomitantly
           - An antidepressant and thyroid hormone used concomitantly
           - An antidepressant and buspirone used concomitantly
   ii. Member has major depressive disorder with both of the following:
      a. Member has current suicidal ideation with intent defined as both of the following:
         - Member has thoughts, even momentarily, of self-harm with at least some intent or awareness that they may die as a result, or member thinks about suicide
         - Member intends to act on thoughts of killing themselves

b. The prescriber represents that, in the absence of the requested drug, within the next 24 to 48 hours the member will require confinement in an acute care psychiatric institution.

V. CONTINUATION OF THERAPY

A. Treatment-resistant depression (TRD)
Authorization of 3 months may be granted for the continuation of treatment of TRD when there is improvement or sustained improvement from baseline in depressive symptoms documented by standardized rating scales that reliably measure depressive symptoms (e.g., Beck Depression Inventory [BDI], Hamilton Depression Rating Scale [HDRS], Montgomery-Asberg Depression Rating Scale [MADRS]).

B. Major depressive disorder (MDD) with acute suicidal ideation or behavior
The use of Spravato beyond 4 weeks has not been systematically evaluated in the treatment of depressive symptoms in patients with MDD with acute suicidal ideation or behavior. Member must meet all initial criteria for approval.

VI. REFERENCES

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Reference number
1782-A

SPECIALTY GUIDELINE MANAGEMENT

SPRYCEL (dasatinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
1. Newly diagnosed adults with Philadelphia chromosome-positive (Ph+) chronic myeloid leukemia (CML) in chronic phase
2. Adults with chronic, accelerated, or myeloid or lymphoid blast phase Ph+ CML with resistance or intolerance to prior therapy including imatinib
3. Adults with Ph+ acute lymphoblastic leukemia (ALL) with resistance or intolerance to prior therapy
4. Pediatric patients 1 year of age and older with Ph+ CML in chronic phase
5. Pediatric patients 1 year of age and older with newly diagnosed Ph+ ALL in combination with chemotherapy

B. Compendial Uses
1. Primary treatment of advanced phase CML (accelerated phase or blast phase)
2. Follow-up therapy for CML patients after hematopoietic stem cell transplant (HSCT)
3. Ph+ B-cell acute lymphoblastic leukemia or lymphoblastic lymphoma (Ph+ B-ALL/LL)
4. Maintenance therapy for Ph+ B-ALL/LL patients after HSCT
5. Induction or consolidation therapy for Ph+ B-ALL/LL
6. Relapsed or refractory Ph+ B-ALL/LL
7. Relapsed or refractory T-cell ALL/LL with ABL-class translocation
8. Induction or consolidation therapy for Ph-like B-ALL/LL with ABL-class kinase fusion
9. Consolidation therapy for Ph-like B-ALL/LL and CRLF2- with ABL-class kinase fusion
10. Metastatic chondrosarcoma
11. Recurrent chordoma
12. Gastrointestinal stromal tumor (GIST)
13. Myeloid/lymphoid neoplasms with eosinophilia and ABL1 rearrangement in chronic phase
14. Lymphoid, myeloid or mixed lineage neoplasms with eosinophilia and ABL1 rearrangement in blast phase

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

The following information is necessary to initiate the prior authorization review:
A. For treatment of CML or Ph+ ALL/LL: results of cytogenetic and/or molecular testing for detection of the Ph chromosome or the BCR-ABL gene
B. For treatment of Ph-like B-ALL/LL: results of cytogenetic and/or molecular testing confirming ABL-class kinase fusion
C. For treatment of T-cell ALL/LL: results of cytogenetic and/or molecular testing confirming ABL-class translocation

D. For members requesting initiation of therapy with the requested medication for treatment of CML or ALL/LL after experiencing resistance to prior tyrosine kinase inhibitor (TKI) therapy: results of BCR-ABL1 mutation testing for T315I/A, F317L/V/I/C, and V299L mutations
E. For treatment of GIST: PDGFRA exon 18 mutation testing (where applicable)
F. For members requesting initiation of therapy with the requested medication for treatment of myeloid and/or lymphoid neoplasms with eosinophilia: results of testing or analysis confirming ABL1 rearrangement

III. CRITERIA FOR INITIAL APPROVAL

A. Chronic Myeloid Leukemia (CML)

Authorization of 7 months may be granted for treatment of CML that has been confirmed by detection of the Ph chromosome or BCR-ABL gene by cytogenetic and/or molecular testing when any of the following criteria are met:

1. Member has not received prior therapy with a TKI (e.g., bosutinib, imatinib, nilotinib, ponatinib)
2. Member experienced toxicity or intolerance to prior therapy with a TKI
3. Member experienced resistance to prior therapy with a TKI and results of BCR-ABL1 mutational testing are negative for all of the following: T315I/A, F317L/V/I/C, and V299L
4. Member has received HSCT for CML and results of BCR-ABL1 mutational testing are negative for all of the following: T315I/A, F317L/V/I/C, and V299L

B. Acute Lymphoblastic Leukemia (ALL)/Lymphoblastic Lymphoma (LL)

1. Authorization of 12 months may be granted for treatment of ALL/LL when both of the following criteria are met:
   i. The member has any of the following:
      a. Ph+ ALL/LL that has been confirmed by detection of the Ph chromosome or BCR-ABL gene by cytogenetic and/or molecular testing
      b. Ph-like B-ALL/LL with ABL-class kinase fusion that has been confirmed by cytogenetic and/or molecular testing
      c. T-cell ALL/LL with ABL-class translocation that has been confirmed by cytogenetic and/or molecular testing and the disease is relapsed or refractory
   ii. The member meets any of the following:
      a. Member has not received prior therapy with a TKI (e.g., bosutinib, imatinib, nilotinib, ponatinib)
      b. Member experienced toxicity or intolerance to prior therapy with a TKI
      c. Member experienced resistance to prior therapy with a TKI and results of BCR-ABL1 mutational testing are negative for all of the following: T315I/A, F317L/V/I/C, and V299L

2. Authorization of 12 months may be granted for members who have received HSCT for Ph+ ALL/LL and results of BCR-ABL1 mutation testing are negative for all of the following: T315I/A, F317L/V/I/C, and V299L

C. Gastrointestinal Stromal Tumor (GIST)

Authorization of 12 months may be granted for treatment of GIST when either of the following criteria are met:

1. The member meets all of the following:
   i. Member has unresectable, recurrent/progressive, or metastatic disease,
   ii. The disease harbors a platelet-derived growth factor receptor alpha (PDGFRA) exon 18 mutation
   iii. Member has received prior therapy with imatinib or avapritinib
   iv. The requested medication will be used as a single agent

2. The requested medication will be used for palliation of symptoms if previously tolerated and effective.

D. Bone Cancer
Authorization of 12 months may be granted for treatment of metastatic chondrosarcoma or recurrent chordoma when the requested medication is used as a single agent.

E. Myeloid/Lymphoid Neoplasms with Eosinophilia
Authorization of 12 months may be granted for treatment of myeloid and/or lymphoid neoplasms with eosinophilia and ABL1 rearrangement in the chronic phase or blast phase.

IV. CONTINUATION OF THERAPY

A. CML
Authorization may be granted for continued treatment of CML that has been confirmed by detection of Ph chromosome or BCR-ABL gene by cytogenetic and/ or molecular testing when either of the following criteria is met:
1. Authorization of 12 months may be granted when any of the following criteria is met:
   i. BCR-ABL1 is less than or equal to 10% and there is no evidence of disease progression or unacceptable toxicity while on the current regimen for members who have been receiving the requested medication for 6 months or greater
   ii. Member has received HSCT and there is no evidence of unacceptable toxicity or disease progression while on the current regimen
2. Authorization of up to 7 months may be granted when the member has completed less than 6 months of therapy with the requested medication.

B. Acute Lymphoblastic Leukemia or Lymphoblastic Lymphoma (ALL/LL)
Authorization of 12 months may be granted for continued treatment of ALL/LL when there is no evidence of unacceptable toxicity or disease progression while on the current regimen and any of the following criteria is met:
1. Member has Ph+ ALL/LL that has been confirmed by detection of Ph chromosome or BCR-ABL gene by cytogenetic and/ or molecular testing.
2. Member has Ph-like B-ALL/LL with ABL-class kinase fusion that has been confirmed by cytogenetic and/or molecular testing.
3. Member has T-cell ALL/LL with ABL-class translocation that has been confirmed by cytogenetic testing and/or molecular testing.
4. Member has received HSCT for ALL/LL

C. GIST, Bone Cancer, and Myeloid/Lymphoid Neoplasms with Eosinophilia
Authorization of 12 months may be granted for continued treatment of GIST, chondrosarcoma, chordoma, or myeloid/lymphoid neoplasms with eosinophilia when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

V. REFERENCES

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3. NCCN Clinical Practice Guidelines in Oncology® Chronic Myeloid Leukemia (Version 3.2022). © 2022 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed April 12, 2022.
4. NCCN Clinical Practice Guidelines in Oncology® Acute Lymphoblastic Leukemia (Version 1.2022).

© 2022 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed April 12, 2022.

Reference number(s)
2010-A

SPECIALTY GUIDELINE MANAGEMENT

STELARA (ustekinumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
1. Moderate to severe plaque psoriasis (PsO) in patients 6 years and older who are candidates for phototherapy or systemic therapy
2. Active psoriatic arthritis (PsA) in patients 6 years and older
3. Moderately to severely active Crohn's disease (CD) in adults
4. Moderately to severely active ulcerative colitis (UC) in adults

B. Compendial Uses
Immune checkpoint inhibitor-related toxicity

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

A. Plaque psoriasis (PsO)
1. Initial requests:
   i. Chart notes or medical record documentation of affected area(s) and body surface area (BSA) affected (if applicable).
   ii. Chart notes, medical record documentation, or claims history supporting previous medications tried (if applicable), including response to therapy. If therapy is not advisable, documentation of clinical reason to avoid therapy.
2. Continuation requests: Chart notes or medical record documentation of decreased body surface area (BSA) affected and/or improvement in signs and symptoms.

B. Psoriatic arthritis (PsA)
1. Initial requests: Chart notes, medical record documentation, or claims history supporting previous medications tried (if applicable), including response to therapy. If therapy is not advisable, documentation of clinical reason to avoid therapy.
2. Continuation requests: Chart notes or medical record documentation supporting positive clinical response.

C. Crohn's disease (CD)

Continuation requests: Chart notes or medical record documentation supporting positive clinical response to therapy or remission.

D. Ulcerative colitis (UC)
Continuation requests: Chart notes or medical record documentation supporting positive clinical response to therapy or remission.

E. Immune checkpoint inhibitor-related toxicity
Chart notes, medical record documentation, or claims history supporting previous medications tried (if applicable), including response to therapy. If therapy is not advisable, documentation of clinical reason to avoid therapy.

III. PRESCRIBER SPECIALTIES

The medication must be prescribed by or in consultation with one of the following:
A. Plaque psoriasis: dermatologist
B. Psoriatic arthritis: rheumatologist or dermatologist
C. Crohn's disease and ulcerative colitis: gastroenterologist
D. Immune checkpoint inhibitor-related toxicity: hematologist or oncologist

IV. CRITERIA FOR INITIAL APPROVAL

A. Plaque psoriasis (PsO)

1. Authorization of 12 months may be granted for members 6 years of age and older who have previously received a biologic or targeted synthetic drug (e.g., Sotyktu, Otezla) indicated for treatment of moderate to severe plaque psoriasis.

2. Authorization of 12 months may be granted for members 6 years of age and older for treatment of moderate to severe plaque psoriasis when any of the following criteria is met:
   i. Crucial body areas (e.g., hands, feet, face, neck, scalp, genitals/groin, intertriginous areas) are affected.
   ii. At least 10% of body surface area (BSA) is affected.
   iii. At least 3% of body surface area (BSA) is affected and the member meets either of the following criteria:
      a. Member has had an inadequate response or intolerance to either phototherapy (e.g., UVB, PUVA) or pharmacologic treatment with methotrexate, cyclosporine, or acitretin.
      b. Member has a clinical reason to avoid pharmacologic treatment with methotrexate, cyclosporine, and acitretin (see Appendix).

B. Psoriatic arthritis (PsA)

1. Authorization of 12 months may be granted for members 6 years of age or older who have previously received a biologic or targeted synthetic drug (e.g., Rinvoq, Otezla) indicated for active psoriatic arthritis.

2. Authorization of 12 months may be granted for members 6 years of age or older for treatment of active psoriatic arthritis when either of the following criteria is met:
   i. Member has mild to moderate disease and meets one of the following criteria:

a. Member has had an inadequate response to methotrexate, leflunomide, or another conventional synthetic drug (e.g., sulfasalazine) administered at an adequate dose and duration.
b. Member has an intolerance or contraindication to methotrexate or leflunomide (see Appendix), or another conventional synthetic drug (e.g., sulfasalazine).
c. Member has enthesitis or predominantly axial disease.

ii. Member has severe disease.

C. Crohn's disease (CD)
Authorization of 12 months may be granted for adult members for treatment of moderately to severely active Crohn's disease.

D. Ulcerative colitis (UC)
Authorization of 12 months may be granted for adult members for treatment of moderately to severely active ulcerative colitis.

E. Immune checkpoint inhibitor-related toxicity
Authorization of 6 months may be granted for the treatment of immune checkpoint inhibitor-related diarrhea or colitis when the member has experienced an inadequate response, intolerance, or contraindication to infliximab or vedolizumab.

V. CONTINUATION OF THERAPY

A. Plaque psoriasis (PsO)
Authorization of 12 months may be granted for all members 6 years of age and older (including new members) who are using the requested medication for moderate to severe plaque psoriasis and who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition when either of the following is met:
1. Reduction in body surface area (BSA) affected from baseline
2. Improvement in signs and symptoms from baseline (e.g., itching, redness, flaking, scaling, burning, cracking, pain)

B. Psoriatic arthritis (PsA)
Authorization of 12 months may be granted for all members 6 years of age or older (including new members) who are using the requested medication for psoriatic arthritis and who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition when there is improvement in any of the following from baseline:
1. Number of swollen joints
2. Number of tender joints
3. Dactylitis
4. Enthesitis
5. Axial disease
6. Skin and/or nail involvement

C. Crohn's Disease (CD)
1. Authorization of 12 months may be granted for all adult members (including new members) who are using the requested medication for moderately to severely active Crohn's disease and who achieve or maintain remission.

2. Authorization of 12 months may be granted for all adult members (including new members) who are using the requested medication for moderately to severely active Crohn's disease and who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition when there is improvement in any of the following from baseline:
   i. Abdominal pain or tenderness
   ii. Diarrhea
   iii. Body weight
   iv. Abdominal mass
   v. Hematocrit
   vi. Appearance of the mucosa on endoscopy, computed tomography enterography (CTE), magnetic resonance enterography (MRE), or intestinal ultrasound
   vii. Improvement on a disease activity scoring tool (e.g., Crohn's Disease Activity Index [CDAI] score)

D. Ulcerative colitis

1. Authorization of 12 months may be granted for all adult members (including new members) who are using the requested medication for moderately to severely active ulcerative colitis and who achieve or maintain remission.

2. Authorization of 12 months may be granted for all adult members (including new members) who are using the requested medication for moderately to severely active ulcerative colitis and who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition when there is improvement in any of the following from baseline:
   i. Stool frequency
   ii. Rectal bleeding
   iii. Urgency of defecation
   iv. C-reactive protein (CRP)
   v. Fecal calprotectin (FC)
   vi. Appearance of the mucosa on endoscopy, computed tomography enterography (CTE), magnetic resonance enterography (MRE), or intestinal ultrasound
   vii. Improvement on a disease activity scoring tool (e.g., Ulcerative Colitis Endoscopic Index of Severity [UCEIS], Mayo score)

E. Immune checkpoint inhibitor-related toxicity

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

VI. OTHER

For all indications: Member has had a documented negative tuberculosis (TB) test (which can include a tuberculosis skin test [PPD], an interferon-release assay [IGRA], or a chest x-ray)* within 6 months of initiating therapy for persons who are naïve to biologic drugs or targeted synthetic drugs associated with an increased risk of TB.

* If the screening testing for TB is positive, there must be further testing to confirm there is no active disease. Do not administer the requested medication to members with active TB infection. If there is latent disease, TB treatment must be started before initiation of the requested medication.

For all indications: Member cannot use the requested medication concomitantly with any other biologic drug or targeted synthetic drug.

Stelara for intravenous administration will only be authorized to use for the treatment of Crohn's disease, ulcerative colitis, and immune checkpoint inhibitor-related toxicity.

VII. DOSAGE AND ADMINISTRATION

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

VIII. APPENDIX

Examples of Clinical Reasons to Avoid Pharmacologic Treatment with Methotrexate, Cyclosporine, Acitretin, or Leflunomide

1. Clinical diagnosis of alcohol use disorder, alcoholic liver disease, or other chronic liver disease
2. Drug interaction
3. Risk of treatment-related toxicity
4. Pregnancy or currently planning pregnancy
5. Breastfeeding
6. Significant comorbidity prohibits use of systemic agents (e.g., liver or kidney disease, blood dyscrasias, uncontrolled hypertension)
7. Hypersensitivity
8. History of intolerance or adverse event

IX. REFERENCES

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Reference number(s)
1950-A

SPECIALTY GUIDELINE MANAGEMENT

STIMATE (desmopressin acetate nasal spray)

POLICY*

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
1. Hemophilia A with Factor VIII coagulant activity level >5%
2. Mild to moderate type 1 von Willebrand disease (VWD) with Factor VIII activity level >5%

B. Compendial Uses
1. Type 2A, 2M, 2N VWD
2. Qualitative platelet disorders
3. Acquired hemophilia A
4. Acquired von Willebrand syndrome

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Von Willebrand Disease
Type 1, 2A, 2M, or 2N VWD
1. Authorization of one month may be granted for treatment of mild or moderate type 1 and type 2A, 2M, or 2N VWD in members who are initiating therapy.
2. Authorization of 12 months may be granted for treatment of mild or moderate type 1 and type 2A, 2M, or 2N VWD in members who are continuing therapy and have demonstrated a response to an initial trial of Stimate.

B. Hemophilia A
Authorization of 12 months may be granted for treatment of hemophilia A with factor VIII activity level greater than 5% (see Appendix).

C. Qualitative Platelet Disorders
Authorization of 12 months may be granted for treatment of a qualitative platelet disorder.

D. Acquired Hemophilia A
Authorization of 12 months may be granted for treatment of acquired hemophilia A.

E. Acquired von Willebrand Syndrome
Authorization of 12 months may be granted for treatment of acquired von Willebrand syndrome.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II when the member is experiencing benefit from therapy (e.g., reduced frequency or severity of bleeds).

IV. APPENDIX

Appendix: Classification of Hemophilia by Clotting Factor Level (% Activity) and Bleeding Episodes

Severity	Clotting Factor Level % activity^	Bleeding Episodes
Severe	<1%	Spontaneous bleeding episodes, predominantly into joints and muscles Severe bleeding with trauma, injury or surgery
Moderate	1% to 5%	Occasional spontaneous bleeding episodes Severe bleeding with trauma, injury or surgery
Mild	6% to 40%	Severe bleeding with serious injury, trauma or surgery

^Factor assay levels are required to determine the diagnosis and are of value in monitoring treatment response.

*Note: **This program addresses the appropriate use of Stimate Nasal Spray only**. Stimate Nasal Spray and DDAVP (desmopressin) Nasal Spray are two distinct products and are not interchangeable. DDAVP Nasal Spray is not indicated for hemophilia or VWD.

V. REFERENCES

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Reference number(s)
1809-A

SPECIALTY GUIDELINE MANAGEMENT

STIVARGA (regorafenib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
1. Colorectal cancer
   Stivarga is indicated for the treatment of patients with metastatic colorectal cancer (CRC) who have been previously treated with fluoropyrimidine-, oxaliplatin- and irinotecan-based chemotherapy, an anti-vascular endothelial growth factor (VEGF) therapy, and, if RAS wild type, an anti-epidermal growth factor receptor (EGFR) therapy.
2. Gastrointestinal stromal tumors
   Stivarga is indicated for the treatment of patients with locally advanced, unresectable or metastatic gastrointestinal stromal tumor (GIST) who have been previously treated with imatinib mesylate and sunitinib malate.
3. Hepatocellular carcinoma
   Stivarga is indicated for the treatment of patients with hepatocellular carcinoma (HCC) who have been previously treated with sorafenib.

B. Compendial Uses
1. Advanced or metastatic colorectal cancer
2. Gastrointestinal stromal tumors (GIST)
3. Soft tissue sarcoma
   a. Non-adipocytic sarcoma
   b. Retroperitoneal/Intra-abdominal
   c. Rhabdomyosarcoma
   d. Angiosarcoma
4. Hepatocellular carcinoma
5. Osteosarcoma
6. Glioblastoma

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Colorectal Cancer (CRC)
Authorization of 12 months may be granted for treatment of advanced or metastatic colorectal cancer, including appendiceal adenocarcinoma and anal adenocarcinoma, as a single agent when the member has progressed on previous treatment with all the following regimens unless the member has a contraindication or intolerance:
1. Fluoropyrimidine-, oxaliplatin- and irinotecan-based chemotherapy; and

2. An anti-vascular endothelial growth factor (VEGF) therapy; and
3. If RAS wild type, an anti-epidermal growth factor receptor (EGFR) therapy, such as Erbitux (cetuximab) or Vectibix (panitumumab), for rectal cancer, appendiceal adenocarcinoma, anal adenocarcinoma, or left-sided colon cancer.

B. Gastrointestinal stromal tumor (GIST)

Authorization of 12 months may be granted for treatment of GIST when any of the following criteria are met:

1. The requested medication will be used for locally advanced, unresectable, recurrent/progressive, or metastatic GIST following disease progression on imatinib and either sunitinib or dasatinib
2. The requested medication will be used for treatment of unresectable, recurrent/progressive, or metastatic GIST in combination with everolimus for disease progression after the member has failed at least four FDA-approved therapies (e.g., imatinib, sunitinib, ripretinib, avapritinib)
3. The requested medication will be used for treatment of unresectable succinate dehydrogenase (SDH)-deficient GIST as a single agent.
4. The requested medication will be used for palliation of symptoms if previously tolerated and effective.

C. Hepatocellular carcinoma

Authorization of 12 months may be granted for treatment of hepatocellular carcinoma as subsequent treatment as a single agent.

D. Soft tissue sarcomas

Authorization of 12 months may be granted for treatment of angiosarcoma, retroperitoneal/intra-abdominal soft tissue sarcoma, rhabdomyosarcoma, and non-adipocytic sarcoma, as a single agent.

E. Osteosarcoma

Authorization of 12 months may be granted for second-line treatment of relapsed/refractory or metastatic osteosarcoma as a single agent.

F. Glioblastoma

Authorization of 12 months may be granted for treatment of recurrent glioblastoma as a single agent.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in section II when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

IV. REFERENCES

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Reference number(s)
1974-A

SPECIALTY GUIDELINE MANAGEMENT

STRENSIQ (asfotase alfa)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Strensiq is indicated for the treatment of patients with perinatal/infantile- and juvenile-onset hypophosphatasia (HPP).

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

A. Initiation of therapy:
   1. Documentation of presence of condition before the age of 18, if applicable
   2. Documentation confirming diagnosis which includes one of the following:
      a. Genetic testing results confirming a mutation in the *ALPL* gene, or
      b. Submission of ALL of the following:
         i. Radiographic imaging demonstrating skeletal abnormalities (See Appendix B)
         ii. A serum alkaline phosphatase (ALP) level below the gender and age-specific reference range of the laboratory performing the test
         iii. Elevated tissue non-specific alkaline phosphatase (TNSALP) substrate level (i.e., serum pyridoxal 5-phosphate (PLP) level, serum or urine proximity extension immunoassay (PEA) level, urinary inorganic pyrophosphate (PPi) level)

B. Continuation of therapy:
   Medical records of at least one of the following:
   1. Radiographic Global Impression of Change (RGI-C) rating
   2. Height and weight measurements as measured by z-scores
   3. Modified Performance Oriented Mobility Assessment-Gait (MPOMA-G) score
   4. Distance walked in the 6 Minute Walk Test (6MWT)

III. CRITERIA FOR INITIAL APPROVAL

Perinatal/infantile- and juvenile-onset hypophosphatasia (HPP)
Authorization of 12 months may be granted for treatment of HPP when all of the following criteria are met:

A. The member has clinical signs and/or symptoms of hypophosphatasia (See Appendix A).
B. The onset of the disease was perinatal/infantile or juvenile. If the member is 18 years of age or older at the time of the request, documentation of the presence of the condition before the age of 18 must be provided (e.g., member began experiencing symptoms at age 10).

C. The diagnosis was confirmed by one of the following (1 or 2):
   1. The presence of a known pathological mutation in the *ALPL* gene as detected by *ALPL* molecular genetic testing
   2. The diagnosis is supported by ALL of the following:
      a. Radiographic imaging demonstrating skeletal abnormalities (See Appendix B)
      b. A serum alkaline phosphatase (ALP) level below the gender- and age-specific reference range of the laboratory performing the test
      c. Elevated tissue-nonspecific alkaline phosphatase (TNSALP) substrate level (i.e., serum PLP level, serum or urine PEA level, urinary PPi level)

D. Member's weekly dose will not exceed the following:
   1. 9 mg/kg weekly in a member with perinatal/infantile-onset HPP
   2. 6 mg/kg weekly in a member with juvenile-onset HPP

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III who are currently receiving the requested medication through a paid pharmacy or medical benefit when both of the following are met:

A. Member is experiencing benefit from therapy as demonstrated by one of the following:
   1. Member has experienced improvement in skeletal manifestations from baseline as assessed by the Radiographic Global Impression of Change (RGI-C) scale
   2. Member is less than 18 years of age and has experienced an improvement in height and weight compared to baseline, as measured by z-scores
   3. Member has experienced an improvement in step length by at least 1 point in either foot compared to baseline based on the Modified Performance Oriented Mobility Assessment-Gait (MPOMA-G) scale
   4. Member has experienced an improvement in 6 Minute Walk Test compared to baseline

B. Member's weekly dose will not exceed the following:
   1. 9 mg/kg weekly in a member with perinatal/infantile-onset HPP
   2. 6 mg/kg weekly in a member with juvenile-onset HPP

V. APPENDIX

Appendix A. Examples of Signs and Symptoms of HPP

A. Perinatal/infantile-onset HPP:
   - Generalized hypomineralization with rachitic features, chest deformities and rib fractures
   - Skeletal abnormalities (e.g., short limbs, abnormally shaped chest, soft skull bone)
   - Respiratory problems (e.g., pneumonia)
   - Hypercalcemia
   - Failure to thrive
   - Severe muscular hypotonia and weakness
   - Nephrocalcinosis secondary to hypercalciuria
   - Swallowing problems
   - Seizures

B. Juvenile-onset HPP:
   - Premature loss of deciduous teeth
   - Failure to thrive with anorexia, nausea, and gastrointestinal problems
   - Short stature with bowed legs or knock knees
   - Skeletal deformities (e.g., enlarged wrist and ankle joints, abnormal skull shape)

- Bone and joint pain
- Rickets
- Fractures
- Delayed walking
- Waddling gait

Appendix B. Examples of Radiographic Findings that Support HPP Diagnosis

- Infantile rickets
- Alveolar bone loss
- Focal bony defects of the metaphyses
- Metatarsal stress fractures
- Osteomalacia with lateral pseudofractures
- Osteopenia, osteoporosis, or low bone mineral content for age (as detected by dual-energy x-ray absorptiometry [DEXA])

VI. REFERENCES

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PRIOR AUTHORIZATION CRITERIA

BRAND NAME*
(generic)

SUCRAID
(sacrosidase)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization with Quantity Limit ***Ref # 3369-C***

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Sucraid (sacrosidase) Oral Solution is indicated as oral replacement therapy of the genetically determined sucrase deficiency, which is part of congenital sucrase-isomaltase deficiency (CSID).

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has a diagnosis of congenital sucrase-isomaltase deficiency

AND

- The diagnosis of congenital sucrase-isomaltase deficiency was confirmed by small bowel biopsy
  OR
- The diagnosis of congenital sucrase-isomaltase deficiency was confirmed by genetic testing
  OR
- The diagnosis of congenital sucrase-isomaltase deficiency was confirmed by sucrose hydrogen breath test

Quantity Limits apply.

QUANTITY LIMIT

PLEASE NOTE: Since manufacturer package sizes may vary, it is the discretion of the dispensing pharmacy to fill quantities per package size up to these quantity limits. In such cases the filling limit and day supply may be less than what is indicated.

Drug	1 Month Limit*	3 Month Limit*
Sucraid Multiple-Dose Bottle (Each bottle contains 4 oz [118 mL total])	354 mL / 25 days	1062 mL / 75 days
Sucraid Single-Use Container (Each carton contains 150 single-use containers of 2 mL each [300 mL total])	300 mL/ 21 days	900 mL/ 63 days

**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing OR the duration of 21 days is used for a 25-day fill period and 63 days is used for a 75-day fill period to allow time for refill processing.*

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Sucraid (sacrosidase) Oral Solution is indicated

CVS caremark®

as oral replacement therapy of the genetically determined sucrase deficiency, which is part of congenital sucrase-isomaltase deficiency (CSID). The definitive test for diagnosis of CSID is the measurement of intestinal disaccharidases following small bowel biopsy.[1] Genetic testing may be indicated in some cases. Other tests may include sucrose hydrogen breath tests[4,5] Therefore, coverage will be considered for patients who have congenital sucrose-isomaltase deficiency that was confirmed by small bowel biopsy, genetic testing, or sucrose hydrogen breath test.

The recommended dosage of Sucraid is 1 mL per meal or snack for patients weighing up to 15 kg, and 2 mL per meal or snack for patients weighing over 15 kg. Sucraid is supplied in 4 ounce (118 mL total) bottles and cartons containing 150 2mL single use containers (300mL total).[1] To accommodate for up to 3 meals and 3 snacks per day at the highest dosage and to accommodate package dispensing requirements, a quantity limit reflective of 12 mL per day for each package size will apply to patients who meet the prior authorization criteria.

REFERENCES

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Written by:	UM Development (DS)
Date Written:	10/2019
Revised:	01/2020 (no clinical changes), 09/2020 (added sucrose hydrogen breath test to confirm dx, updated title), 09/2021 (no clinical changes), (VLS) 06/2022 (added 2mL single-dose package)
Reviewed:	Medical Affairs (CHART) 10/24/2019, 01/23/2020, 09/24/2020, 12/31/2020, 09/30/2021 External Review: 12/2019, 04/2020, 12/2020, 12/2021, (FYI) 08/2022

CRITERIA FOR APPROVAL

1	Does the patient have a diagnosis of congenital sucrase-isomaltase deficiency? [If yes, go to 2. If no, then no further questions.]	Yes	No
2	Was the diagnosis of congenital sucrase-isomaltase deficiency confirmed by small bowel biopsy? [If yes, go to 5. If no, go to 3.]	Yes	No
3	Was the diagnosis of congenital sucrase-isomaltase deficiency confirmed by genetic testing? [If yes, go to 5. If no, go to 4.]	Yes	No
4	Was the diagnosis of congenital sucrase-isomaltase deficiency confirmed by sucrose hydrogen breath test? [If yes, go to 5. If no, then no further questions.]	Yes	No
5	Does the patient require an amount for coadministration with more than three meals and three snacks per day with the requested drug? [No further questions] [RPh Note: If yes, then deny and enter a partial approval per Quantity Limit Chart.]	Yes	No

Mapping Instructions			
	Yes	**No**	**DENIAL REASONS**
1.	Go to 2	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have congenital sucrase-isomaltase deficiency. Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]
2.	Go to 5	Go to 3	
3.	Go to 5	Go to 4	
4.	Go to 5	Deny	You do not meet the requirements of your plan. Your plan covers this drug when your diagnosis was confirmed by one of the following: - small bowel biopsy - genetic testing - sucrose hydrogen breath test Your request has been denied based on the information we have. [Short Description: No confirmation of diagnosis]
5.	Deny	Approve, 12 months, See Quantity Limit Chart	You have requested more than the maximum quantity allowed by your plan. Your current plan approved criteria cover up to: - 354 mL/30 days of the Sucraid Multiple-Dose Bottle - 300 mL/25 days of the Sucraid Single-Use Containers Your request has been partially approved. You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity]

PRIOR AUTHORIZATION CRITERIA

DRUG CLASS	**NARCOLEPSY AGENTS**
BRAND NAME (generic)	**SUNOSI (solriamfetol)**

Status: CVS Caremark Criteria
Type: Initial Prior Authorization with Quantity Limit

POLICY

FDA-APPROVED INDICATIONS
Sunosi is indicated to improve wakefulness in adult patients with excessive daytime sleepiness associated with narcolepsy or obstructive sleep apnea (OSA).

Limitations of use
Sunosi is not indicated to treat the underlying airway obstruction in OSA. Ensure that the underlying airway obstruction is treated (e.g., with continuous positive airway pressure (CPAP)) for at least one month prior to initiating Sunosi for excessive daytime sleepiness. Modalities to treat the underlying airway obstruction should be continued during treatment with Sunosi. Sunosi is not a substitute for these modalities.

COVERAGE CRITERIA
The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has excessive daytime sleepiness associated with narcolepsy
  AND
  - The request is for continuation of therapy
    AND
  - The patient experienced a decrease in daytime sleepiness with narcolepsy

  OR
  - The requested drug is being prescribed by, or in consultation with, a sleep specialist
    AND
  - The diagnosis has been confirmed by sleep lab evaluation
    AND
  - The patient has experienced an inadequate treatment response to armodafinil OR modafinil
    OR
  - The patient has experienced an intolerance to armodafinil OR modafinil
    OR
  - The patient has a contraindication that would prohibit a trial of ALL of the following: A) armodafinil, B) modafinil

OR

- The patient has excessive daytime sleepiness associated with obstructive sleep apnea (OSA)
  AND
  - The request is for continuation of therapy
    AND
  - The patient has experienced a decrease in daytime sleepiness with obstructive sleep apnea (OSA)
    AND

- The patient is compliant with using continuous positive airway pressure (CPAP) or bilevel positive airway pressure (BIPAP)

OR

- The requested drug is being prescribed by, or in consultation with, a sleep specialist

AND

- The diagnosis has been confirmed by polysomnography

AND

- The patient has been receiving treatment for the underlying airway obstruction (continuous positive airway pressure [CPAP] or bilevel positive airway pressure [BIPAP]) for at least one month

AND

- Treatment with continuous positive airway pressure (CPAP) or bilevel positive airway pressure (BIPAP) will continue

AND

- The patient has experienced an inadequate treatment response to armodafinil OR modafinil

  OR

- The patient has experienced an intolerance to armodafinil OR modafinil

  OR

- The patient has a contraindication that would prohibit a trial of ALL of the following: A) armodafinil, B) modafinil

Quantity Limits Apply. The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.

REFERENCES

1. Sunosi [package insert]. Palo Alto, California: Jazz Pharmaceuticals, Inc.; October 2021.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2022; Accessed February 2, 2022.
3. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed January 28, 2022.
4. American Academy of Sleep Medicine. *International Classification of Sleep Disorders: Diagnostic and Coding Manual*. 3rd edition. Westchester, IL: American Academy of Sleep Medicine; 2014.
5. Morgenthaler TI, Vishesh KK, Brown T, et al. Practice Parameters for the Treatment of Narcolepsy and other Hypersomnias of Central Origin. *Sleep* 2007;30(12):1705-11.
6. Maski K, Trotti LM, Kotagal S, et al. Treatment of central disorders of hypersomnolence: an American Academy of Sleep Medicine clinical practice guideline. *J Clin Sleep Med* 2021;17(9):1881-1893.
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8. Epstein LJ, Kristo D, Strollo PJ et al. Clinical Guidelines for the Evaluation, Management and Long-term Care of Obstructive Sleep Apnea in Adults. *J Clin Sleep Med* 2009:5(3):263-276.
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Reference number
2022-A

SPECIALTY GUIDELINE MANAGEMENT

SUTENT (sunitinib)
sunitinib

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
1. Gastrointestinal Stromal Tumor (GIST)
   Sutent is indicated for the treatment of adult patients with gastrointestinal stromal tumor after disease progression on or intolerance to imatinib mesylate.
2. Advanced Renal Cell Carcinoma (RCC)
   Sutent is indicated for the treatment of adult patients with advanced renal cell carcinoma.
3. Adjuvant Treatment of Renal Cell Carcinoma (RCC)
   Sutent is indicated for the adjuvant treatment of adult patients at high risk of recurrent RCC following nephrectomy.
4. Advanced Pancreatic Neuroendocrine Tumors (pNET)
   Sutent is indicated for the treatment of progressive, well-differentiated pancreatic neuroendocrine tumors in adult patients with unresectable locally advanced or metastatic disease.

B. Compendial Uses
1. Relapsed or stage IV RCC
2. Soft tissue sarcoma subtypes:
   a. Angiosarcoma
   b. Solitary fibrous tumor
   c. Alveolar soft part sarcoma
3. Gastrointestinal stromal tumors
4. Thymic carcinomas
5. Differentiated thyroid carcinoma (papillary, Hürthle cell, or follicular)
6. Medullary thyroid carcinoma
7. Meningioma
8. Recurrent chordoma
9. Lymphoid, myeloid or mixed lineage neoplasms with eosinophilia and FLT3 rearrangement in chronic or blast phase
10. Pheochromocytoma/Paraganglioma

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: Testing or analysis confirming FLT3 rearrangement (if applicable)

III. CRITERIA FOR INITIAL APPROVAL

A. Renal Cell Carcinoma

1. Authorization of 12 months may be granted for treatment of relapsed, advanced, or stage IV renal cell carcinoma as a single agent.

2. Authorization of up to 54 weeks total may be granted for adjuvant treatment of members who are at high risk of recurrent renal cell carcinoma following nephrectomy.

B. Soft Tissue Sarcoma

Authorization of 12 months may be granted for treatment of the following subtypes of soft tissue sarcoma as single-agent therapy: alveolar soft-part sarcoma, angiosarcoma, or solitary fibrous tumor.

C. Gastrointestinal Stromal Tumor (GIST)

Authorization of 12 months may be granted for treatment of gastrointestinal stromal tumor when any of the following criteria are met:

1. The requested medication will be used after failure of imatinib due to disease progression or intolerable side effects as a single agent.
2. The requested medication will be used for treatment of unresectable, recurrent/progressive, or metastatic GIST in combination with everolimus for disease progression after the member has failed at least four FDA-approved therapies (e.g., imatinib, avapritinib, regorafenib and ripretinib).
3. The requested medication will be used for treatment of unresectable succinate dehydrogenase (SDH)-deficient GIST as a single agent.
4. The requested medication will be used for palliation of symptoms if previously tolerated and effective.

D. Pancreatic Neuroendocrine Tumor

Authorization of 12 months may be granted for treatment of pancreatic neuroendocrine tumors as a single agent.

E. Pheochromocytoma/Paraganglioma

Authorization of 12 months may be granted for treatment of locally unresectable or metastatic pheochromocytoma or paraganglioma as a single agent.

F. Thymic Carcinoma

Authorization of 12 months may be granted for treatment of thymic carcinoma with failure or intolerance of one previous chemotherapy regimen as a single agent.

G. Papillary, Hürthle cell, or Follicular Thyroid Carcinoma

Authorization of 12 months may be granted for treatment of progressive and/or symptomatic papillary, Hürthle cell, or follicular thyroid carcinoma not amenable to radioactive iodine (RAI) therapy.

H. Medullary Thyroid Carcinoma

Authorization of 12 months may be granted for treatment of recurrent or metastatic medullary thyroid carcinoma when either of the following criteria are met:

1. Member has a contraindication or intolerance to FDA approved systemic therapy options (e.g., vandetanib [Caprelsa], cabozantinib [Cometriq]); OR
2. Member has disease progression while on FDA approved systemic therapy options (e.g., vandetanib [Caprelsa], cabozantinib [Cometriq]).

I. Meningioma
Authorization of 12 months may be granted for treatment of surgically inaccessible recurrent or progressive meningioma for which radiation is not possible.

J. Chordoma
Authorization of 12 months may be granted for treatment of recurrent chordoma as single-agent therapy.

K. Myeloid/Lymphoid Neoplasms with Eosinophilia
Authorization of 12 months may be granted for treatment of myeloid and/or lymphoid neoplasms with eosinophilia and FLT3 rearrangement in the chronic phase or blast phase.

IV. CONTINUATION OF THERAPY

A. Authorization of 12 months may be granted for continued treatment in members requesting reauthorization when there is no evidence of unacceptable toxicity or disease progression while on the current regimen for the specified indications below:
   1. Relapsed, advanced, or stage IV renal cell carcinoma
   2. Soft tissue sarcoma
   3. Gastrointestinal stromal tumor
   4. Pancreatic neuroendocrine tumor
   5. Thymic carcinoma
   6. Papillary, Hürthle cell, or Follicular thyroid carcinoma
   7. Medullary thyroid carcinoma
   8. Meningioma
   9. Chordoma
   10. Myeloid and/or lymphoid neoplasms with eosinophilia
   11. Pheochromocytoma/Paraganglioma

B. Authorization of up to 54 weeks total may be granted for continued treatment in members requesting reauthorization for adjuvant treatment of renal cell carcinoma when the following criteria are met:
   1. Disease is not recurrent; AND
   2. Member has not exceeded a maximum of nine 6 week cycles.

V. REFERENCES

1. Sutent [package insert]. New York, NY: Pfizer Labs.; August 2021.
2. The NCCN Drugs & Biologics Compendium 2022 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed May 25, 2022.
3. Kaley TJ, Web P, Schiff D, et al. Phase II Trial of Sunitinib for Recurrent and Progressive Atypical and Anaplastic Meningioma. *Neuro Oncol.* 2015:17(1):116-21.

Reference number(s)
2516-A

SPECIALTY GUIDELINE MANAGEMENT

SYMDEKO (tezacaftor/ivacaftor)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Symdeko is indicated for the treatment of cystic fibrosis (CF) in patients age 6 years and older who are homozygous for the *F508del* mutation or who have at least one mutation in the cystic fibrosis transmembrane conductance regulator (*CFTR*) gene that is responsive to tezacaftor/ivacaftor based on *in vitro* data and/or clinical evidence.

If the patient's genotype is unknown, an FDA-cleared CF mutation test should be used to detect the presence of *CFTR* mutation followed by verification with bi-directional sequencing when recommended by the mutation test instructions for use.

All other indications are considered experimental/investigational and are not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: genetic testing report confirming the presence of the appropriate *CFTR* gene mutation.

III. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with a pulmonologist.

IV. CRITERIA FOR INITIAL APPROVAL

Cystic Fibrosis
Authorization of 12 months may be granted for treatment of cystic fibrosis when all of the following criteria are met:
A. Genetic testing was conducted to detect a mutation in the *CFTR* gene.
B. The member is homozygous for the *F508del* mutation, or the member has one of the following mutations in the *CFTR* gene: A120T, A234D, A349V, A455E, A554E, A1006E, A1067T, D110E, D110H, D192G, D443Y, D443Y;G576A;R668C, D579G, D614G, D836Y, D924N, D979V, D1152H, D1270N, E56K, E60K, E92K, E116K, E193K, E403D, E588V, E822K, E831X, F191V, F311del, F311L, F508C, F508C;S1251N, F575Y, F1016S, F1052V, F1074L, F1099L, G126D, G178E, G178R, G194R, G194V, G314E, G551D, G551S, G576A, G576A;R668C, G622D, G970D, G1069R, G1244E, G1249R, G1349D, H939R, H1054D, H1375P, I148T, I175V, I336K, I601F, I618T, I807M, I980K, I1027T, I1139V, I1269N, I1366N, K1060T, L15P, L206W, L320V, L346P, L967S, L997F, L1324P, L1335P, L1480P, M152V, M265R, M952I, M952T,

P5L, P67L, P205S, Q98R, Q237E, Q237H, Q359R, Q1291R, R31L, R74Q, R74W, R74W;D1270N, R74W;V201M, R74W;V201M;D1270N, R75Q, R117C, R117G, R117H, R117L, R117P, R170H, R258G, R334L, R334Q, R347H, R347L, R347P, R352Q, R352W, R553Q, R668C, R751L, R792G, R933G, R1066H, R1070Q, R1070W, R1162L, R1283M, R1283S, S549N, S549R, S589N, S737F, S912L, S945L, S977F, S1159F, S1159P, S1251N, S1255P, T338I, T1036N, T1053I, V201M, V232D, V562I, V754M, V1153E, V1240G, V1293G, W1282R, Y109N, Y161S, Y1014C, Y1032C, 546insCTA, 711+3A→G, 2789+5G→A, 3272-26A→G, 3849+10kbC→T.

C. The member is at least 6 years of age.
D. Symdeko will not be used in combination with other medications containing ivacaftor.

V. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section IV who are experiencing benefit from therapy as evidenced by disease stability or disease improvement (e.g., improvement in FEV1 from baseline).

VI. REFERENCES

1. Symdeko [package insert]. Boston, MA: Vertex Pharmaceuticals Inc.; December 2020.
2. Rowe SM, Daines C, Ringshausen FC, et al. Tezacaftor-Ivacaftor in Residual Function Heterozygotes with Cystic Fibrosis. *N Engl J Med*. 2017;377:2024-2035.
3. Taylor-Cousar JL, Munck A, McKone EF, et al. Tezacaftor–ivacaftor in patients with cystic fibrosis homozygous for Phe508del. *N Engl J Med* 2017;377:2013-2023.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME
(generic)

SYMLINPEN
(pramlintide acetate)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

POLICY

FDA-APPROVED INDICATIONS
Symlin is indicated as an adjunctive treatment in patients with type 1 or type 2 diabetes who use mealtime insulin therapy and who have failed to achieve desired glucose control despite optimal insulin therapy.

COVERAGE CRITERIA
The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has a diagnosis of diabetes mellitus

AND

- The patient has NOT been receiving a stable maintenance dose of the requested drug for at least 3 months **AND**
    - The patient has failed to achieve desired glucose control despite receiving optimal insulin therapy, including mealtime insulin

OR

- The patient has been receiving a stable maintenance dose of the requested drug for at least 3 months **AND**
    - The patient has demonstrated a reduction in A1c (hemoglobin A1c) since starting this therapy

REFERENCES

1. SymlinPen [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; December 2019.
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3. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed June 22, 2022.
4. American Diabetes Association. Standards of Medical Care in Diabetes-2022. Diabetes Care 2022;45(Supplement1):S1-S264.
5. Garber AJ, Handelsman Y, Grunberger G, et al. Consensus Statement by the American Association of Clinical Endocrinologists and American College of Endocrinology on the Comprehensive Type 2 Diabetes Management Algorithm-2020 Executive Summary. Endocr Pract. 2020;26(No 1):107-139.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME
(generic)

SYMPROIC
(naldemedine)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

POLICY

FDA-APPROVED INDICATIONS
Symproic is indicated for the treatment of opioid-induced constipation (OIC) in adult patients with chronic non-cancer pain, including patients with chronic pain related to prior cancer or its treatment who do not require frequent (e.g., weekly) opioid dosage escalation.

COVERAGE CRITERIA
The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for the treatment of opioid-induced constipation (OIC) in an adult patient with chronic non-cancer pain, including chronic pain related to prior cancer or its treatment who does not require frequent (e.g., weekly) opioid dosage escalation

REFERENCES

1. Symproic [package insert]. Raleigh, NC: BioDelivery Sciences International, Inc.; July 2021.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2021; Accessed September 2, 2021.
3. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed September 2, 2021.

Reference number(s)
1640-A

SPECIALTY GUIDELINE MANAGEMENT

Adcirca (tadalafil tablet)
Alyq (tadalafil tablet)
Tadliq (tadalafil oral suspension)
tadalafil tablet

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication
Indicated for the treatment of pulmonary arterial hypertension (PAH) (World Health Organization [WHO] Group 1) to improve exercise ability. Studies establishing effectiveness included predominately patients with New York Heart Association (NYHA) Functional Class II – III symptoms and etiologies of idiopathic or heritable PAH or PAH associated with connective tissue diseases.

B. Compendial Use
Secondary Raynaud's phenomenon

All other indications are considered experimental/investigational and not medically necessary.

II. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with a pulmonologist or cardiologist for the diagnosis of pulmonary arterial hypertension (PAH).

III. CRITERIA FOR INITIAL APPROVAL

A. Pulmonary Arterial Hypertension (PAH)
Authorization of 12 months may be granted for treatment of PAH when ALL of the following criteria are met:
1. Member has PAH defined as WHO Group 1 class of pulmonary hypertension (refer to Appendix).
2. PAH was confirmed by either criterion (i) or criterion (ii) below:
   i. Pretreatment right heart catheterization with all of the following results:
      a. Mean pulmonary arterial pressure (mPAP) > 20 mmHg
      b. Pulmonary capillary wedge pressure (PCWP) ≤ 15 mmHg
      c. Pulmonary vascular resistance (PVR) ≥ 3 Wood units in adult patients or pulmonary vascular resistance index (PVRI) ≥ 3 Wood units x m^2 in pediatric patients
   ii. For infants less than one year of age, PAH was confirmed by Doppler echocardiogram if right heart catheterization cannot be performed.

B. Secondary Raynaud's Phenomenon

Authorization of 12 months may be granted for treatment of secondary Raynaud's phenomenon when the member has had an inadequate response to one of the following medications:

1. Calcium channel blockers
2. Angiotensin II receptor blockers
3. Selective serotonin reuptake inhibitors
4. Alpha blockers
5. Topical nitrates

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for members with an indication listed in Section III who are currently receiving a tadalafil product through a paid pharmacy or medical benefit, and who are experiencing benefit from therapy as evidenced by disease stability or disease improvement.

V. APPENDIX

WHO Classification of Pulmonary Hypertension

1 PAH

1.1 Idiopathic (PAH)
1.2 Heritable PAH
1.3 Drug- and toxin-induced PAH
1.4. PAH associated with:
- 1.4.1 Connective tissue diseases
- 1.4.2 HIV infection
- 1.4.3 Portal hypertension
- 1.4.4 Congenital heart diseases
- 1.4.5 Schistosomiasis

1.5 PAH long-term responders to calcium channel blockers
1.6 PAH with overt features of venous/capillaries (PVOD/PCH) involvement
1.7 Persistent PH of the newborn syndrome

2 PH due to left heart disease

2.1 PH due to heart failure with preserved LVEF
2.2 PH due to heart failure with reduced LVEF
2.3 Valvular heart disease
2.4 Congenital/acquired cardiovascular conditions leading to post-capillary PH

3 PH due to lung diseases and/or hypoxia

3.1 Obstructive lung disease
3.2 Restrictive lung disease
3.3 Other lung disease with mixed restrictive/obstructive pattern
3.4 Hypoxia without lung disease
3.5 Developmental lung disorders

4 PH due to pulmonary artery obstruction

4.1 Chronic thromboembolic PH
4.2 Other pulmonary artery obstructions
- 4.2.1 Sarcoma (high or intermediate grade) or angiosarcoma
- 4.2.2 Other malignant tumors
  - Renal carcinoma
  - Uterine carcinoma

Germ cell tumours of the testis
Other tumours
4.2.3 Non-malignant tumours
Uterine leiomyoma
4.2.4 Arteritis without connective tissue disease
4.2.5 Congenital pulmonary artery stenosis
4.2.6 Parasites
Hydatidosis

5 PH with unclear and/or multifactorial mechanisms

5.1 Hematologic disorders: Chronic hemolytic anemia, myeloproliferative disorders
5.2 Systemic and metabolic disorders: Pulmonary Langerhans cell histiocytosis, Gaucher disease, glycogen storage disease, neurofibromatosis, sarcoidosis
5.3 Others: chronic renal failure with or without hemodialysis, fibrosing mediastinitis
5.4 Complex congenital heart disease

IV. REFERENCES

1. Adcirca [package insert]. Indianapolis, IN: Eli Lilly and Company; September 2020.
2. Tadalafil [package insert]. Bridgewater, NJ: Ajanta Pharma USA Inc.; July 2022.
3. Alyq [package insert]. North Wales, PA: Teva Pharmaceuticals USA, Inc.; September 2021.
4. Tadliq [package insert]. Farmville, NC: CMP Pharma, Inc.; June 2022.
5. IBM Micromedex® DRUGDEX® (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed April 12, 2023.
6. Chin KM, Rubin LJ. Pulmonary arterial hypertension. *J Am Coll Cardiol*. 2008;51(16):1527-1538.
7. McLaughlin VV, Archer SL, Badesch DB, et al. ACCF/AHA 2009 expert consensus document on pulmonary hypertension a report of the American College of Cardiology Foundation Task Force on Expert Consensus Documents and the American Heart Association developed in collaboration with the American College of Chest Physicians, American Thoracic Society, Inc., and the Pulmonary Hypertension Association. *J Am Coll Cardiol*. 2009;53(17):1573-1619.
8. Badesch DB, Champion HC, Gomez-Sanchez MA, et al. Diagnosis and assessment of pulmonary arterial hypertension. *J Am Coll Cardiol.* 2009;54:S55-S66.
9. Rubin LJ; American College of Chest Physicians. Diagnosis and management of pulmonary arterial hypertension: ACCP evidence-based clinical practice guidelines. *Chest*. 2004;126(1 Suppl):7S-10S.
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11. Taichman DB, Ornelas J, Chung L, et al. Pharmacologic therapy for pulmonary arterial hypertension in adults. CHEST guideline and expert panel report. *Chest*. 2014;46(2):449-475.
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15. Simonneau G, Montani D, Celermajer DS, et al. Haemodynamic definitions and updated clinical classification of pulmonary hypertension. *Eur Respir J.* 2019;53:1801913; doi:10.1183/13993003.01913-2018.
16. Hughes M, Ong VH, Anderson ME, et al. Consensus best practice pathway of the UK Scleroderma Study Group: digital vasculopathy in systemic sclerosis. *Rheumatology*. 2015;54:2015-2024.

17. Roustit M, Blaise S, Allanore Y, et al. Phosphodiesterase-5 inhibitors for the treatment of secondary Raynaud's phenomenon: systematic review and meta-analysis of randomized trials. *Ann Rheum Dis*. 2013;72(10):1696-1699.
18. Walker KM, Pope J, et al. Treatment of systemic sclerosis complications: what to use when first-line treatment fails – a consensus of systemic sclerosis experts. *Semin Arthritis Rheum*. 2012;42(1):42-55.

Reference number(s)
1683-A

SPECIALTY GUIDELINE MANAGEMENT

TAFINLAR (dabrafenib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met, and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
1. Tafinlar is indicated as a single agent for the treatment of patients with unresectable or metastatic melanoma with BRAF V600E mutation as detected by an FDA-approved test.
2. Tafinlar is indicated, in combination with trametinib, for the treatment of patients with unresectable or metastatic melanoma with BRAF V600E or V600K mutations as detected by an FDA-approved test.
3. Tafinlar is indicated, in combination with trametinib, for the adjuvant treatment of patients with melanoma with BRAF V600E or V600K mutations as detected by an FDA-approved test, and involvement of lymph node(s), following complete resection.
4. Tafinlar is indicated, in combination with trametinib, for the treatment of patients with metastatic non-small cell lung cancer (NSCLC) with BRAF V600E mutation as detected by an FDA-approved test.
5. Tafinlar is indicated, in combination with trametinib, for the treatment of patients with locally advanced or metastatic anaplastic thyroid cancer (ATC) with BRAF V600E mutation and no satisfactory locoregional treatment options.
6. Tafinlar is indicated, in combination with trametinib, for the treatment of adult and pediatric patients 6 years of age and older with unresectable or metastatic solid tumors with BRAF V600E mutation who have progressed following prior treatment and have no satisfactory alternative treatment options.

   Limitations of Use: Tafinlar is not indicated for treatment of patients with colorectal cancer because of known intrinsic resistance to BRAF inhibition. Tafinlar is not indicated for treatment of patients with wild-type BRAF solid tumors.

B. Compendial Uses
1. Melanoma, BRAF V600 activating mutation-positive
2. Brain metastases from melanoma
3. NSCLC, BRAF V600E
4. Glioma, BRAF V600 activating mutation-positive
5. Meningioma, BRAF V600 activating mutation-positive
6. Astrocytoma, BRAF V600 activating mutation-positive
7. Thyroid Carcinoma
   a. Anaplastic carcinoma
   b. Papillary carcinoma
   c. Follicular carcinoma
   d. Hűrthle cell carcinoma
8. Hepatobiliary Cancers
   a. Gallbladder Cancer
   b. Extrahepatic Cholangiocarcinoma
   c. Intrahepatic Cholangiocarcinoma

9. Histiocytic Neoplasms
    a. Erdheim-Chester Disease
    b. Langerhans Cell Histiocytosis
10. Ovarian cancer/fallopian tube cancer/primary peritoneal cancer

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of BRAF mutation documentation is necessary to initiate prior authorization review.

III. CRITERIA FOR INITIAL APPROVAL

A. Cutaneous melanoma
Authorization of 12 months may be granted for treatment of melanoma with a BRAF V600 activating mutation (e.g., V600E or V600K) in any of the following settings:
1. Unresectable or metastatic cutaneous melanoma as a single agent or in combination with trametinib (Mekinist).
2. Brain metastases from melanoma in combination with trametinib (Mekinist).
3. Adjuvant treatment of resected stage III cutaneous melanoma in combination with trametinib (Mekinist).
4. Limited resectable local satellite/in-transit recurrent disease in combination with trametinib (Mekinist).

B. Non-Small Cell Lung Cancer (NSCLC)
Authorization of 12 months may be granted for treatment of BRAF V600E mutation-positive advanced or metastatic NSCLC as a single agent or in combination with trametinib (Mekinist).

C. Central Nervous System Cancer
Authorization of 12 months may be granted for treatment of BRAF V600 mutation-positive gliomas, meningiomas, or astrocytomas.

D. Thyroid Cancer
Authorization of 12 months may be granted for treatment of thyroid carcinoma when any of the following criteria are met:
1. Member has progressive and/or symptomatic BRAF-positive follicular, Hürthle cell, or papillary thyroid carcinoma that is not amenable to radioactive iodine (RAI) therapy.
2. Member has BRAF V600E mutation positive locally advanced, metastatic, or borderline resectable anaplastic thyroid carcinoma and the requested medication will be used in combination with trametinib (Mekinist).

E. Hepatobiliary Cancers
Authorization of 12 months may be granted for subsequent treatment of progressive BRAF-V600E mutated unresectable or metastatic gallbladder cancer, extrahepatic cholangiocarcinoma, or intrahepatic cholangiocarcinoma in combination with trametinib (Mekinist).

F. Histiocytic Neoplasms
Authorization of 12 months may be granted for treatment of BRAF V600E mutation-positive Erdheim-Chester disease or Langerhans cell histiocytosis as a single agent.

G. Solid Tumors

Authorization of 12 months may be granted for treatment of unresectable or metastatic solid tumors when all of the following criteria are met:

1. The tumors are BRAF V600E mutation positive.
2. The disease has progressed following prior treatment and there are no satisfactory alternative treatment options.
3. The member is 6 years of age or older.
4. The requested medication will not be used for the treatment of colorectal cancer.
5. The requested medication will be used in combination with trametinib (Mekinist).

H. Ovarian Cancer, Fallopian Tube Cancer, and Primary Peritoneal Cancer

Authorization of 12 months may be granted for treatment of persistent or recurrent BRAF-V600E positive epithelial ovarian cancer, fallopian tube cancer, primary peritoneal cancer, carcinosarcoma (malignant mixed Mullerian tumors), clear cell carcinoma of the ovary, grade 1 endometrioid carcinoma, low-grade serious carcinoma/ovarian borderline epithelial tumor (low malignant potential), or mucinous carcinoma of the ovary, in combination with trametinib (Mekinist).

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III when there is no evidence of unacceptable toxicity or disease progression or recurrence while on the current regimen. For patients using Tafinlar for adjuvant treatment of cutaneous melanoma, only 12 months of therapy total will be approved.

V. REFERENCES

1. Tafinlar [package insert]. East Hanover, NJ: Novartis Pharmaceutical Corporation; June 2022.
2. The NCCN Drugs & Biologics Compendium® © 2022 National Comprehensive Cancer Network, Inc. Available at: https://www.nccn.org. Accessed November 17, 2022.
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Reference number(s)
1663-A

SPECIALTY GUIDELINE MANAGEMENT

TAGRISSO (osimertinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. Tagrisso is indicated for the first-line treatment of adult patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 L858R mutations, as detected by an FDA-approved test.
   2. Tagrisso is indicated for the treatment of adult patients with metastatic epidermal growth factor receptor (EGFR) T790M mutation-positive non-small cell lung cancer (NSCLC), as detected by an FDA-approved test, whose disease has progressed on or after EGFR tyrosine kinase inhibitor (TKI) therapy.
   3. Tagrisso is indicated for adjuvant therapy after tumor resection in adult patients with non-small cell lung cancer (NSCLC) whose tumors have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 L858R mutations, as detected by and FDA approved test.

B. Compendial Uses
   1. EGFR mutation-positive recurrent, advanced or metastatic NSCLC.
   2. Adjuvant treatment of completely resected stage IB-IIIA EGFR-mutation positive NSCLC.
   3. Brain metastases from sensitizing EGFR mutation-positive NSCLC.
   4. Leptomeningeal metastases from EGFR mutation-positive NSCLC.

All other indications are considered experimental/investigational and not medically necessary.

II. REQUIRED DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: EGFR mutation testing results.

III. CRITERIA FOR INITIAL APPROVAL

Non-small cell lung cancer (NSCLC)

A. Authorization of 12 months may be granted for treatment of recurrent, advanced, or metastatic NSCLC (including brain and/or leptomeningeal metastases from NSCLC) in members with sensitizing EGFR mutation-positive disease as a single agent.
B. Authorization of 12 months may be granted for the adjuvant treatment of NSCLC following complete tumor resection in members with EGFR mutation-positive disease as a single agent.

IV. CONTINUATION OF THERAPY

Non-small cell lung cancer (NSCLC)

A. Authorization of 12 months (up to a maximum duration of 3 years) may be granted for continued treatment in members requesting reauthorization for adjuvant treatment of NSCLC when there is no evidence of unacceptable toxicity or disease recurrence while on the current regimen.

B. Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for recurrent, advanced, or metastatic NSCLC when there is no evidence of unacceptable toxicity while on the current regimen.

V. REFERENCES

1. Tagrisso [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; January 2022.
2. The NCCN Drugs & Biologics Compendium® © 2022 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed March 4, 2022.

Reference number(s)
2668-A

SPECIALTY GUIDELINE MANAGEMENT

TAKHZYRO (lanadelumab-flyo)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Takhzyro is indicated for prophylaxis to prevent attacks of hereditary angioedema (HAE) in adult and pediatric patients 12 years of age and older.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
A. For initial authorization, the following should be documented:
   1. C1 inhibitor functional and antigenic protein levels
   2. F12, angiopoietin-1, plasminogen, kininogen-1 (KNG1), heparan sulfate-glucosamine 3-O-sulfotransferase 6 (HS3ST6), or myoferlin (MYOF) gene mutation testing, if applicable
   3. Chart notes confirming family history of angioedema and the angioedema was refractory to a trial of high-dose antihistamine therapy, if applicable
B. For continuation of therapy, chart notes demonstrating a reduction in frequency of attacks

III. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with a prescriber who specializes in the management of HAE.

IV. CRITERIA FOR INITIAL APPROVAL

Hereditary angioedema (HAE)
Authorization of 6 months may be granted for prevention of HAE attacks when the requested medication will not be used in combination with any other medication used for the prophylaxis of HAE attacks and either of the following criteria is met at the time of diagnosis:
A. Member has C1 inhibitor deficiency or dysfunction as confirmed by laboratory testing and meets one of the following criteria:
   1. C1 inhibitor (C1-INH) antigenic level below the lower limit of normal as defined by the laboratory performing the test, or
   2. Normal C1-INH antigenic level and a low C1-INH functional level (functional C1-INH less than 50% or C1-INH functional level below the lower limit of normal as defined by the laboratory performing the test).

B. Member has normal C1 inhibitor as confirmed by laboratory testing and meets one of the following criteria:
   1. Member has an F12, angiopoietin-1, plasminogen, kininogen-1 (KNG1), heparan sulfate-glucosamine 3-O-sulfotransferase 6 (HS3ST6), or myoferlin (MYOF) gene mutation as confirmed by genetic testing, or
   2. Member has a documented family history of angioedema and the angioedema was refractory to a trial of high-dose antihistamine therapy (i.e., cetirizine at 40 mg per day or the equivalent) for at least one month.

V. CONTINUATION OF THERAPY

Authorization of 6 months may be granted for continuation of therapy when all of the following criteria are met:
A. Member meets the criteria for initial approval.
B. Member has experienced a significant reduction in frequency of attacks (e.g., ≥ 50%) since starting treatment.
C. Member has reduced the use of medications to treat acute attacks since starting treatment.
D. The requested drug is being dosed every 4 weeks or dosing every 4 weeks has been considered if the member is well-controlled on therapy for more than 6 months.

VI. REFERENCES

1. Takhzyro [package insert]. Lexington, MA: Dyax Corp., a Takeda company; February 2022.
2. Maurer M, Magerl M, Ansotegui I, et al. The international WAO/EAACI guideline for the management of hereditary angioedema – the 2021 revision and update. *Allergy*. 2022 Jan 10. doi: 10.1111/all. 15214. Online ahead of print.
3. Henao MP, Kraschnewski J, Kelbel T, Craig T. Diagnosis and screening of patients with hereditary angioedema in primary care. *Therapeutics and Clin Risk Management.* 2016; 12: 701-711.
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5. Busse PJ, Christiansen, SC, Riedl MA, et al. US HAEA Medical Advisory Board 2020 Guidelines for the Management of Hereditary Angioedema. *J Allergy Clin Immunol: In Practice.* 2021 Jan;9(1):132-150.e3.
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Reference number(s)
2013-A

SPECIALTY GUIDELINE MANAGEMENT

TALTZ (ixekizumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

1. Moderate to severe plaque psoriasis in patients 6 years of age and older who are candidates for systemic therapy or phototherapy
2. Adult patients with active psoriatic arthritis
3. Adult patients with active ankylosing spondylitis
4. Adult patients with active non-radiographic axial spondyloarthritis (nr-axSpA) with objective signs of inflammation

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

A. Plaque psoriasis
   1. Initial requests:
      i. Chart notes or medical record documentation of affected area(s) and body surface area (BSA) affected.
      ii. Chart notes, medical record documentation, or claims history supporting previous medications tried (if applicable), including response to therapy. If therapy is not advisable, documentation of clinical reason to avoid therapy.
   2. Continuation requests: Chart notes or medical record documentation of decreased body surface area (BSA) affected and/or improvement in signs and symptoms.

B. Psoriatic arthritis: For continuation requests: Chart notes or medical record documentation supporting positive clinical response.

C. Ankylosing spondylitis and axial spondyloarthritis:
   1. Initial requests: Chart notes, medical record documentation, or claims history supporting previous medications tried (if applicable), including response to therapy. If therapy is not advisable, documentation of clinical reason to avoid therapy.
   2. Continuation requests: Chart notes or medical record documentation supporting positive clinical response.

III. CRITERIA FOR INITIAL APPROVAL

A. Moderate to severe plaque psoriasis (PsO)

1. Authorization of 12 months may be granted for members who have previously received Otezla or a biologic indicated for the treatment of moderate to severe plaque psoriasis.

2. Authorization of 12 months may be granted for treatment of moderate to severe plaque psoriasis in members when any of the following criteria is met:
   a. Crucial body areas (e.g., hands, feet, face, neck, scalp, genitals/groin, intertriginous areas) are affected.
   b. At least 10% of the body surface area (BSA) is affected.
   c. At least 3% of body surface area (BSA) is affected and the member meets any of the following criteria:
      i. Member has had an inadequate response or intolerance to either phototherapy (e.g., UVB, PUVA) or pharmacologic treatment with methotrexate, cyclosporine or acitretin.
      ii. Member has a clinical reason to avoid pharmacologic treatment with methotrexate, cyclosporine and acitretin (see Appendix).

B. Active psoriatic arthritis (PsA)

Authorization of 12 months may be granted for treatment of active psoriatic arthritis.

C. Active ankylosing spondylitis (AS) and active axial spondyloarthritis

1. Authorization of 12 months may be granted for members who have previously received a biologic indicated for active ankylosing spondylitis or active axial spondyloarthritis.

2. Authorization of 12 months may be granted for treatment of active ankylosing spondylitis or active axial spondyloarthritis when any of the following criteria is met:
   a. Member has experienced an inadequate response to at least two non-steroidal anti-inflammatory drugs (NSAIDs).
   b. Member has an intolerance or contraindication to two or more NSAIDs.

IV. CONTINUATION OF THERAPY

A. Moderate to severe plaque psoriasis (PsO)

Authorization of 12 months may be granted for all members (including new members) who are using the requested medication for moderate to severe plaque psoriasis and who achieve or maintain positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition when any of the following is met:

1. Reduction in body surface area (BSA) affected from baseline
2. Improvement in signs and symptoms from baseline (e.g., itching, redness, flaking, scaling, burning, cracking, pain)

B. Active psoriatic arthritis (PsA)

Authorization of 12 months may be granted for all members (including new members) who are using the requested medication for active psoriatic arthritis and who achieve or maintain positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition when there is improvement in any of the following from baseline:

1. Number of swollen joints
2. Number of tender joints
3. Dactylitis
4. Enthesitis
5. Skin and/or nail involvement

C. Active ankylosing spondylitis (AS) and active axial spondyloarthritis

Authorization of 12 months may be granted for all members (including new members) who are using the requested medication for active ankylosing spondylitis or active axial spondyloarthritis and who achieve or maintain positive clinical response with the requested medication as evidenced by low disease activity or improvement in signs and symptoms of the condition when there is improvement in any of the following from baseline:

1. Functional status
2. Total spinal pain
3. Inflammation (e.g., morning stiffness)

V. OTHER

For all indications: Member has had a documented negative TB test (which can include a tuberculosis skin test [PPD], an interferon-release assay [IGRA], or a chest x-ray)* within 6 months of initiating therapy for persons who are naïve to biologic DMARDs or targeted synthetic DMARDs associated with an increased risk of TB.

* If the screening testing for TB is positive, there must be further testing to confirm there is no active disease. Do not administer the requested medication to members with active TB infection. If there is latent disease, TB treatment must be started before initiation of the requested medication.

For all indications: Member cannot use the requested medication concomitantly with any other biologic DMARD or targeted synthetic DMARD.

VI. DOSAGE AND ADMINISTRATION

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

VII. APPENDIX

Examples of Clinical Reasons to Avoid Pharmacologic Treatment with Methotrexate, Cyclosporine or Acitretin

1. Clinical diagnosis of alcohol use disorder, alcoholic liver disease or other chronic liver disease
2. Breastfeeding
3. Drug interaction
4. Cannot be used due to risk of treatment-related toxicity
5. Pregnancy or currently planning pregnancy
6. Significant comorbidity prohibits use of systemic agents (examples include liver or kidney disease, blood dyscrasias, uncontrolled hypertension)

VIII. REFERENCES

1. Taltz [package insert]. Indianapolis, IN: Eli Lilly and Company; November 2021.
2. Menter A, Korman NJ, Elmets CA, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis. Section 6: Guidelines of care for the treatment of psoriasis and psoriatic arthritis: case-based presentations and evidence-based conclusions. *J Am Acad Dermatol*. 2011;65(1):137-174.

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6. McInnes IB, Mease PJ, Kirkham B, et al. Secukinumab, a human anti-interleukin-17A monoclonal antibody, in patients with psoriatic arthritis (FUTURE 2): a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet*. 2015;386(9999):1137-46.
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9. Braun J, van den Berg R, Baraliakos X, et al. 2010 update of the ASAS/EULAR recommendations for the management of ankylosing spondylitis. *Ann Rheum Dis* 2011;70:896–904.
10. Ward MM, Deodhar A, Gensler LS, et al. 2019 Update of the American College of Rheumatology/Spondylitis Association of America/Spondyloarthritis Research and Treatment Network Recommendations for the treatment of ankylosing spondylitis and nonradiographic axial spondyloarthritis. Arthritis Rheumatol. 2019;71(10):1285-1299.
11. Singh JA, Guyatt G, Ogdie A, et al. 2018 American College of Rheumatology/National Psoriasis Foundation Guideline for the Treatment of Psoriatic Arthritis. *Arthritis Rheum.* 2018;71:5-32.
12. Gossec L, Baraliakos X, Kerschbaumer A, et al. European League Against Rheumatism (EULAR) recommendations for the management of psoriatic arthritis with pharmacological therapies: 2019 update. *Ann Rheum Dis*. 2020;79(6):700-712.

Reference number(s)
2782-A

SPECIALTY GUIDELINE MANAGEMENT

TALZENNA (talazoparib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. Breast Cancer
      Talzenna is indicated as a single agent for the treatment of adult patients with deleterious or suspected deleterious germline breast cancer susceptibility gene (BRCA)-mutated (*gBRCAm*) human epidermal growth factor receptor 2 (HER2)-negative locally advanced or metastatic breast cancer. Select patients for therapy based on an FDA-approved companion diagnostic for Talzenna.
   2. Prostate Cancer
      Talzenna is indicated in combination with enzalutamide for the treatment of adult patients with homologous recombination repair (HRR) gene-mutated metastatic castration-resistant prostate cancer (mCRPC).

B. Compendial Uses
   1. Human epidermal growth factor receptor 2 (HER2)-negative, BRCA 1/2-germline mutated breast cancer
   2. HER2-positive BRCA 1/2-germline mutated breast cancer

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: BRCA mutation or HRR gene testing results.

III. CRITERIA FOR INITIAL APPROVAL

1. Breast Cancer
Authorization of 12 months may be granted for treatment of breast cancer with no response to preoperative systemic therapy, or for locally advanced, recurrent, or metastatic breast cancer as a single agent in members with deleterious or suspected deleterious germline BRCA mutations.

2. Metastatic Castration-Resistant Prostate Cancer
Authorization of 12 months may be granted for treatment of metastatic castration-resistant prostate cancer when all of the following criteria are met:
   i. The member has homologous recombination repair (HRR)-gene mutation which includes ATM, ATR, BRCA1, BRCA2, CDK12, CHEK2, FANCA, MLH1, MRE11A, NBN, PALB2, or RAD51C

ii. The requested medication will be used in combination with enzalutatmide (Xtandi)
iii. The member has had a bilateral orchiectomy or will be using the requested medication in combination with a gonadotropin-releasing hormone (GnRH) analog.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

V. REFERENCES

1. Talzenna [package insert]. New York, NY: Pfizer Inc.; June 2023.
2. The NCCN Drugs & Biologics Compendium 2022 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed December 6, 2022.

Reference number
1793-A

SPECIALTY GUIDELINE MANAGEMENT

TASIGNA (nilotinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. Adult patients and pediatric patients greater than or equal to 1 year of age with newly diagnosed Philadelphia chromosome positive chronic myeloid leukemia (Ph+ CML) in chronic phase
   2. Adult patients with chronic phase and accelerated phase Ph+ CML resistant or intolerant to prior therapy that included imatinib
   3. Pediatric patients greater than or equal to 1 year of age with chronic phase and accelerated phase Ph+ CML with resistance or intolerance to prior tyrosine-kinase inhibitor (TKI) therapy.

B. Compendial Uses
   1. Primary treatment of advanced phase CML (accelerated phase or blast phase)
   2. Follow-up therapy for CML patients after hematopoietic stem cell transplant (HSCT)
   3. Ph+ acute lymphoblastic leukemia or lymphoblastic lymphoma (Ph+ ALL/LL)
   4. Maintenance therapy for Ph+ ALL/LL patients after HSCT
   5. Gastrointestinal stromal tumor (GIST)
   6. Myeloid/lymphoid neoplasms with eosinophilia and ABL1 rearrangement in chronic phase
   7. Lymphoid, myeloid or mixed lineage neoplasms with eosinophilia and ABL1 rearrangement in blast phase
   8. Pigmented Villonodular Synovitis/Tenosynovial Giant Cell Tumor (PVNS/TGCT)

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

The following information is necessary to initiate the prior authorization review:
A. For treatment of CML or Ph+ ALL/LL: results of cytogenetic and/or molecular testing for detection of the Ph chromosome or the BCR-ABL gene
B. For members requesting initiation of therapy with the requested medication for treatment of CML or ALL/LL after experiencing resistance to prior tyrosine kinase inhibitor (TKI) therapy: results of BCR-ABL1 mutation testing for T315I, Y253H, E255K/V, F359V/C/I, and G250E mutations, where applicable
C. For members requesting initiation of therapy with the requested medication for treatment of myeloid and/or lymphoid neoplasms with eosinophilia: results of testing or analysis confirming ABL1 rearrangement

III. CRITERIA FOR INITIAL APPROVAL

A. Chronic Myeloid Leukemia (CML)

Authorization of 7 months may be granted for treatment of CML that has been confirmed by detection of the Ph chromosome or BCR-ABL gene by cytogenetic and/or molecular testing when any of the following criteria are met:

1. Member has not received prior therapy with a TKI (e.g., bosutinib, dasatinib, imatinib, ponatinib)
2. Member experienced toxicity or intolerance to prior therapy with a TKI
3. Member experienced resistance to prior therapy with a TKI and results of BCR-ABL1 mutational testing are negative for all of the following: T315I, Y253H, E255K/V, F359V/C/I
4. Member has received HSCT for CML and results of BCR-ABL1 mutational testing are negative for all of the following: T315I, Y253H, E255K/V, F359V/C/I

B. Ph+ Acute Lymphoblastic Leukemia (ALL)/Lymphoblastic Lymphoma (LL)

Authorization of 12 months may be granted for treatment of Ph+ ALL/LL that has been confirmed by detection of the Ph chromosome or BCR-ABL gene by cytogenetic and/or molecular testing when any of the following criteria are met:

1. Member has not received prior therapy with a TKI (e.g., bosutinib, dasatinib, imatinib, ponatinib)
2. Member experienced toxicity or intolerance to prior therapy with a TKI
3. Member experienced resistance to prior therapy with a TKI and results of BCR-ABL1 mutational testing are negative for all of the following: T315I, Y253H, E255K/V, F359V/C/I, and G250E
4. Member has received HSCT for Ph+ ALL/LL and results of BCR-ABL1 mutational testing are negative for all of the following: T315I, Y253H, E255K/V, F359V/C/I, and G250E

C. Gastrointestinal Stromal Tumor (GIST)

Authorization of 12 months may be granted for treatment of GIST when either of the following criteria are met:

1. The requested medication will be used as a single agent for unresectable, recurrent/progressive, or metastatic disease and the member has failed at least four FDA-approved therapies (e.g., imatinib, sunitinib, regorafenib, ripretinib)
2. The requested medication will be used for palliation of symptoms if previously tolerated and effective

D. Myeloid/Lymphoid Neoplasms with Eosinophilia

Authorization of 12 months may be granted for treatment of myeloid and/or lymphoid neoplasms with eosinophilia and ABL1 rearrangement in the chronic phase or blast phase.

E. Pigmented Villonodular Synovitis/Tenosynovial Giant Cell Tumor (PVNS/TGCT)

Authorization of 12 months may be granted for the treatment of pigmented villonodular synovitis (PVNS) or tenosynovial giant cell tumor (TGCT) as a single agent.

IV. CONTINUATION OF THERAPY

A. CML

Authorization may be granted for continued treatment of CML that has been confirmed by detection of Ph chromosome or BCR-ABL gene by cytogenetic and/ or molecular testing when either of the following criteria is met:

1. Authorization of 12 months may be granted when any of the following criteria is met:
   a. BCR-ABL1 is less than or equal to 10% and there is no evidence of disease progression or unacceptable toxicity while on the current regimen for members who have been receiving treatment with the requested medication for 6 months or greater
   b. Member has received HSCT and there is no evidence of unacceptable toxicity or disease progression while on the current regimen

2. Authorization of up to 7 months may be granted when the member has completed less than 6 months of therapy with the requested medication.

B. Ph+ ALL/LL

Authorization of 12 months may be granted for continued treatment of ALL/LL when there is no evidence of unacceptable toxicity or disease progression while on the current regimen and either of the following criteria is met:

1. Member has Ph+ ALL/LL that has been confirmed by detection of Ph chromosome or BCR-ABL gene by cytogenetic and/ or molecular testing
2. Member has received HSCT for ALL/LL

C. GIST, Myeloid/Lymphoid Neoplasms with Eosinophilia, or PVNS/TGCT

Authorization of 12 months may be granted for continued treatment of GIST, myeloid/lymphoid neoplasms with eosinophilia, or PVNS/TGCT when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

V. REFERENCES

1. Tasigna [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; September 2021.
2. The NCCN Drugs & Biologics Compendium® © 2022 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed April 13, 2022.
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4. NCCN Clinical Practice Guidelines in Oncology® Acute Lymphoblastic Leukemia (Version 1.2022). © 2022 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed April 13, 2022.
5. Micromedex Solutions [database online]. Ann Arbor, MI: Truven Health Analytics, Inc. Updated periodically. Available at: https://www.micromedexsolutions.com [available with subscription]. Accessed April 14, 2022.

Reference number(s)
2560-A

SPECIALTY GUIDELINE MANAGEMENT

TAVALISSE (fostamatinib disodium hexahydrate)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Treatment of thrombocytopenia in adult patients with chronic immune thrombocytopenia (ITP) who have had an insufficient response to a previous treatment.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: pretreatment and current platelet counts

III. EXCLUSIONS

Coverage will not be provided for members with the following exclusion: concomitant use of Tavalisse with thrombopoietin receptor agonists (e.g., Promacta, Nplate, Doptelet, Mulpleta)

IV. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with a hematologist.

V. CRITERIA FOR INITIAL APPROVAL

Chronic immune thrombocytopenia (ITP)
Authorization of 12 weeks may be granted to members with chronic ITP who meet all of the following criteria:
A. Inadequate response or intolerance to prior therapy (for example, corticosteroids or immunoglobulins).
B. Untransfused platelet count at any point prior to the initiation of the requested medication is less than $30x10^9$/L OR $30x10^9$/L to $50x10^9$/L with symptomatic bleeding (e.g., significant mucous membrane bleeding, gastrointestinal bleeding or trauma) or risk factors for bleeding (see Section VI).

VI. CONTINUATION OF THERAPY

Chronic immune thrombocytopenia (ITP)

A. Authorization of 3 months may be granted to members with current platelet count less than $50x10^9$/L for whom the platelet count is not sufficient to prevent clinically important bleeding and who have not received a maximal Tavalisse dose for at least 8 weeks.
B. Authorization of 12 months may be granted to members with current platelet count less than $50x10^9$/L for whom the current platelet count is sufficient to prevent clinically important bleeding.
C. Authorization of 12 months may be granted to members with current platelet count of $50x10^9$/L to $200x10^9$/L.
D. Authorization of 12 months may be granted to members with current platelet count greater than $200x10^9$/L to less than or equal to $400x10^9$/L for whom Tavalisse dosing will be adjusted to achieve a platelet count sufficient to avoid clinically important bleeding.

VII. APPENDIX

Examples of risk factors for bleeding (not all inclusive)

- Undergoing a medical or dental procedure where blood loss is anticipated
- Comorbidity (e.g., peptic ulcer disease, hypertension)
- Mandated anticoagulation therapy
- Profession (e.g., construction worker) or lifestyle (e.g., plays contact sports) that predisposes patient to trauma

VIII. REFERENCES

1. Tavalisse [package insert]. South San Francisco, CA: Rigel Pharmaceuticals, Inc.; November 2020.
2. Nuenert C, Terrel DR, Arnold DM, et al. American Society of Hematology 2019 guidelines for immune thrombocytopenia. *Blood Adv* 2019;3(23):3829–3866.
3. Provan D, Arnold DM, Bussel JB, et al. Updated international consensus report on the investigation and management of primary immune thrombocytopenia. *Blood Adv* 2019;3(22): 3780–3817.
4. Rodeghiero F, Stasi R, Gernsheimer T, et al. Standardization of terminology, definitions and outcome criteria in immune thrombocytopenic purpura of adults and children: report from an international working group. *Blood*. 2009;113(11):2386-2393.
5. Bussel J, Arnold DM, Grossbard E, et al. Fostamatinib for the treatment of adult chronic and persistent immune thrombocytopenia: Results of two, phase III, randomized placebo-controlled trials. *Am J Hematol.* 2018; published online: https://doi.org/10.1002/ajh.25125.

PRIOR AUTHORIZATION CRITERIA

DRUG CLASS	**RETINOID (TOPICAL)**
BRAND NAME (generic)	**TAZORAC (ALL TOPICAL) (tazarotene)**

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

POLICY

FDA-APPROVED INDICATIONS

Tazorac (tazarotene) Cream
Tazorac Cream 0.05% and 0.1% are indicated for the topical treatment of patients with plaque psoriasis.
Tazorac Cream 0.1% is also indicated for the topical treatment of patients with acne vulgaris.

Tazorac (tazarotene) Gel
Tazorac Gel 0.05% and 0.1% are indicated for the topical treatment of patients with plaque psoriasis of up to 20% body surface area involvement.
Tazorac Gel 0.1% is also indicated for the topical treatment of patients with facial acne vulgaris of mild to moderate severity.
The efficacy of Tazorac Gel in the treatment of acne previously treated with other retinoids or resistant to oral antibiotics has not been established.

Limitations of Use
The safety of Tazorac Gel use on more than 20% body surface area has not been established in psoriasis or acne.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has a diagnosis of acne vulgaris

OR

- The requested drug is being prescribed for plaque psoriasis to treat less than or equal to 20 percent of the patient's body surface area
  AND
- The patient has experienced an inadequate treatment response to at least one topical corticosteroid
  [Note: The patient may continue to use a corticosteroid product (e.g., clobetasol, fluocinonide, mometasone, triamcinolone, etc.).]
  OR
- The patient has experienced an intolerance to at least one topical corticosteroid
  OR
- The patient has a contraindication that would prohibit a trial of topical corticosteroids

REFERENCES

1. Tazorac Cream [package insert]. Exton, PA: Almirall, LLC.; August 2019.
2. Tazorac Gel [package insert]. Exton, PA: Almirall, LLC; August 2019.

3. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, Ohio: UpToDate, Inc.; 2021; Accessed February 16, 2022.
4. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed February 16, 2022.
5. Elmets C, Korman N, Prater E, et al. Joint AAD-NPF Guidelines of care for the management and treatment of psoriasis with topical therapies and alternative medicine modalities for psoriasis severity measures. *J Am Acad Dermatol* 2021; 84:432-70.
6. Zaenglein AL, Pathy AL, Schlosser BJ, et al. Guidelines of care for the management of acne vulgaris. *J Am Acad Dermatol*. 2016; 74:945-73.

Reference number(s)
3502-A

Specialty Guideline Management

TAZVERIK (tazemetostat)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
1. Tazverik is indicated for the treatment of adults and pediatric patients aged 16 years and older with metastatic or locally advanced epithelioid sarcoma not eligible for complete resection.
2. Tazverik is indicated for the treatment of adult patients with relapsed or refractory (R/R) follicular lymphoma (FL) whose tumors are positive for an EZH2 mutation as detected by an FDA-approved test and who have received at least 2 prior systemic therapies.
3. Tazverik is indicated for the treatment of adult patients with R/R FL who have no satisfactory alternative treatment options.

B. Compendial Use
Follicular Lymphoma- Relapsed/Refractory disease irrespective of EZH2 mutation

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Epithelioid Sarcoma
Authorization of 12 months may be granted for the treatment of metastatic or locally advanced epithelioid sarcoma as a single agent when the member is 16 years of age or older and the disease is not eligible for complete resection.

B. Follicular Lymphoma
Authorization of 12 months may be granted for the treatment of relapsed or refractory follicular lymphoma when the member is 18 years of age or older and either of the following criteria is met:
1. The member has received at least 2 prior therapies
2. The member does not have any satisfactory alternative treatment options

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

IV. REFERENCES

1. Tazverik [package insert]. Cambridge, MA: Epizyme, Inc.; July 2020.

2. The NCCN Drugs & Biologics Compendium® © 2023 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed January 31, 2023.

PRIOR AUTHORIZATION CRITERIA

DRUG CLASS	**TESTOSTERONE PRODUCTS – ORAL**
BRAND NAME (generic)	
	METHITEST (methyltestosterone oral tablet)
	(methyltestosterone oral capsule)
Status: CVS Caremark Criteria	
Type: Initial Prior Authorization	

POLICY

FDA-APPROVED INDICATIONS

Males

Androgens are indicated for replacement therapy in conditions associated with deficiency or absence of endogenous testosterone:

Primary hypogonadism (congenital or acquired) - testicular failure due to cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, or orchidectomy.

Hypogonadotropic hypogonadism (congenital or acquired) - gonadotropin or luteinizing hormone-releasing hormone (LHRH) deficiency, or pituitary-hypothalamic injury from tumors, trauma, or radiation. (Appropriate adrenal cortical and thyroid hormone replacement therapy are still necessary, however, and are actually of primary importance.)

If the above conditions occur prior to puberty, androgen replacement therapy will be needed during the adolescent years for development of secondary sexual characteristics. Prolonged androgen treatment will be required to maintain sexual characteristics in these and other males who develop testosterone deficiency after puberty.

Safety and efficacy of oral methyltestosterone in men with “age-related hypogonadism” (also referred to as “late-onset hypogonadism”) have not been established.

Androgens may be used to stimulate puberty in carefully selected males with clearly delayed puberty. These patients usually have a familial pattern of delayed puberty that is not secondary to a pathological disorder; puberty is expected to occur spontaneously at a relatively late date. Brief treatment with conservative doses may occasionally be justified in these patients if they do not respond to psychological support. The potential adverse effect on bone maturation should be discussed with the patient and parents prior to androgen administration. An X-ray of the hand and wrist to determine bone age should be obtained every 6 months to assess the effect of treatment on the epiphyseal centers.

Females

Androgens may be used secondarily in women with advancing inoperable metastatic (skeletal) mammary cancer who are 1 to 5 years postmenopausal. Primary goals of therapy in these women include ablation of the ovaries. Other methods of counteracting estrogen activity are adrenalectomy, hypophysectomy, and/or anti-estrogen therapy. This treatment has also been used in premenopausal women with breast cancer who have benefited from oophorectomy and are considered to have a hormone-responsive tumor. Judgment concerning androgen therapy should be made by an oncologist with expertise in this field.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has experienced an inadequate treatment response to an alternative testosterone product (e.g., topical testosterone, transdermal testosterone, injectable testosterone)

OR

- The patient has experienced an intolerance to an alternative testosterone product (e.g., topical testosterone, transdermal testosterone, injectable testosterone)

OR

- The patient has a contraindication that would prohibit a trial of alternative testosterone products (e.g., topical testosterone, transdermal testosterone, injectable testosterone)

AND

- The requested drug is NOT being prescribed for "age-related hypogonadism" (also referred to as "late-onset hypogonadism")

AND

- The requested drug is being prescribed for primary or hypogonadotropic hypogonadism

  AND

  - The request is NOT for continuation of therapy

    AND

    - Before the start of testosterone therapy, the patient has at least two confirmed low morning testosterone levels according to current practice guidelines or your standard lab reference values

  OR

  - The request is for continuation of therapy

    AND

    - Before the patient started testosterone therapy, the patient had a confirmed low morning testosterone level according to current practice guidelines or your standard lab reference values

OR

- The requested drug is being prescribed for inoperable metastatic breast cancer in a patient who is 1 to 5 years postmenopausal and had an incomplete response to other therapy for metastatic breast cancer

OR

- The requested drug is being prescribed for a premenopausal patient with breast cancer who has benefited from oophorectomy and is considered to have a hormone-responsive tumor

OR

- The requested drug is being prescribed for delayed puberty

REFERENCES

1. Methitest [package insert]. Bridgewater, NJ: Amneal Pharmaceuticals LLC; October 2018.
2. Methyltestosterone capsule [package insert]. East Windsor, NJ: Novitium Pharma LLC; June 2021.
3. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2023; Accessed January 3, 2023.
4. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed January 3, 2023.
5. Bhasin S, Brito JP, Cunningham GR, et al. Testosterone Therapy in Men with Hypogonadism: An Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab.* 2018;103(5):1715-1744.

Reference number(s)
2266-A

SPECIALTY GUIDELINE MANAGEMENT

XENAZINE (tetrabenazine)
tetrabenazine (generic)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication
Treatment of chorea associated with Huntington's disease

B. Compendial Uses
1. Tic disorders
2. Tardive dyskinesia
3. Hemiballismus
4. Chorea not associated with Huntington's disease

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary for both initial approval and continuation of therapy prior authorization reviews (where applicable): Documentation of score of items 1 to 7 of the Abnormal Involuntary Movement Scale (AIMS).

III. CRITERIA FOR INITIAL APPROVAL

A. Chorea associated with Huntington's disease
Authorization of 6 months may be granted for treatment of chorea associated with Huntington's disease when both of the following criteria are met:
1. Member demonstrates characteristic motor examination features
2. Member meets one of the following conditions:
   i. Laboratory results indicate an expanded *HTT* CAG repeat sequence of at least 36
   ii. Member has a positive family history for Huntington's disease

B. Chorea not associated with Huntington's disease
Authorization of 6 months may be granted for treatment of chorea not associated with Huntington's disease.

C. Tic disorders
Authorization of 6 months may be granted for treatment of tic disorders.

D. Tardive dyskinesia
Authorization of 6 months may be granted for the treatment of tardive dyskinesia when the baseline AIMS score for items 1 to 7 is obtained.

E. Hemiballismus
Authorization of 6 months may be granted for the treatment of hemiballismus.

IV. CONTINUATION OF THERAPY

A. Tardive dyskinesia
Authorization of 12 months may be granted for treatment of tardive dyskinesia when the member's tardive dyskinesia symptoms have improved as indicated by a decreased AIMS score (items 1 to 7) from baseline.

B. Other indications
Authorization of 12 months may be granted for treatment of all other indications listed in Section III when the member has experienced improvement or stabilization.

V. REFERENCES

1. Xenazine [package insert]. Deerfield, IL: Lundbeck Inc.; November 2019.
2. Micromedex® (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. Available at: http://www.micromedexsolutions.com. Accessed March 7, 2023.
3. AHFS Drug Information. http://online.lexi.com/lco. Accessed March 7, 2023.
4. Guay DR. Tetrabenazine, a monoamine-depleting drug used in the treatment of hyperkinetic movement disorders. *Am J Geriatr Pharmacother*. 2010; 8:331-373.
5. Armstrong MJ, Miyasaki JM. Evidence-based guideline: pharmacologic treatment of chorea in Huntington disease: Report of the Guideline Development Subcommittee of the American Academy of Neurology. *Neurology*. 2012; 79(6):597-603.
6. Kenney C, Hunter C, Jankovic J. Long-term tolerability of tetrabenazine in the treatment of hyperkinetic movement disorders. Movement Disorders. 2007; 22(2): 193-7.
7. Tetrabenazine [package insert]. Weston, FL: Apotex Corp.; October 2021.
8. American Psychiatric Association. (2021). *Practice Guideline for the Treatment of Patients With Schizophrenia, third edition.* https://doi.org/10.1176/appi.books.9780890424841

QUANTITY LIMIT PRIOR AUTHORIZATION CRITERIA

BRAND NAME
(generic)

(tetracycline capsules)

Status: CVS Caremark Criteria
Type: Quantity Limit; Post Limit Prior Authorization

POLICY

FDA-APPROVED INDICATIONS

To reduce the development of drug-resistant bacteria and maintain the effectiveness of tetracycline hydrochloride and other antibacterial drugs, tetracycline hydrochloride should be used only to treat infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.
Tetracycline is indicated in the treatment of infections caused by susceptible strains of the designated organisms in the conditions listed below:

- Upper respiratory tract infections caused by Streptococcus pyogenes, Streptococcus pneumoniae and Hemophilus influenzae. Note: Tetracycline should not be used for streptococcal disease unless the organism has been demonstrated to be susceptible.
- Lower respiratory tract infections caused by Streptococcus pyogenes, Streptococcus pneumoniae, Mycoplasma pneumoniae (Eaton agent, and Klebsiella sp.)
- Skin and soft tissue infections caused by Streptococcus pyogenes, Staphylococcus aureus. (Tetracyclines are not the drugs of choice in the treatment of any type of staphylococcal infections.)
- Infections caused by rickettsia including Rocky Mountain spotted fever, typhus group infections, Q fever, rickettsial pox.
- Psittacosis caused by Chlamydophila psittaci.
- Infections caused by Chlamydia trachomatis such as uncomplicated urethral, endocervical or rectal infections, inclusion conjunctivitis, trachoma, and lymphogranuloma venereum.
- Granuloma inguinale caused by Klebsiella granulomatis.
- Relapsing fever caused by Borrelia sp.
- Bartonellosis caused by Bartonella bacilliformis.
- Chancroid caused by Hemophilus ducreyi.
- Tularemia caused by Francisella tularensis.
- Plague caused by Yersinia pestis.
- Cholera caused by Vibrio cholerae.
- Brucellosis caused by Brucella species (tetracycline may be used in conjunction with an aminoglycoside).
- Infections due to Campylobacter fetus.
- As adjunctive therapy in intestinal amebiasis caused by Entamoeba histolytica.
- Urinary tract infections caused by susceptible strains of Escherichia coli, Klebsiella, etc.
- Other infections caused by susceptible gram-negative organisms such as E. coli, Enterobacter aerogenes, Shigella sp., Acinetobacter sp., Klebsiella sp., and Bacteroides sp.
- In severe acne, adjunctive therapy with tetracycline may be useful.

When penicillin is contraindicated, tetracyclines are alternative drugs in the treatment of the following infections:

- Syphilis and yaws caused by Treponema pallidum and pertenue, respectively,
- Vincent's infection caused by Fusobacterium fusiforme,
- Infections caused by Neisseria gonorrhoeae,
- Anthrax caused by Bacillus anthracis,
- Infections due to Listeria monocytogenes,
- Actinomycosis caused by Actinomyces species,
- Infections due to Clostridium species.

Compendial Uses:
Melioidosis caused by Burkholderia pseudomallei[3]
Balantidiasis caused by Balantidium coli [2]
Dientamoeba fragilis Infections[2]
Diverticulitis[3]
Necrotizing ulcerative gingivitis, acute[3]
Leptospirosis[2]
Lyme Disease[2]
Malaria[2,3]
Pinta[2]
Rosacea[3]

INITIAL QUANTITY LIMIT**

LIMIT CRITERIA
Limits do not accumulate together; patient is allowed the maximum limit for each drug and strength

Drug	1 Month Limit*	3 Month Limit*
Tetracycline Capsules	120 caps / 25 days	360 caps / 75 days

**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*

**If the patient is requesting more than the initial quantity limit, the claim will reject with a message indicating that a prior authorization is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

COVERAGE CRITERIA
The requested drug will be covered with prior authorization when the following criteria are met:
- The requested drug is not being used in a footbath

AND
- The requested drug is being prescribed for the treatment of Plague caused by Yersinia pestis
  OR
- The requested drug is being prescribed for the treatment of melioidosis caused by Burkholderia pseudomallei

Quantity Limits apply.
240 capsules / 25 days*, 720 capsules / 75 days* for the treatment of Plague caused by Yersinia pestis
180 capsules / 25 days*, 540 capsules / 75 days* for the treatment of melioidosis caused by Burkholderia pseudomallei
**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*

REFERENCES

1. Tetracycline Capsules [package insert]. Congers, NY: Chartwell Pharmaceuticals, LLC.; February 2021.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2022; Accessed February 6, 2023.
3. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed February 6, 20023.
4. Centers for Disease Control and Prevention. Available at: https://www.cdc.gov/diseasesconditions/az/y.html. Accessed February 2023.

PRIOR AUTHORIZATION CRITERIA

DRUG CLASS	**TRICYCLIC ANTIDEPRESSANT (TCA) AGENTS – ELDERLY**
BRAND NAME (generic)	
	(amitriptyline)
	(amitriptyline/chlordiazepoxide)
	(amitriptyline/perphenazine)
	(amoxapine)
	ANAFRANIL (clomipramine)
	(doxepin)
	(imipramine hydrochloride)
	(imipramine pamoate)
	NORPRAMIN (desipramine)
	PAMELOR (nortriptyline)
	(protriptyline)
	SILENOR (doxepin)
	(trimipramine)

Quantity limits applies only to patients 65 years of age or older.

Status: CVS Caremark Criteria
Type: Post Limit Prior Authorization

POLICY

FDA-APPROVED INDICATIONS

Amitriptyline
Amitriptyline is indicated for the relief of symptoms of depression. Endogenous depression is more likely to be alleviated than are other depressive states.

Amitriptyline/Chlordiazepoxide
Chlordiazepoxide and amitriptyline hydrochloride is indicated for the treatment of patients with moderate to severe depression associated with moderate to severe anxiety.
The therapeutic response to chlordiazepoxide and amitriptyline hydrochloride occurs earlier and with fewer treatment failures than when either amitriptyline or chlordiazepoxide is used alone.
Symptoms likely to respond in the first week of treatment include: insomnia, feelings of guilt or worthlessness, agitation, psychic and somatic anxiety, suicidal ideation and anorexia.

Amitriptyline/Perphenazine
Perphenazine and amitriptyline hydrochloride tablets are recommended for treatment of (1) patients with moderate to severe anxiety and/or agitation and depressed mood, (2) patients with depression in whom anxiety and/or agitation are severe, and (3) patients with depression and anxiety in association with chronic physical disease. In many of these patients, anxiety masks the depressive state so that, although therapy with a tranquilizer appears to be indicated, the administration of a tranquilizer alone will not be adequate.
Schizophrenic patients who have associated depressive symptoms should be considered for therapy with perphenazine and amitriptyline hydrochloride tablets.

Amoxapine
Amoxapine is indicated for the relief of symptoms of depression in patients with neurotic or reactive depressive disorders as well as endogenous and psychotic depressions. It is indicated for depression accompanied by anxiety or agitation.

Anafranil
Anafranil (clomipramine hydrochloride) is indicated for the treatment of obsessions and compulsions in patients with Obsessive-Compulsive Disorder (OCD).

Doxepin
Doxepin hydrochloride capsules are recommended for the treatment of psychoneurotic patients with depression and/or anxiety, depression and/or anxiety associated with alcoholism (not to be taken concomitantly with alcohol), depression and/or anxiety associated with organic disease (the possibility of drug interaction should be considered if the patient is receiving other drugs concomitantly), psychotic depressive disorders with associated anxiety including involutional depression and manic-depressive disorders

Imipramine Hydrochloride
Depression – For the relief of symptoms of depression. Endogenous depression is more likely to be alleviated than other depressive states. One to three weeks of treatment may be needed before optimal therapeutic effects are evident.
Childhood Enuresis – May be useful as temporary adjunctive therapy in reducing enuresis in children aged 6 years and older, after possible organic causes have been excluded by appropriate tests. In patients having daytime symptoms of frequency and urgency, examination should include voiding cystourethrography and cystoscopy, as necessary. The effectiveness of treatment may decrease with continued drug administration.

Imipramine Pamoate
For the relief of symptoms of depression. Endogenous depression is more likely to be alleviated than other depressive states. One to three weeks of treatment may be needed before optimal therapeutic effects are evident.

Norpramin
Norpramin is indicated for the treatment of depression.

Pamelor
Pamelor (nortriptyline HCl) is indicated for the relief of symptoms of depression. Endogenous depressions are more likely to be alleviated than are other depressive states.

Protriptyline
Protriptyline hydrochloride tablets are indicated for the treatment of symptoms of mental depression in patients who are under close medical supervision. Its activating properties make it particularly suitable for withdrawn and anergic patients.

Silenor
Silenor is indicated for the treatment of insomnia characterized by difficulty with sleep maintenance. The clinical trials performed in support of efficacy were up to 3 months in duration.

Trimipramine
Trimipramine Maleate Capsules are indicated for the relief of symptoms of depression. Endogenous depression is more likely to be alleviated than other depressive states.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization in patients 65 years of age or older when the following criteria are met:

- The request is for one of the following A) amitriptyline, amoxapine, desipramine, imipramine hydrochloride, imipramine pamoate, nortriptyline, protriptyline, or trimipramine for depression, B) doxepin for depression and/or anxiety, C) amitriptyline/perphenazine for depression with anxiety and/or agitation D) amitriptyline/chlordiazepoxide for depression associated with anxiety

Quantity Limits apply.

POST LIMIT QUANTITY**

Generic Drug (Brand if available)	Strength	1 Month Limit *	3 Month Limit *
amitriptyline	10 mg	180 tabs/25 days	540 tabs/75 days
amitriptyline	25 mg	120 tabs/25 days	360 tabs/75 days
amitriptyline	50 mg	90 tabs/25 days	270 tabs/75 days
amitriptyline	75 mg	60 tabs/25 days	180 tabs/75 days
amitriptyline	100 mg, 150 mg	30 tabs/25 days	90 tabs/75 days
amitriptyline/chlordiazepoxide	12.5 mg/5 mg, 25 mg/10 mg	180 tabs/25 days	540 tabs/75 days
amitriptyline/perphenazine	10 mg/2 mg	180 tabs/25 days	540 tabs/75 days
amitriptyline/perphenazine	10 mg/4 mg, 25 mg/2 mg, 25 mg/4 mg	120 tabs/25 days	360 tabs/75 days
amitriptyline/perphenazine	50 mg/4 mg	90 tabs/25 days	270 tabs/75 days
amoxapine	25 mg, 50 mg, 100 mg	120 tabs/25 days	360 tabs/75 days
amoxapine	150 mg	60 tabs/25 days	180 tabs/75 days
clomipramine (Anafranil)	25 mg, 50 mg	150 caps/25 days	450 caps/75 days
clomipramine (Anafranil)	75 mg	90 caps/25 days	270 caps/75 days
desipramine (Norpramin)	10 mg, 25 mg, 50 mg	120 tabs/25 days	360 tabs/75 days
desipramine (Norpramin)	75 mg, 100 mg	90 tabs/25 days	270 tabs/75 days
desipramine (Norpramin)	150 mg	60 tabs/25 days	180 tabs/75 days
doxepin (Silenor)	3 mg, 6 mg	30 tabs/25 days	90 tabs/75 days
doxepin	10 mg, 25 mg, 50 mg, 75 mg	120 caps/25 days	360 caps/75 days
doxepin	100 mg	90 caps/25 days	270 caps/75 days
doxepin	150 mg	60 caps/25 days	180 caps/75 days
doxepin	10 mg/mL	900 mL/25 days	2,700 mL/75 days
imipramine hydrochloride	10 mg, 25 mg	150 tabs/25 days	450 tabs/75 days
imipramine hydrochloride	50 mg	120 tabs/25 days	360 tabs/75 days
imipramine pamoate	75 mg, 100 mg	60 caps/25 days	180 caps/75 days
imipramine pamoate	125 mg, 150 mg	30 caps/25 days	90 caps/75 days
nortriptyline (Pamelor)	10 mg	180 caps/25 days	540 caps/75 days
nortriptyline (Pamelor)	25 mg, 50 mg	90 caps/25 days	270 caps/75 days
nortriptyline (Pamelor)	75 mg	60 caps/25 days	180 caps/75 days
nortriptyline	10 mg/5mL	2,250 mL/25 days	6,750 mL/75 days

protriptyline	5 mg	120 tabs/25 days	360 tabs/75 days
protriptyline	10 mg	180 tabs/25 days	540 tabs/75 days
trimipramine	25 mg, 50 mg	120 caps/25 days	360 caps/75 days
trimipramine	100 mg	60 caps/25 days	180 caps/75 days
**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*			

** The initial limits for amitriptyline/perphenazine 10 mg/4 mg, amoxapine 150 mg, clomipramine (Anafranil) 25 mg, 50 mg, 75 mg, doxepin (Silenor) 3 mg, 6 mg are set at the maximum daily dose. Additional quantities exceed the maximum daily dosage; therefore, no additional post limit quantities will be available for this drug.

REFERENCES

1. Amitriptyline [package insert]. Princeton, NJ: Sandoz Inc.; November 2021.
2. Amitriptyline/Chlordiazepoxide [package insert]. Morgantown, WV: Mylan Pharmaceuticals; March 2021.
3. Amitriptyline/Perphenazine [package insert]. Morgantown, WV: Mylan Pharmaceuticals; September 2019.
4. Amoxapine [package insert]. Parsippany, NJ: Actavis Pharma, Inc; February 2015.
5. Anafranil [package insert]. Webster Groves, MO: Mallinckrodt Inc; March 2019.
6. Doxepin [package insert]. Morgantown, WV: Mylan Pharmaceuticals; March 2022.
7. Doxepin 150mg [package insert]. Chestnut Ridge, NY: Par Pharmaceutical; June 2021.
8. Doxepin Solution [package insert]. Philadelphia, PA: Lannett Company, Inc.; March 2020.
9. Imipramine Hydrochloride [package insert]. Birmingham, AL: Oxford Pharmaceuticals LLC; January 2022.
10. Imipramine Pamoate [package insert]. Eatontown, NJ: West-Ward Pharmaceutical Corp; August 2016.
11. Norpramin [package insert]. Parsippany, NJ: Validus Pharmaceuticals LLC; November 2018.
12. Nortriptyline Solution [package insert]. Greenville, SC: Pharmaceutical Associates, Inc.; January 2015.
13. Pamelor [package insert]. Webster Groves, MO: SpecGx LLC; April 2019.
14. Protriptyline [package insert]. Eatontown, NJ: West-Ward Pharmaceuticals Corp.; March 2016.
15. Silenor [package insert]. Morristown, NJ: Currax Pharmaceuticals LLC; October 2020.
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PRIOR AUTHORIZATION CRITERIA

DRUG CLASS	**TRICYCLIC ANTIDEPRESSANT (TCA) AGENTS – ELDERLY**
BRAND NAME (generic)	
	(amitriptyline)
	(amitriptyline/chlordiazepoxide)
	(amitriptyline/perphenazine)
	(amoxapine)
	ANAFRANIL (clomipramine)
	(doxepin)
	(imipramine hydrochloride)
	(imipramine pamoate)
	NORPRAMIN (desipramine)
	PAMELOR (nortriptyline)
	(protriptyline)
	SILENOR (doxepin)
	(trimipramine)

Quantity limits applies only to patients 65 years of age or older.

Status: CVS Caremark Criteria
Type: Post Limit Prior Authorization

POLICY

FDA-APPROVED INDICATIONS

Amitriptyline
Amitriptyline is indicated for the relief of symptoms of depression. Endogenous depression is more likely to be alleviated than are other depressive states.

Amitriptyline/Chlordiazepoxide
Chlordiazepoxide and amitriptyline hydrochloride is indicated for the treatment of patients with moderate to severe depression associated with moderate to severe anxiety.
The therapeutic response to chlordiazepoxide and amitriptyline hydrochloride occurs earlier and with fewer treatment failures than when either amitriptyline or chlordiazepoxide is used alone.
Symptoms likely to respond in the first week of treatment include: insomnia, feelings of guilt or worthlessness, agitation, psychic and somatic anxiety, suicidal ideation and anorexia.

Amitriptyline/Perphenazine
Perphenazine and amitriptyline hydrochloride tablets are recommended for treatment of (1) patients with moderate to severe anxiety and/or agitation and depressed mood, (2) patients with depression in whom anxiety and/or agitation are severe, and (3) patients with depression and anxiety in association with chronic physical disease. In many of these patients, anxiety masks the depressive state so that, although therapy with a tranquilizer appears to be indicated, the administration of a tranquilizer alone will not be adequate.
Schizophrenic patients who have associated depressive symptoms should be considered for therapy with perphenazine and amitriptyline hydrochloride tablets.

Amoxapine
Amoxapine is indicated for the relief of symptoms of depression in patients with neurotic or reactive depressive disorders as well as endogenous and psychotic depressions. It is indicated for depression accompanied by anxiety or agitation.

Anafranil
Anafranil (clomipramine hydrochloride) is indicated for the treatment of obsessions and compulsions in patients with Obsessive-Compulsive Disorder (OCD).

Doxepin
Doxepin hydrochloride capsules are recommended for the treatment of psychoneurotic patients with depression and/or anxiety, depression and/or anxiety associated with alcoholism (not to be taken concomitantly with alcohol), depression and/or anxiety associated with organic disease (the possibility of drug interaction should be considered if the patient is receiving other drugs concomitantly), psychotic depressive disorders with associated anxiety including involutional depression and manic-depressive disorders

Imipramine Hydrochloride
Depression – For the relief of symptoms of depression. Endogenous depression is more likely to be alleviated than other depressive states. One to three weeks of treatment may be needed before optimal therapeutic effects are evident.
Childhood Enuresis – May be useful as temporary adjunctive therapy in reducing enuresis in children aged 6 years and older, after possible organic causes have been excluded by appropriate tests. In patients having daytime symptoms of frequency and urgency, examination should include voiding cystourethrography and cystoscopy, as necessary. The effectiveness of treatment may decrease with continued drug administration.

Imipramine Pamoate
For the relief of symptoms of depression. Endogenous depression is more likely to be alleviated than other depressive states. One to three weeks of treatment may be needed before optimal therapeutic effects are evident.

Norpramin
Norpramin is indicated for the treatment of depression.

Pamelor
Pamelor (nortriptyline HCl) is indicated for the relief of symptoms of depression. Endogenous depressions are more likely to be alleviated than are other depressive states.

Protriptyline
Protriptyline hydrochloride tablets are indicated for the treatment of symptoms of mental depression in patients who are under close medical supervision. Its activating properties make it particularly suitable for withdrawn and anergic patients.

Silenor
Silenor is indicated for the treatment of insomnia characterized by difficulty with sleep maintenance. The clinical trials performed in support of efficacy were up to 3 months in duration.

Trimipramine
Trimipramine Maleate Capsules are indicated for the relief of symptoms of depression. Endogenous depression is more likely to be alleviated than other depressive states.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization in patients 65 years of age or older when the following criteria are met:

- The request is for one of the following A) amitriptyline, amoxapine, desipramine, imipramine hydrochloride, imipramine pamoate, nortriptyline, protriptyline, or trimipramine for depression, B) doxepin for depression and/or anxiety, C) amitriptyline/perphenazine for depression with anxiety and/or agitation D) amitriptyline/chlordiazepoxide for depression associated with anxiety

Quantity Limits apply.

POST LIMIT QUANTITY**

Generic Drug (Brand if available)	Strength	1 Month Limit *	3 Month Limit *
amitriptyline	10 mg	180 tabs/25 days	540 tabs/75 days
amitriptyline	25 mg	120 tabs/25 days	360 tabs/75 days
amitriptyline	50 mg	90 tabs/25 days	270 tabs/75 days
amitriptyline	75 mg	60 tabs/25 days	180 tabs/75 days
amitriptyline	100 mg, 150 mg	30 tabs/25 days	90 tabs/75 days
amitriptyline/chlordiazepoxide	12.5 mg/5 mg, 25 mg/10 mg	180 tabs/25 days	540 tabs/75 days
amitriptyline/perphenazine	10 mg/2 mg	180 tabs/25 days	540 tabs/75 days
amitriptyline/perphenazine	10 mg/4 mg, 25 mg/2 mg, 25 mg/4 mg	120 tabs/25 days	360 tabs/75 days
amitriptyline/perphenazine	50 mg/4 mg	90 tabs/25 days	270 tabs/75 days
amoxapine	25 mg, 50 mg, 100 mg	120 tabs/25 days	360 tabs/75 days
amoxapine	150 mg	60 tabs/25 days	180 tabs/75 days
clomipramine (Anafranil)	25 mg, 50 mg	150 caps/25 days	450 caps/75 days
clomipramine (Anafranil)	75 mg	90 caps/25 days	270 caps/75 days
desipramine (Norpramin)	10 mg, 25 mg, 50 mg	120 tabs/25 days	360 tabs/75 days
desipramine (Norpramin)	75 mg, 100 mg	90 tabs/25 days	270 tabs/75 days
desipramine (Norpramin)	150 mg	60 tabs/25 days	180 tabs/75 days
doxepin (Silenor)	3 mg, 6 mg	30 tabs/25 days	90 tabs/75 days
doxepin	10 mg, 25 mg, 50 mg, 75 mg	120 caps/25 days	360 caps/75 days
doxepin	100 mg	90 caps/25 days	270 caps/75 days
doxepin	150 mg	60 caps/25 days	180 caps/75 days
doxepin	10 mg/mL	900 mL/25 days	2,700 mL/75 days
imipramine hydrochloride	10 mg, 25 mg	150 tabs/25 days	450 tabs/75 days
imipramine hydrochloride	50 mg	120 tabs/25 days	360 tabs/75 days
imipramine pamoate	75 mg, 100 mg	60 caps/25 days	180 caps/75 days
imipramine pamoate	125 mg, 150 mg	30 caps/25 days	90 caps/75 days
nortriptyline (Pamelor)	10 mg	180 caps/25 days	540 caps/75 days
nortriptyline (Pamelor)	25 mg, 50 mg	90 caps/25 days	270 caps/75 days
nortriptyline (Pamelor)	75 mg	60 caps/25 days	180 caps/75 days
nortriptyline	10 mg/5mL	2,250 mL/25 days	6,750 mL/75 days

protriptyline	5 mg	120 tabs/25 days	360 tabs/75 days
protriptyline	10 mg	180 tabs/25 days	540 tabs/75 days
trimipramine	25 mg, 50 mg	120 caps/25 days	360 caps/75 days
trimipramine	100 mg	60 caps/25 days	180 caps/75 days
**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*			

** The initial limits for amitriptyline/perphenazine 10 mg/4 mg, amoxapine 150 mg, clomipramine (Anafranil) 25 mg, 50 mg, 75 mg, doxepin (Silenor) 3 mg, 6 mg are set at the maximum daily dose. Additional quantities exceed the maximum daily dosage; therefore, no additional post limit quantities will be available for this drug.

REFERENCES

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2. Amitriptyline/Chlordiazepoxide [package insert]. Morgantown, WV: Mylan Pharmaceuticals; March 2021.
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4. Amoxapine [package insert]. Parsippany, NJ: Actavis Pharma, Inc; February 2015.
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10. Imipramine Pamoate [package insert]. Eatontown, NJ: West-Ward Pharmaceutical Corp; August 2016.
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QUANTITY LIMIT CRITERIA

DRUG CLASS	**TRICYCLIC ANTIDEPRESSANT (TCA) AGENTS – ELDERLY**
BRAND NAME* (generic)	
	(amitriptyline)
	(amitriptyline/chlordiazepoxide)
	(amitriptyline/perphenazine)
	(amoxapine)
	ANAFRANIL (clomipramine)
	(doxepin)
	(imipramine hydrochloride)
	(imipramine pamoate)
	NORPRAMIN (desipramine)
	PAMELOR (nortriptyline)
	(protriptyline)
	SILENOR (doxepin)
	(trimipramine)

Quantity limit applies only to patients 65 years of age or older.

Status: CVS Caremark Criteria
Type: Quantity Limit with Age Edit ***Ref # 754-I***

**Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Amitriptyline

Amitriptyline is indicated for the relief of symptoms of depression. Endogenous depression is more likely to be alleviated than are other depressive states.

Amitriptyline/Chlordiazepoxide
Chlordiazepoxide and amitriptyline hydrochloride is indicated for the treatment of patients with moderate to severe depression associated with moderate to severe anxiety.
The therapeutic response to chlordiazepoxide and amitriptyline hydrochloride occurs earlier and with fewer treatment failures than when either amitriptyline or chlordiazepoxide is used alone.
Symptoms likely to respond in the first week of treatment include: insomnia, feelings of guilt or worthlessness, agitation, psychic and somatic anxiety, suicidal ideation and anorexia.

Amitriptyline/Perphenazine
Perphenazine and amitriptyline hydrochloride tablets are recommended for treatment of (1) patients with moderate to severe anxiety and/or agitation and depressed mood, (2) patients with depression in whom anxiety and/or agitation are severe, and (3) patients with depression and anxiety in association with chronic physical disease. In many of these patients, anxiety masks the depressive state so that, although therapy with a tranquilizer appears to be indicated, the administration of a tranquilizer alone will not be adequate.
Schizophrenic patients who have associated depressive symptoms should be considered for therapy with perphenazine and amitriptyline hydrochloride tablets.

Amoxapine
Amoxapine is indicated for the relief of symptoms of depression in patients with neurotic or reactive depressive disorders as well as endogenous and psychotic depressions. It is indicated for depression accompanied by anxiety or agitation.

Anafranil
Anafranil (clomipramine hydrochloride) is indicated for the treatment of obsessions and compulsions in patients with Obsessive-Compulsive Disorder (OCD).

Doxepin
Doxepin hydrochloride capsules are recommended for the treatment of psychoneurotic patients with depression and/or anxiety, depression and/or anxiety associated with alcoholism (not to be taken concomitantly with alcohol), depression and/or anxiety associated with organic disease (the possibility of drug interaction should be considered if the patient is receiving other drugs concomitantly), psychotic depressive disorders with associated anxiety including involutional depression and manic-depressive disorders.

Imipramine Hydrochloride
Depression – For the relief of symptoms of depression. Endogenous depression is more likely to be alleviated than other depressive states. One to three weeks of treatment may be needed before optimal therapeutic effects are evident.
Childhood Enuresis – May be useful as temporary adjunctive therapy in reducing enuresis in children aged 6 years and older, after possible organic causes have been excluded by appropriate tests. In patients having daytime symptoms of frequency and urgency, examination should include voiding cystourethrography and cystoscopy, as necessary. The effectiveness of treatment may decrease with continued drug administration.

Imipramine Pamoate
For the relief of symptoms of depression. Endogenous depression is more likely to be alleviated than other depressive states. One to three weeks of treatment may be needed before optimal therapeutic effects are evident.

Norpramin
Norpramin is indicated for the treatment of depression.

Pamelor
Pamelor (nortriptyline HCl) is indicated for the relief of symptoms of depression. Endogenous depressions are more likely to be alleviated than are other depressive states.

Protriptyline
Protriptyline hydrochloride tablets are indicated for the treatment of symptoms of mental depression in patients who are under close medical supervision. Its activating properties make it particularly suitable for withdrawn and anergic patients.

Silenor

Silenor is indicated for the treatment of insomnia characterized by difficulty with sleep maintenance. The clinical trials performed in support of efficacy were up to 3 months in duration.

Trimipramine
Trimipramine Maleate Capsules are indicated for the relief of symptoms of depression. Endogenous depression is more likely to be alleviated than other depressive states.

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. The initial limit is set to allow up to the FDA-approved maximum elderly dose for each of the included tricyclic antidepressants (TCAs). This initial limit is coded to apply only to patients 65 years of age or older. If the prescribing information has no maximum elderly dose, the initial limit is set to allow up to the FDA-approved maximum adult dose.

Older adults, 65 years of age or older, have increased sensitivity to TCAs; in general, all TCAs increase risk of cognitive impairment, delirium, falls, fractures, and motor vehicle crashes in older adults.[19]

If the patient is requesting more than the initial quantity limit, the claim will reject with a message indicating that a prior authorization is required (does not apply to amoxapine 150 mg, amitriptyline/perphenazine 10 mg/4 mg, Silenor (all strengths), or Anafranil [all strengths]).

If the patient is requesting more than the initial quantity limit of amoxapine 150 mg, amitriptyline/perphenazine 10 mg/4 mg, Silenor (all strengths), or Anafranil (all strengths), the claim will reject with a message indicating that quantity limits are exceeded.

The chart below details dosing for the drugs targeted by this criteria document.

Generic Drug (Brand if available)	Maximum Adult Daily Dose	Maximum Elderly Daily Dose
amitriptyline	150 mg	50 mg
amitriptyline/perphenazine	amitriptyline: 150 mg perphenazine: 16 mg	amitriptyline: 50 mg perphenazine: 16 mg
amoxapine	400 mg	300 mg
chlordiazepoxide/amitriptyline	amitriptyline: 150 mg chlordiazepoxide: 60 mg	amitriptyline: 50 mg chlordiazepoxide: 60 mg
clomipramine (Anafranil)	250 mg	250 mg
desipramine (Norpramin)	300 mg	150 mg
doxepin	300 mg	150 mg
doxepin (Silenor)	6 mg	6 mg
imipramine (Tofranil)	200 mg	100 mg
imipramine pamoate	200 mg	100 mg
nortriptyline (Pamelor)	150 mg	50 mg
protriptyline	60 mg	20 mg
trimipramine	200 mg	100 mg

REFERENCES

1. Amitriptyline [package insert]. Princeton, NJ: Sandoz Inc.; November 2021.
2. Amitriptyline/Chlordiazepoxide [package insert]. Morgantown, WV: Mylan Pharmaceuticals; March 2021.
3. Amitriptyline/Perphenazine [package insert]. Morgantown, WV: Mylan Pharmaceuticals; September 2019.
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5. Anafranil [package insert]. Webster Groves, MO: Mallinckrodt Inc; March 2019.
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Written by:	UM Development (NB) 02/2012
Revised:	(MS) 04/2013; (CF) 11/2013, 11/2014, 11/2015; (MS) 11/2016 (no clinical changes); (JG) 11/2017 (no clinical changes), (ME) 11/2018 (removed brand Limbitrol), 10/2019 (removed brand Elavil), 05/2020 (no clinical changes), 05/2021 (removed brand Surmontil), (TM) 05/2022 (removed brand Tofranil)
Reviewed:	Medical Affairs (KP) 02/2012, 04/2013, 07/2013 (removed Tofranil NON-PM 75 mg and 100 mg); (LCB) 11/2013; (KJC) 11/2014; (LCB) 11/2015; (ME) 11/2016, (DNC) 10/2018, CHART 10/31/19, CHART 05/28/20, CHART 05/27/21, 05/26/22
External Review:	06/2012, 06/2013, 04/2014, 02/2015, 02/2016, 02/2017, 02/2018, 02/2019, 02/2020, 08/2020, 08/2021, 08/2022

LIMIT CRITERIA**
These limits are only intended to address dosing for patients 65 years of age or older.
Limits do not accumulate together; patient is allowed the maximum limit for each drug and strength.

Generic Drug (Brand if available)	Strength	1 Month Limit *	3 Month Limit *
amitriptyline	10 mg	150 tabs/25 days	450 tabs/75 days
amitriptyline	25 mg	60 tabs/25 days	180 tabs/75 days
amitriptyline	50 mg	30 tabs/25 days	90 tabs/75 days
amitriptyline	75 mg, 100 mg, 150 mg	0** tabs/25 days	0** tabs/75 days
amitriptyline/chlordiazepoxide	12.5 mg/5 mg	120 tabs/25 days	360 tabs/75 days
amitriptyline/chlordiazepoxide	25 mg/10 mg	60 tabs/25 days	180 tabs/75 days
amitriptyline/perphenazine	10 mg/2 mg	150 tabs/25 days	450 tabs/75 days
amitriptyline/perphenazine	10 mg/4 mg	120*** tabs/25 days	360*** tabs/75 days
amitriptyline/perphenazine	25 mg/2 mg, 25 mg/4 mg	60 tabs/25 days	180 tabs/75 days
amitriptyline/perphenazine	50 mg/4 mg	30 tabs/25 days	90 tabs/75 days
amoxapine	25 mg, 50 mg, 100 mg	90 tabs/25 days	270 tabs/75 days
amoxapine	150 mg	60*** tabs/25 days	180*** tabs/75 days
clomipramine (Anafranil)	25 mg, 50 mg	150*** caps/25 days	450 caps***/75 days
clomipramine (Anafranil)	75 mg	90*** caps/25 days	270 caps***/75 days
desipramine (Norpramin)	10 mg, 25 mg, 50 mg	90 tabs/25 days	270 tabs/75 days
desipramine (Norpramin)	75 mg	60 tabs/25 days	180 tabs/75 days
desipramine (Norpramin)	100 mg, 150 mg	30 tabs/25 days	90 tabs/75 days
doxepin (Silenor)	3 mg, 6 mg	30*** tabs/25 days	90 tabs***/75 days
doxepin	10 mg, 25 mg, 50 mg	90 caps/25 days	270 caps/75 days
doxepin	75 mg	60 caps/25 days	180 caps/75 days
doxepin	100 mg, 150 mg	30 caps/25 days	90 caps/75 days
doxepin	10 mg/mL	450 mL/25 days	1,350 mL/75 days
imipramine hydrochloride	10 mg, 25 mg	120 tabs/25 days	360 tabs/75 days
imipramine hydrochloride	50 mg	60 tabs/25 days	180 tabs/75 days
imipramine pamoate	75 mg, 100 mg	30 caps/25 days	90 caps/75 days
imipramine pamoate	125 mg, 150 mg	0** caps/25 days	0** caps/25 days
nortriptyline (Pamelor)	10 mg	150 caps/25 days	450 caps/75 days

nortriptyline (Pamelor)	25 mg	60 caps/25 days	180 caps/75 days
nortriptyline (Pamelor)	50 mg	30 caps/25 days	90 caps/75 days
nortriptyline (Pamelor)	75 mg	0** caps/25 days	0** caps/25 days
nortriptyline	10 mg/5mL	750 mL/25 days	2,250 mL/75 days
protriptyline	5 mg	90 tabs/25 days	270 tabs/75 days
protriptyline	10 mg	60 tabs/25 days	180 tabs/75 days
trimipramine	25 mg, 50 mg	60 caps/25 days	180 caps/75 days
trimipramine	100 mg	30 caps/25 days	90 caps/75 days
** The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*			

**The initial limit is zero as the dose of one unit per day would exceed the maximum elderly daily dose. All requests for this drug and strength will be considered through post limit prior authorization.
***Additional quantities exceed the maximum daily dosage; therefore, no additional post limit quantities will be available for this drug.

PRIOR AUTHORIZATION CRITERIA

DRUG CLASS	**TRICYCLIC ANTIDEPRESSANT (TCA) AGENTS – ELDERLY**
BRAND NAME* **(generic)**	
	(amitriptyline)
	(amitriptyline/chlordiazepoxide)
	(amitriptyline/perphenazine)
	(amoxapine)
	ANAFRANIL **(clomipramine)**
	(doxepin)
	(imipramine hydrochloride)
	(imipramine pamoate)
	NORPRAMIN **(desipramine)**
	PAMELOR **(nortriptyline)**
	(protriptyline)
	SILENOR **(doxepin)**
	(trimipramine)

Quantity limits applies only to patients 65 years of age or older.

Status: CVS Caremark Criteria
Type: Post Limit Prior Authorization ***Ref # 755-J***

**Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Amitriptyline
Amitriptyline is indicated for the relief of symptoms of depression. Endogenous depression is more likely to be alleviated than are other depressive states.

Amitriptyline/Chlordiazepoxide
Chlordiazepoxide and amitriptyline hydrochloride is indicated for the treatment of patients with moderate to severe depression associated with moderate to severe anxiety.
The therapeutic response to chlordiazepoxide and amitriptyline hydrochloride occurs earlier and with fewer treatment failures than when either amitriptyline or chlordiazepoxide is used alone.
Symptoms likely to respond in the first week of treatment include: insomnia, feelings of guilt or worthlessness, agitation, psychic and somatic anxiety, suicidal ideation and anorexia.

Amitriptyline/Perphenazine
Perphenazine and amitriptyline hydrochloride tablets are recommended for treatment of (1) patients with moderate to severe anxiety and/or agitation and depressed mood, (2) patients with depression in whom anxiety and/or agitation are severe, and (3) patients with depression and anxiety in association with chronic physical disease. In many of these patients, anxiety masks the depressive state so that, although therapy with a tranquilizer appears to be indicated, the administration of a tranquilizer alone will not be adequate.
Schizophrenic patients who have associated depressive symptoms should be considered for therapy with perphenazine and amitriptyline hydrochloride tablets.

Amoxapine
Amoxapine is indicated for the relief of symptoms of depression in patients with neurotic or reactive depressive disorders as well as endogenous and psychotic depressions. It is indicated for depression accompanied by anxiety or agitation.

Anafranil
Anafranil (clomipramine hydrochloride) is indicated for the treatment of obsessions and compulsions in patients with Obsessive-Compulsive Disorder (OCD).

Doxepin
Doxepin hydrochloride capsules are recommended for the treatment of psychoneurotic patients with depression and/or anxiety, depression and/or anxiety associated with alcoholism (not to be taken concomitantly with alcohol), depression and/or anxiety associated with organic disease (the possibility of drug interaction should be considered if the patient is receiving other drugs concomitantly), psychotic depressive disorders with associated anxiety including involutional depression and manic-depressive disorders.

Imipramine Hydrochloride
Depression – For the relief of symptoms of depression. Endogenous depression is more likely to be alleviated than other depressive states. One to three weeks of treatment may be needed before optimal therapeutic effects are evident.
Childhood Enuresis – May be useful as temporary adjunctive therapy in reducing enuresis in children aged 6 years and older, after possible organic causes have been excluded by appropriate tests. In patients having daytime symptoms of frequency and urgency, examination should include voiding cystourethrography and cystoscopy, as necessary. The effectiveness of treatment may decrease with continued drug administration.

Imipramine Pamoate
For the relief of symptoms of depression. Endogenous depression is more likely to be alleviated than other depressive states. One to three weeks of treatment may be needed before optimal therapeutic effects are evident.

Norpramin
Norpramin is indicated for the treatment of depression.

Pamelor
Pamelor (nortriptyline HCl) is indicated for the relief of symptoms of depression. Endogenous depressions are more likely to be alleviated than are other depressive states.

Protriptyline
Protriptyline hydrochloride tablets are indicated for the treatment of symptoms of mental depression in patients who are under close medical supervision. Its activating properties make it particularly suitable for withdrawn and anergic patients.

Silenor
Silenor is indicated for the treatment of insomnia characterized by difficulty with sleep maintenance. The clinical trials performed in support of efficacy were up to 3 months in duration.

Trimipramine
Trimipramine Maleate Capsules are indicated for the relief of symptoms of depression. Endogenous depression is more likely to be alleviated than other depressive states.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization in patients 65 years of age or older when the following criteria are met:

- The request is for one of the following A) amitriptyline, amoxapine, desipramine, imipramine hydrochloride, imipramine pamoate, nortriptyline, protriptyline, or trimipramine for depression, B) doxepin for depression and/or anxiety, C) amitriptyline/perphenazine for depression with anxiety and/or agitation D) amitriptyline/chlordiazepoxide for depression associated with anxiety

AND

- The patient has experienced an inadequate treatment response or intolerance to at least TWO of the following agents: A) a serotonin-norepinephrine reuptake inhibitor (SNRI), B) a selective serotonin reuptake inhibitor (SSRI), C) mirtazapine, D) bupropion, E) trazodone

AND

- The request is for desipramine (Norpramin) or nortriptyline (Pamelor)
  OR
- The patient experienced an inadequate treatment response or intolerance to a trial of desipramine (Norpramin) or nortriptyline (Pamelor)

Quantity Limits apply.

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines once the initial quantity limits have been exceeded for patients 65 years of age or older. Older adults, 65 years of age or older, have increased sensitivity to Tricyclic antidepressants (TCAs); in general, all TCAs increase risk of cognitive impairment, delirium, falls, fractures, and motor vehicle crashes in older adults.[22] Amitriptyline is indicated for the relief of symptoms of depression. Amitriptyline/perphenazine is recommended for treatment of patients with moderate to severe anxiety and/or agitation and depressed mood, patients with depression in whom anxiety and/or agitation are severe, and patients with depression and anxiety in association with chronic physical disease. Amoxapine is indicated for the relief of symptoms of depression in patients with neurotic or reactive depressive disorders as well as endogenous and psychotic depressions. It is indicated for depression accompanied by anxiety or agitation. Chlordiazepoxide/amitriptyline is indicated for the treatment of patients with moderate to severe depression associated with moderate to severe anxiety. Doxepin hydrochloride capsules are recommended for the treatment of psychoneurotic patients with depression and/or anxiety, depression and/or anxiety associated with alcoholism (not to be taken concomitantly with alcohol), depression and/or anxiety associated with organic disease (the possibility of drug interaction should be considered if the patient is receiving other drugs concomitantly), psychotic depressive disorders with associated anxiety including involutional depression and manic-depressive disorders. Imipramine pamoate is indicated for the relief of symptoms of depression. Norpramin (desipramine) is indicated for the treatment of depression. Pamelor (nortriptyline HCl) is indicated for the relief of symptoms of depression. Protriptyline hydrochloride tablets are indicated for the treatment of symptoms of mental depression in patients who are under close medical supervision. Trimipramine is indicated for the relief of symptoms of depression. Tofranil (imipramine) is indicated for the relief of symptoms of depression.[1-17]

TCAs may be considered for certain patients who do not respond to two or more trials with first line antidepressants or who have previously achieved remission with a TCA. Tricyclic antidepressants should be used cautiously in the elderly.[19] If the use of a TCA is necessary, nortriptyline and desipramine should be considered first.[18,19] Among the TCAs, desipramine and nortriptyline should be considered before amitriptyline, imipramine, and doxepin, due to increasing sensitivity to side effects and toxicity with advancing age.[18] Due to increased side effects (e.g., central nervous system [CNS], anticholinergic, cardiovascular effects) associated with amitriptyline, imipramine, and doxepin, the primary care physician should avoid the use of these agents in elderly patients.[19]

The American College of Physicians (ACP) guidelines summarized results of individual studies and stated that the available evidence does not support clinically significant differences in efficacy, effectiveness, or quality of life among selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), selective serotonin-norepinephrine reuptake inhibitors (SSNRIs), or other second generation antidepressants for the treatment of acute-phase major depressive disorder (MDD). Evidence from head-to-head trials, meta-analyses, and placebo-controlled trials showed no differences in efficacy of second-generation antidepressants in elderly (65 to 80 years), very elderly (>80 years), or younger patients. Therefore, existing evidence does not justify the choice of any second-generation antidepressant including bupropion, citalopram, duloxetine, escitalopram, fluoxetine, fluvoxamine, mirtazapine, nefazodone paroxetine, sertraline, trazodone, and venlafaxine over another on the basis of greater efficacy and effectiveness.[16] The Institute for Clinical Systems Improvement guidelines state that SSRIs, as well as venlafaxine, duloxetine, desvenlafaxine, mirtazapine and bupropion, are frequently recommended as first-line antidepressant treatment options due to the quality and quantity of published data, relative tolerability of side effects compared to TCAs and Monoamine Oxidase Inhibitors (MAOIs), and their overall relative safety. Elderly individuals with dementia generally do best when given antidepressant medications with the lowest possible degree of anticholinergic effect, e.g., bupropion, fluoxetine, sertraline, trazodone, and of the tricyclic agents, desipramine or nortriptyline. Nefazodone has been associated with rare, but potentially fatal liver failure which has limited its use in recent years.[18] Because of associated side effects, TCAs are used less frequently as first-line agents. However, the literature clearly supports the effectiveness of TCAs.[17]

If the patient meets the post limit prior authorization criteria, the approval quantity will be the maximum FDA approved adult daily dose.[1-19] The initial limits for amitriptyline/perphenazine 10 mg/4 mg, amoxapine 150 mg, clomipramine (Anafranil) 25 mg, 50 mg, 75 mg, doxepin (Silenor) 3 mg, 6 mg are set at the maximum daily dose. Additional quantities exceed the maximum daily dosage; therefore, no additional post limit quantities will be available for these drugs.

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Written by:	UM Development (NB) 02/2012
Revised:	10/2012 (extended duration), 12/2012 (shortened duration); (MS) 04/2013, 07/2013 (removed Tofranil NON-PM 75mg and 100mg); (CF) 11/2013, 11/2014, (LN) 04/2015 (added denial reasons); (CF) 11/2015; (MS) 11/2016 (removed 3 contraindication questions that were not leading to denials, added multi-single partial approval questions); (JG) 11/2017 (no clinical changes), (ME) 11/2018 (removed brand Limbitrol), 10/2019 (removed brand Elavil), 05/2020 (no clinical changes), 05/2021 (removed brand Surmontil), (TM) 05/2022 (removed brand Tofranil)
Reviewed:	Medical Affairs (KP) 02/2012, 10/2012, 04/2013; (LCB) 11/2013; (KJC) 11/2014; (LCB) 11/2015; (ME) 11/2016, (DNC) 10/2018, CHART 10/31/19, CHART 05/28/20, CHART 05/27/21, 05/26/22
External Review:	06/2012, 06/2013, 04/2014, 02/2015, 02/2016, 02/2017, 02/2018, 02/2019, 02/2020, 08/2020, 08/2021, 08/2022

CRITERIA FOR APPROVAL

1	Is this request for one of the following: A) amitriptyline/perphenazine 10 mg/4 mg, B) amoxapine 150 mg, C) clomipramine (Anafranil) 25 mg, 50 mg or 75 mg, D) doxepin (Silenor) 3 mg, 6 mg? [If yes, then no further questions. If no, go to 2.] [RPh Note: If yes, then deny. No override is required because no additional quantities are available with this post limit criteria.]	Yes	No
2	Has the patient experienced an inadequate treatment response or intolerance to at least TWO of the following agents: A) a serotonin-norepinephrine reuptake inhibitor (SNRI), B) a selective serotonin reuptake inhibitor (SSRI), C) mirtazapine, D) bupropion, E) trazodone? [If yes, go to 3. If no, then no further questions.]	Yes	No
3	Is this request for one of the following: [please check the one that applies, (brand or generic)] [] desipramine (Norpramin) for depression (If checked, go to 6) [] nortriptyline (Pamelor) for depression (If checked, go to 7) [] None of the above (If checked, go to 4)		
4	Has the patient experienced an inadequate treatment response or intolerance to desipramine (Norpramin) or nortriptyline (Pamelor)? [If yes, go to 5. If no, then no further questions.]	Yes	No
5	Is this request for one of the following: [please check the one that applies, (brand or generic)] [] amitriptyline for depression (If checked, go to 8) [] amitriptyline/chlordiazepoxide for depression associated with anxiety (If checked, go to 9)		

	[] amitriptyline/perphenazine for depression with anxiety and/or agitation (If checked, go to 10) [] amoxapine for depression (If checked, go to 11) [] doxepin for depression and/or anxiety (If checked, go to 12) [] imipramine hydrochloride for depression (If checked, go to 13) [] imipramine pamoate for depression (If checked, go to 14) [] protriptyline for depression (If checked, go to 15) [] trimipramine for depression (If checked, go to 16) [] None of the above (If checked, no further questions)		
6	Does the patient require MORE than the plan allowance PER MONTH of any of the following: A) 120 tablets of desipramine (Norpramin) 10 mg, 25 mg, 50 mg, B) 90 tablets of desipramine (Norpramin) 75 mg, 100 mg, C) 60 tablets of desipramine (Norpramin) 150 mg? [No further questions] [RPh Note: If yes, then deny and enter a partial approval for ONE of the following per 25 days: A) 120 tablets of desipramine (Norpramin) 10 mg, 25 mg, 50 mg, B) 90 tablets of desipramine (Norpramin) 75 mg, 100 mg, C) 60 tablets of desipramine (Norpramin) 150 mg.]	Yes	No
7	Does the patient require MORE than the plan allowance PER MONTH of any of the following: A) 180 capsules of nortriptyline (Pamelor) 10 mg, B) 90 capsules of nortriptyline (Pamelor) 25 mg, 50 mg, C) 60 capsules of nortriptyline (Pamelor) 75 mg, D) 2,250 mL of nortriptyline 10 mg/5mL solution? [No further questions] [RPh Note: If yes, then deny and enter a partial approval for ONE of the following per 25 days: A) 180 caps of nortriptyline (Pamelor) 10 mg, B) 90 caps of nortriptyline (Pamelor) 25 mg, 50 mg, C) 60 caps of nortriptyline (Pamelor) 75 mg, D) 2,250 mL of nortriptyline soln.]	Yes	No
8	Does the patient require MORE than the plan allowance PER MONTH of any of the following: A) 180 tablets of amitriptyline 10 mg, B) 120 tablets of amitriptyline 25 mg, C) 90 tablets of amitriptyline 50 mg, D) 60 tablets of amitriptyline 75 mg, E) 30 tablets of amitriptyline 100 mg, 150 mg? [No further questions] [RPh Note: If yes, then deny and enter a partial approval for ONE of the following per 25 days: A)180 tabs of amitriptyline 10mg, B)120 tabs of amitriptyline 25mg, C)90 tabs of amitriptyline 50mg, D)60 tabs of amitriptyline 75mg, E)30 tabs of amitriptyline 100mg, 150mg.]	Yes	No
9	Does the patient require MORE than the plan allowance PER MONTH of 180 tablets of amitriptyline/chlordiazepoxide 12.5 mg/5 mg or 25 mg/10 mg?	Yes	No

	[No further questions] [RPh Note: If yes, then deny and enter a partial approval per 25 days for 180 tablets of amitriptyline/chlordiazepoxide 12.5 mg/5 mg or 25 mg/10 mg.]		
10	Does the patient require MORE than the plan allowance PER MONTH of any of the following: A) 180 tablets of amitriptyline/perphenazine 10 mg/2 mg, B) 120 tablets of amitriptyline/perphenazine 25 mg/2 mg, 25 mg/4 mg, C) 90 tablets of amitriptyline/perphenazine 50 mg/4 mg? [No further questions] [RPh Note: If yes, then deny and enter a partial approval for ONE of the following per 25 days: A)180 tabs of amitriptyline/perphenazine 10mg/2mg, B)120 tabs of amitriptyline/perphenazine 25mg/2mg, 25mg/4mg, C)90 tabs of amitriptyline/perphenazine 50mg/4mg.]	Yes	No
11	Does the patient require MORE than the plan allowance PER MONTH of 120 tablets of amoxapine 25 mg, 50 mg, or 100 mg? [No further questions] [RPh Note: If yes, then deny and enter a partial approval per 25 days for 120 tablets of amoxapine 25 mg, 50 mg, 100 mg.]	Yes	No
12	Does the patient require MORE than the plan allowance PER MONTH of any of the following: A) 120 capsules of doxepin 10 mg, 25 mg, 50 mg, 75 mg, B) 90 capsules of doxepin 100 mg, C) 60 capsules of doxepin 150 mg, D) 900 mL of doxepin 10 mg/mL? [No further questions] [RPh Note: If yes, then deny and enter a partial approval for ONE of the following per 25 days: A) 120 capsules of doxepin 10 mg, 25 mg, 50 mg, 75 mg, B) 90 capsules of doxepin 100 mg, C) 60 capsules of doxepin 150 mg, D) 900 mL of doxepin 10 mg/mL solution.]	Yes	No
13	Does the patient require MORE than the plan allowance PER MONTH of any of the following: A) 150 tablets of imipramine hydrochloride 10 mg, 25 mg, B) 120 tablets of imipramine hydrochloride 50 mg? [No further questions] [RPh Note: If yes, then deny and enter a partial approval for ONE of the following per 25 days: A) 150 tablets of imipramine hydrochloride 10 mg, 25 mg, B) 120 tablets of imipramine hydrochloride 50 mg.]	Yes	No
14	Does the patient require MORE than the plan allowance PER MONTH of any of the following: A) 60 capsules of imipramine pamoate 75 mg, 100mg, B) 30 capsules of imipramine pamoate 125 mg, 150 mg? [No further questions] [RPh Note: If yes, then deny and enter a partial approval for ONE of the following per 25 days: A) 60 capsules of imipramine pamoate 75 mg, 100mg, B) 30 capsules of imipramine pamoate 125 mg, 150	Yes	No

	mg.]		
15	Does the patient require MORE than the plan allowance PER MONTH of any of the following: A) 120 tablets of protriptyline 5 mg, B) 180 tablets of protriptyline 10 mg? [No further questions] [RPh Note: If yes, then deny and enter a partial approval for ONE of the following per 25 days: A) 120 tablets of protriptyline 5 mg, B) 180 tablets of protriptyline 10 mg.]	Yes	No
16	Does the patient require MORE than the plan allowance PER MONTH of any of the following: A) 120 capsules of trimipramine 25 mg, 50 mg, B) 60 capsules of trimipramine 100 mg? [No further questions] [RPh Note: If yes, then deny and enter a partial approval for ONE of the following per 25 days: A) 120 capsules of trimipramine 25 mg, 50 mg, B) 60 capsules of trimipramine 100 mg.]	Yes	No

Mapping Instructions			
	Yes	**No**	**DENIAL REASONS**
1.	Deny, No override required. (No additional quantities are available on this post limit.) For the denial verbiage, only include the requested drug. Remove all the other drugs from the verbiage	Go to 2	You do not meet the requirements of your plan. Your plan covers a sufficient quantity of the requested drug up to a maximum of: - 120 tablets per month of amitriptyline/perphenazine 10 mg/4 mg - 60 tablets per month of amoxapine 150 mg - 150 capsules per month of clomipramine (Anafranil) 25 mg, 50 mg - 90 capsules per month of clomipramine (Anafranil) 75 mg - 30 tablets per month of doxepin (Silenor) 3 mg, 6 mg Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity]
2.	Go to 3	Deny	You do not meet the requirements of your plan. Your plan covers additional quantities of this drug when you tried 2 of the following: bupropion, mirtazapine, trazodone, a serotonin-norepinephrine reuptake inhibitor (SNRI), a selective serotonin reuptake inhibitor (SSRI) and they either did not work for you or you cannot use them. Your request has been denied based on the information we have. [Short Description: No inadequate response or intolerance to bupropion, mirtazapine, trazodone, SNRI, SSRI]
3.	1=6 ;2=7 ;3=4		
4.	Go to 5	Deny	You do not meet the requirements of your plan. Your plan covers additional quantities of this drug when you tried desipramine (Norpramin) or

			nortriptyline (Pamelor) and it either did not work for you or you cannot use it. [Short Description: No inadequate response or intolerance to desipramine (Norpramin) or nortriptyline (Pamelor)]
5.	1=8 ;2=9 ;3=10 ;4=11 ;5=12 ;6=13 ;7=14 ;8=15 ;9=16 ;10=Deny		You do not meet the requirements of your plan. Your plan covers additional quantities of this drug when you have any of these conditions: - Depression (amitriptyline, amoxapine, desipramine, imipramine hydrochloride, imipramine pamoate, nortriptyline, protriptyline, trimipramine) - Depression and/or anxiety (doxepin) - Depression with anxiety and/or agitation (amitriptyline/perphenazine) - Depression associated with anxiety (amitriptyline/chlordiazepoxide) Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]
6.	Deny	Approve, 12 Months, See Post Limit Quantity Chart	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to: - 120 tablets/month of desipramine (Norpramin) 10 mg, 25 mg or 50 mg - 90 tablets/month of desipramine (Norpramin) 75 mg or 100 mg - 60 tablets/month of desipramine (Norpramin) 150 mg You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity - desipramine]
7.	Deny	Approve, 12 Months, See Post Limit Quantity Chart	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to: - 180 capsules/month of nortriptyline (Pamelor) 10 mg - 90 capsules/month of nortriptyline (Pamelor) 25 mg or 50 mg - 60 capsules/month of nortriptyline (Pamelor) 75 mg - 2,250 mL /month of nortriptyline 10 mg/5mL solution You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity - nortriptyline (Pamelor)]
8.	Deny	Approve, 12 Months, See Post Limit Quantity Chart	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to: - 180 tablets/month of amitriptyline 10 mg - 120 tablets/month of amitriptyline 25 mg - 90 tablets/month of amitriptyline 50 mg - 60 tablets/month of amitriptyline 75 mg - 30 tablets/month of amitriptyline 100 mg or 150 mg You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity - amitriptyline]
9.	Deny	Approve, 12 Months, See	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 180 tablets/month of

		Post Limit Quantity Chart	amitriptyline/chlordiazepoxide 12.5 mg/5 mg or 25 mg/10 mg. You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity - amitriptyline/chlordiazepoxide]
10.	Deny	Approve, 12 Months, See Post Limit Quantity Chart	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to: - 180 tablets/month of amitriptyline/perphenazine 10 mg/2 mg - 120 tablets/month of amitriptyline/perphenazine 25 mg/2 mg or 25 mg/4 mg - 90 tablets/month of amitriptyline/perphenazine 50 mg/4 mg You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity - amitriptyline/perphenazine]
11.	Deny	Approve, 12 Months, See Post Limit Quantity Chart	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 120 tablets/month of amoxapine 25 mg, 50 mg, or 100 mg. You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity - amoxapine]
12.	Deny	Approve, 12 Months, See Post Limit Quantity Chart	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to: - 120 capsules/month of doxepin 10 mg, 25 mg, 50 mg or 75 mg - 90 capsules/month of doxepin 100 mg - 60 capsules/month of doxepin 150 mg - 900 mL/month of doxepin 10 mg/mL solution You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity - doxepin]
13.	Deny	Approve, 12 Months, See Post Limit Quantity Chart	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to: - 150 tablets/month of imipramine hydrochloride 10 mg or 25 mg - 120 tablets/month of imipramine hydrochloride 50 mg You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity - imipramine hydrochloride]
14.	Deny	Approve, 12 Months, See Post Limit Quantity Chart	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to: - 60 capsules/month of imipramine pamoate 75 mg or 100mg - 30 capsules/month of imipramine pamoate 125 mg or 150 mg. You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied.

			[Short Description: Over max quantity - imipramine pamoate]
15.	Deny	Approve, 12 Months, See Post Limit Quantity Chart	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to: - 120 tablets/month of protriptyline 5 mg - 180 tablets/month of protriptyline 10 mg You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity - protriptyline]
16.	Deny	Approve, 12 Months, See Post Limit Quantity Chart	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to: - 120 capsules/month of trimipramine 25 mg or 50 mg - 60 capsules/month of trimipramine 100 mg You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity - trimipramine]

POST LIMIT QUANTITY**

Generic Drug (Brand if available)	Strength	1 Month Limit *	3 Month Limit *
amitriptyline	10 mg	180 tabs/25 days	540 tabs/75 days
amitriptyline	25 mg	120 tabs/25 days	360 tabs/75 days
amitriptyline	50 mg	90 tabs/25 days	270 tabs/75 days
amitriptyline	75 mg	60 tabs/25 days	180 tabs/75 days
amitriptyline	100 mg, 150 mg	30 tabs/25 days	90 tabs/75 days
amitriptyline/chlordiazepoxide	12.5 mg/5 mg, 25 mg/10 mg	180 tabs/25 days	540 tabs/75 days
amitriptyline/perphenazine	10 mg/2 mg	180 tabs/25 days	540 tabs/75 days
amitriptyline/perphenazine	25 mg/2 mg, 25 mg/4 mg, 10 mg/4 mg	120 tabs/25 days	360 tabs/75 days
amitriptyline/perphenazine	50 mg/4 mg	90 tabs/25 days	270 tabs/75 days
amoxapine	25 mg, 50 mg, 100 mg	120 tabs/25 days	360 tabs/75 days
amoxapine	150 mg	60 tabs/25 days	180 tabs/75 days
clomipramine (Anafranil)	25 mg, 50 mg	150 caps/25 days	450 caps/75 days
clomipramine (Anafranil)	75 mg	90 caps/25 days	270 caps/75 days
desipramine (Norpramin)	10 mg, 25 mg, 50 mg	120 tabs/25 days	360 tabs/75 days
desipramine (Norpramin)	75 mg, 100 mg	90 tabs/25 days	270 tabs/75 days
desipramine (Norpramin)	150 mg	60 tabs/25 days	180 tabs/75 days
doxepin (Silenor)	3 mg, 6 mg	30 tabs/25 days	90 tabs/75 days
doxepin	10 mg, 25 mg, 50 mg, 75 mg	120 caps/25 days	360 caps/75 days
doxepin	100 mg	90 caps/25 days	270 caps/75 days
doxepin	150 mg	60 caps/25 days	180 caps/75 days
doxepin	10 mg/mL	900 mL/25 days	2,700 mL/75 days
imipramine hydrochloride	10 mg, 25 mg	150 tabs/25 days	450 tabs/75 days
imipramine hydrochloride	50 mg	120 tabs/25 days	360 tabs/75 days
imipramine pamoate	75 mg, 100 mg	60 caps/25 days	180 caps/75 days
imipramine pamoate	125 mg, 150 mg	30 caps/25 days	90 caps/75 days

nortriptyline (Pamelor)	10 mg	180 caps/25 days	540 caps/75 days
nortriptyline (Pamelor)	25 mg, 50 mg	90 caps/25 days	270 caps/75 days
nortriptyline (Pamelor)	75 mg	60 caps/25 days	180 caps/75 days
nortriptyline	10 mg/5mL	2,250 mL/25 days	6,750 mL/75 days
protriptyline	5 mg	120 tabs/25 days	360 tabs/75 days
protriptyline	10 mg	180 tabs/25 days	540 tabs/75 days
trimipramine	25 mg, 50 mg	120 caps/25 days	360 caps/75 days
trimipramine	100 mg	60 caps/25 days	180 caps/75 days
** The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*			

** The initial limits for amitriptyline/perphenazine 10 mg/4 mg, amoxapine 150 mg, clomipramine (Anafranil) 25 mg, 50 mg, 75 mg, doxepin (Silenor) 3 mg, 6 mg are set at the maximum daily dose. Additional quantities exceed the maximum daily dosage; therefore, no additional post limit quantities will be available for this drug.

Reference number(s)
2773-A

SPECIALTY GUIDELINE MANAGEMENT

TEGSEDI (inotersen)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Tegsedi is indicated for the treatment of the polyneuropathy of hereditary transthyretin-mediated amyloidosis in adults.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
A. Testing or analysis confirming a mutation of the TTR gene
B. Medical record documentation confirming the member demonstrates signs and symptoms of polyneuropathy and an improvement in these signs and symptoms since starting therapy for continuation

III. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with a neurologist, geneticist, or physician specializing in the treatment of amyloidosis.

IV. CRITERIA FOR INITIAL APPROVAL

Polyneuropathy of Hereditary Transthyretin-mediated Amyloidosis
Authorization of 12 months may be granted for treatment of polyneuropathy of hereditary transthyretin-mediated amyloidosis (also called transthyretin-type familial amyloid polyneuropathy [ATTR-FAP]) when all of the following criteria are met:
A. The diagnosis is confirmed by detection of a mutation of the TTR gene.
B. Member exhibits clinical manifestations of ATTR-FAP (e.g., amyloid deposition in biopsy specimens, TTR protein variants in serum, progressive peripheral sensory-motor polyneuropathy).
C. The member is not a liver transplant recipient.
D. The requested medication will not be used in combination with patisiran (Onpattro), tafamidis (Vyndaqel, Vyndamax) or vutrisiran (Amvuttra).

V. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for the continued treatment of ATTR-FAP when all of the following criteria are met:

A. The member must have met all initial authorization criteria.
B. The member must have demonstrated a beneficial response to treatment with Tegsedi therapy compared to baseline (e.g., improvement of neuropathy severity and rate of disease progression as demonstrated by the modified Neuropathy Impairment Scale+7 (mNIS+7) composite score, the Norfolk Quality of Life-Diabetic Neuropathy (QoL-DN) total score, polyneuropathy disability (PND) score, FAP disease stage, manual grip strength). Documentation from the medical record must be provided.

VI. REFERENCES

1. Tegsedi [package insert]. Waltham, MA: Sobi, Inc.; June 2022.
2. Benson MD, et. al., Inotersen Treatment for Patients with Hereditary Transthyretin Amyloidosis. N Engl J Med. 2018 Jul 5; 379(1):22-31.
3. Ando Y, Coelho T, Berk JL, Cruz MW, Ericzon BG, Ikeda S, Lewis WD, Obici L, Planté-Bordeneuve V, Rapezzi C, et al. Guideline of transthyretin-related hereditary amyloidosis for clinicians. Orphanet J Rare Dis. 2013; 8:31.
4. Sekijima Y. Hereditary Transthyretin Amyloidosis. 2001 Nov 5 [Updated 2021 June 17]. In: Adam MP, Ardinger HH, Pagon RA, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2022. Available from: https://www.ncbi.nlm.nih.gov/books/NBK1194/. Accessed April 1, 2022.

Reference number(s)
1665-A

SPECIALTY GUIDELINE MANAGEMENT

Temodar (temozolomide)
temozolomide (generic)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
1. Newly Diagnosed Glioblastoma
   Temodar is indicated for the treatment of adult patients with newly diagnosed glioblastoma concomitantly with radiotherapy and then as maintenance treatment.

2. Refractory Anaplastic Astrocytoma
   Temodar is indicated for the treatment of adult patients with refractory anaplastic astrocytoma who have experienced disease progression on a drug regimen containing nitrosourea and procarbazine.

B. Compendial Uses
1. Central nervous system (CNS) cancer
2. Ewing sarcoma
3. Neuroendocrine tumors of the pancreas, gastrointestinal tract, lung, and thymus
4. Well-differentiated grade 3 neuroendocrine tumors
5. Poorly differentiated (high grade) neuroendocrine carcinoma/large or small cell carcinoma
6. Pheochromocytoma/paraganglioma
7. Cutaneous melanoma
8. Uveal melanoma
9. Mycosis fungoides (MF)/Sézary syndrome (SS)
10. Small cell lung cancer
11. Soft tissue sarcoma
12. Uterine sarcoma

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Central nervous system (CNS) cancer
Authorization of 12 months may be granted for treatment of CNS cancers.

B. Ewing sarcoma
Authorization of 12 months may be granted for treatment of Ewing sarcoma.

C. Neuroendocrine tumors
Authorization of 12 months may be granted for treatment of neuroendocrine tumors.

D. Poorly differentiated (high-grade) neuroendocrine carcinoma/large or small cell carcinoma
Authorization of 12 months may be granted for treatment of poorly differentiated (high-grade) neuroendocrine carcinoma or large or small cell carcinoma.

E. Pheochromocytoma/paraganglioma
Authorization of 12 months may be granted for treatment of pheochromocytoma or paraganglioma.

F. Cutaneous Melanoma
Authorization of 12 months may be granted for treatment of cutaneous melanoma for metastatic or unresectable disease.

G. Uveal Melanoma
Authorization of 12 months may be granted for treatment of uveal melanoma for distant metastatic disease.

H. Mycosis fungoides (MF)/Sézary syndrome (SS)
Authorization of 12 months may be granted for treatment of MF or SS.

I. Small cell lung cancer (SCLC)
Authorization of 12 months may be granted for treatment of SCLC.

J. Soft tissue sarcoma (STS)
Authorization of 12 months may be granted for treatment of STS.

K. Uterine sarcoma
Authorization of 12 months may be granted for treatment of uterine sarcoma.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

IV. REFERENCES

1. Temodar [package insert]. Whitehouse Station, NJ: Merck & Co., Inc.; November 2019.
2. Temozolomide [package insert]. Durham, NC: Accord Healthcare, Inc.; October 2021.
3. The NCCN Drugs & Biologics Compendium® © 2022 National Comprehensive Cancer Network, Inc. Available at: https://www.nccn.org. Accessed January 12, 2022.

Reference number(s)
4492-A

SPECIALTY GUIDELINE MANAGEMENT

TEPMETKO (tepotinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication
Tepmetko is indicated for the treatment of adult patients with metastatic non-small cell lung cancer (NSCLC) harboring mesenchymal-epithelial transition (MET) exon 14 skipping alterations.

B. Compendial Use
Non-small cell lung cancer

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: Documentation of a mutation that leads to mesenchymal-epithelial transition (MET) exon 14 skipping or MET amplification in tumor or plasma specimens.

III. CRITERIA FOR INITIAL APPROVAL

Non-small cell lung cancer
Authorization of 12 months may be granted for treatment of NSCLC when either of the following criteria are met:
A. The requested medication will be used as a single agent for advanced or metastatic NSCLC with MET exon 14 skipping positive tumors.
B. The requested medication will be used for NSCLC with high-level MET amplification.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

V. REFERENCES

1. Tepmetko [package insert]. Rockland, MA: EMD Serono, Inc.; February 2021.
2. The NCCN Drugs & Biologics Compendium® © 2022 National Comprehensive Cancer Network, Inc. Available at: https://www.nccn.org. Accessed July 6, 2022.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME*
(generic)

(terbinafine tablets)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization ***Ref # 364-A***

** Drugs that are listed in the target drug box include both brand and generic and all dosages forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Terbinafine tablets are indicated for the treatment of onychomycosis of the toenail or fingernail due to dermatophytes (tinea unguium).
Prior to initiating treatment, appropriate nail specimens for laboratory testing [potassium hydroxide (KOH) preparation, fungal culture, or nail biopsy] should be obtained to confirm the diagnosis of onychomycosis.

Compendial Uses
Tinea Capitis[2-4]
Tinea Corporis[2,4], Tinea Cruris[2,4] –extensive disease, dermatophyte folliculitis is present, did not respond to topical therapy, is immunocompromised

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for the treatment of onychomycosis due to dermatophytes (tinea unguium) confirmed by a fungal diagnostic test (e.g., potassium hydroxide [KOH] preparation, fungal culture, or nail biopsy)
  OR
- The requested drug is being prescribed for the treatment of tinea capitis
  OR
- The requested drug is being prescribed for the treatment of tinea corporis or tinea cruris
  AND
  - The patient meets any of the following: A) has extensive disease, B) dermatophyte folliculitis is present, C) did not respond to topical therapy, D) is immunocompromised

  AND
- The requested drug is not being used in a footbath

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Terbinafine tablets are indicated for the treatment of onychomycosis of the toenail or fingernail due to dermatophytes (tinea unguium). Prior to initiating treatment, appropriate nail specimens for laboratory testing (KOH preparation, fungal culture, or nail biopsy) should be obtained to confirm the diagnosis of onychomycosis.[1]

Accurate diagnosis of onychomycosis involves physical and microscopic examination and culture. Only 50% of nail problems are caused by onychomycosis, and clinical diagnosis by physical examination alone can be inaccurate. When onychomycosis is suspected, samples should be taken to conduct diagnostic tests. Samples are then prepared with potassium hydroxide (KOH) solution to be viewed under a microscope to look for the presence of a fungal infection. Once fungal infection is confirmed, cultures can then be performed to identify the organism causing the infection.[5]

The recommended dosage for fingernail onychomycosis is one 250 mg tablet once daily for 6 weeks. The recommended dosage for toenail onychomycosis is one 250 mg tablet once daily for 12 weeks.[1]

The compendia support use of oral terbinafine in the treatment of Tinea capitis. Tinea capitis requires treatment with an oral antifungal; however, topical therapies are sometimes used as adjuncts to oral antifungal treatment.[2] According to the American Academy of Family Physicians, griseofulvin has been the first-line treatment for Tinea capitis for many years due to its long track record of safety and effectiveness. However, randomized clinical trials have confirmed that newer agents, such as terbinafine, have equal effectiveness and safety and shorter treatment courses. Terbinafine may be superior to griseofulvin for *Trichophyton* species, whereas griseofulvin may be superior to terbinafine for the less common *Microsporum* species. Because 95% of Tinea capitis cases in the United States are caused by *Trichophyton* species, terbinafine is a reasonable first choice for treatment. The recommended dosage for Tinea capitis is 125 mg once daily for patients weighing less than 25 kg, 187.5 mg once daily for patients weighing 25 to 35 kg and 250 mg once daily for patients weighing more than 35 kg for 6 weeks.[4]

Per the compendia, oral terbinafine has been used for the treatment of tinea corporis or tinea cruris.[2] Topical antifungals usually are effective for the treatment of uncomplicated tinea corporis. An oral antifungal (griseofulvin, fluconazole, itraconazole, terbinafine) may be necessary if tinea corporis is extensive, dermatophyte folliculitis is present, the infection does not respond to topical therapy or the patient is immunocompromised because of coexisting disease or concomitant therapy. Additionally, the American Academy of Family Physicians states that although tinea corporis and tinea cruris are generally responsive to topical antifungals, an oral antifungal agent (i.e., griseofulvin, fluconazole, itraconazole, terbinafine) may be indicated for extensive disease, failed topical treatment and immunocompromised patients.[4] Oral Lamisil (terbinafine) tablets are given in a dosage of 250 mg daily for 2 to 4 weeks for the treatment of tinea corporis or tinea cruris.[2]

Approval duration will be 3 months to account for the dosing regimens for all indications.

The prior authorization criteria do not approve terbinafine for use in a footbath, as this is not an FDA-approved use.

REFERENCES

1. Terbinafine tablets [package insert]. Warren, NJ: Cipla USA, Inc.; January 2021.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2021; Accessed August 5, 2021.
3. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed August 5, 2021.
4. Ely, JW, Rosenfeld, S, Stone, MS. Diagnosis and Management of Tinea Infections. American Family Physician 2014;90(10):702-712.
5. Westerberg, DP, Voyack MJ. Onychomycosis: Current Trends in Diagnosis and Treatment. American Family Physician 2013;88(11):762-70.

Written by:	UM Development (NB)
Date Written:	12/2008
Revised:	(SE) 07/2009, (TM) 07/2010, 10/2010; (SE) 12/2010 (removed requirement for no use previous 12 mo per CMS file submission), (TM) 08/2011; (RP) 08/2012, (TM) 08/2013, 08/2014; (MS) 05/2015, 05/2016 (removed Terbinex kit). (SF) 05/2017 (combined questions); (KC) 04/2018, (ME) 02/2019 (no clinical changes), (DFW) 02/2020 (removed MDC designation from title/document), 08/2020 (updated denial reasons); (PM) 12/2020 (added footbath question), 09/2021 (no clinical changes)
Reviewed:	CDPR/Medical Affairs (WF) 12/2008, 07/2009, (KP) 07/2010, 10/2010, (KP) 08/2011; (DC) 08/2012, (DC) 09/2013, (LMS) 08/2014; (KC) 05/2015; (JG) 05/2017; (DC) 04/2018, (CHART) 02/27/2020, 12/31/2020, 09/30/2021 External Review 12/2008, 10/2009, 12/2010, 12/2011, 12/2012, 12/2013, 10/2014, 10/2015, 08/2016, 08/2017, 06/2018, 06/2019, 06/2020, 04/2021, 12/2021

CRITERIA FOR APPROVAL

1	Is the requested drug being prescribed for the treatment of onychomycosis due to dermatophytes (tinea unguium) confirmed by a fungal diagnostic test (e.g., potassium hydroxide [KOH] preparation, fungal culture or nail biopsy)? [If yes, then skip to question 5.]	Yes	No

2	Is the requested drug being prescribed for the treatment of tinea capitis? [If yes, then skip to question 5.]	Yes	No
3	Is the requested drug being prescribed for the treatment of tinea corporis or tinea cruris? [If no, then no further questions.]	Yes	No
4	Does the patient meet any of the following: A) has extensive disease, B) dermatophyte folliculitis is present, C) did not respond to topical therapy, D) is immunocompromised? [If no, then no further questions.]	Yes	No
5	Is the requested drug being used in a footbath?	Yes	No

Mapping Instructions				
	Yes	**No**	**DENIAL REASONS (Non-Medicaid, Non-Medicare Part D)**	**DENIAL REASONS (Medicaid)**
1.	Go to 5	Go to 2		
2.	Go to 5	Go to 3		
3.	Go to 4	Deny	Coverage for this medication is denied for the following reason(s). We reviewed the information we received about your condition and circumstances. We used the policy (INSERT CRITERIA NAME) when making this decision. The policy states that this medication may be approved when the member has any of the following diagnoses: -A fungal infection of the nail which has been confirmed by fungal diagnostic testing (e.g., potassium hydroxide preparation, fungal culture, or nail biopsy) -A fungal infection of the scalp (tinea capitis) -A fungal infection of the body or groin (tinea corporis or tinea cruris). Based on the policy and the information we have, the request is denied. The information provided to us indicates that you do not have a diagnosis listed above. [Short Description: No approvable diagnosis]	You do not meet the requirements of your plan. Your plan covers this drug when you meet any of these conditions: - You have a specific fungal infection of the nail and you had a test to confirm the fungus - You have a fungal infection of the scalp - You have a fungal infection of the body or groin Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]
4.	Go to 5	Deny	Coverage for this medication is denied for the following reason(s). We reviewed the information we received about your condition and circumstances. We used the policy (INSERT CRITERIA NAME) when making this decision. The policy states that this medication may be approved when the member has a diagnosis of a fungal infection of the body or groin (tinea corporis or tinea cruris) and meets any of the following conditions:	You do not meet the requirements of your plan. You plan covers this drug when you are using it for a fungal infection of the body or groin and you have any of the following: - Extensive disease - The hair follicle is inflamed - You did not respond to topical treatment - You have a weak immune system Your request has been denied based on the information we have.

			-Extensive fungal infection -Dermatophyte folliculitis -The condition did not respond to topical therapy -The member is immunocompromised. Based on the policy and the information we have, the request is denied. The information provided to us indicates that you are requesting the drug for a fungal infection of the body or groin (tinea corporis or tinea cruris) but do not meet any of the conditions listed above. [Short Description: No conditions beyond diagnosis]	[Short Description: No indication for oral therapy]
5.	Deny	Approve, 3 months	Coverage for this medication is denied for the following reason(s). We reviewed the information we received about your condition and circumstances. We used the policy (INSERT CRITERIA NAME) when making this decision. The policy states that this medication may be approved when the member is not using this drug in a footbath. Based on the policy and the information we have, the request is denied. The information provided to us indicates that you are requesting this drug for use in a footbath. [Short Description: Use in footbath]	You do not meet the requirements of your plan. Your plan covers this drug when it is not being used in a footbath. Your request has been denied based on the information we have. [Short Description: Use in footbath]

These criteria apply to the following:			
✓ ACF	✓ BC	☐ MMT	✓ Aetna FI ACF
✓ ACFC	✓ BCC	☐ Marketplace (MF)	✓ Aetna FI ACFC
✓ SF	✓ VF	☐ Aetna SG ACA (Aetna Health Exchanges)	☐ Aetna FI SOO
✓ SFC	✓ VFC	☐ Aetna IVL	

MEDICAL NECESSITY CRITERIA

DIABETIC TEST STRIPS (NON-PREFERRED)

Status: CVS Caremark Criteria
Type: Medical Necessity Criteria ***Ref # 1520-A***

COVERAGE CRITERIA
The requested non-preferred diabetic test strips will be covered with prior authorization when the following criteria are met:

- The patient cannot be switched to a preferred product (Available Formulary Alternatives: Accu-Chek and OneTouch products)

AND

- The request is for a Contour test strip product for use in association with a MiniMed insulin pump or OmniPod Dash insulin pump. Documentation is required for approval.

OR

- The request is for a Freestyle test strip product for use in association with an OmniPod insulin pump

OR

- The patient has an insulin pump that is incompatible with an Accu-Chek or OneTouch product

RATIONALE
All non-preferred diabetic test strips should be targeted within this criterion. The intent is to allow a participant to receive a non-preferred diabetic test strip if the patient cannot be switched to a preferred product and if the patient is using a diabetic test strip product that can only be used with a compatible pump.

REFERENCES
N/A

Written by:	UM Development (JK/NB)
Date Written:	10/2016 (combined 719-A, 1021-A and 1153-A per PA Admin team)
Revised:	(ME) 10/2017 (added MiniMed 670G), 09/2018 (criteria will apply to all non-preferred test strips), 09/2019 (added pump specific questions), (MAC) 11/2019 (added BF to title, no clinical changes), (ME) 01/2020 (added OmniPod Dash), 08/2020 (updated denial reasons), 09/2020 (added documentation requirements), 09/2020 (changed preferred products to OneTouch and updated questions), 10/2020 (added continuation question for Accu-check grandfathering), 12/2020 (updated denial reasons), 01/2021 (added MiniMed 770G with documentation requirements to #8), 01/2021 (updated document title with VF), 04/2021 (added Accu-Chek as preferred in addition to OneTouch), 09/2021 (no clinical changes); (MRS) 04/2022 (added BC and BCC to title and LOB header, no clinical changes); (ASA) 08/2022 (removed BF from title and LOB header, no clinical changes)
Reviewed:	Medical Affairs: (ME) 10/2016, (AM) 10/2017, (DNC) 10/2018, (AN) 10/2019, (AN) 02/2020, (AN) 09/2020, (AN) 10/2020, (AN) 01/2021, (AN) 01/2021, (CHART) 05/13/21, (CHART) 09/30/21, 08/25/2022 MD Committee: 12/2021, 08/2022 External Review: 06/2022 (FYI), 12/2022 (MD Subcommittee)

These criteria apply to the following:			
✓ ACF	✓ BC	☐ MMT	✓ Aetna FI ACF
✓ ACFC	✓ BCC	☐ Marketplace (MF)	✓ Aetna FI ACFC
✓ SF	✓ VF	☐ Aetna SG ACA (Aetna Health Exchanges)	☐ Aetna FI SOO
✓ SFC	✓ VFC	☐ Aetna IVL	

CRITERIA FOR APPROVAL

1	Preferred products are available at a lower cost. Can your patient be switched to a preferred product? Available Formulary Alternatives: Accu-Chek and OneTouch products [If yes, provide your patient with a new prescription for the preferred product.] [If yes, then no further questions.] [Tech Note: If the prescriber agrees to switch to a preferred product, inform the prescriber that coverage for the prescribed, non-preferred product is not provided.]	Yes	No
2	Is the request for a Contour test strip product? [If no, then skip to question 4.]	Yes	No
3	Are the Contour test strips for use in association with a MiniMed insulin pump or OmniPod Dash insulin pump? [If yes, then documentation is required for approval.] Document the insulin pump the patient is using: _____ [No further questions.]	Yes	No
4	Is the request for a Freestyle test strip product? [If no, then skip to question 6.]	Yes	No
5	Are the Freestyle test strips for use in association with an OmniPod insulin pump? [No further questions.]	Yes	No
6	Does the patient have an insulin pump that is incompatible with an Accu-Chek or OneTouch product?	Yes	No

Mapping Instructions				
	Yes	**No**	**DENIAL REASONS (Non-Medicaid, Non-Medicare Part D)**	**DENIAL REASONS (Medicaid)**
1.	Deny, Inform prescriber to provide patient with a new prescription for the preferred product.	Go to 2	Coverage for this product is denied for the following reason(s). We reviewed the information we received about your condition and circumstances. We used the policy (INSERT CRITERIA NAME) when making this decision. The policy states that this product may be approved when the member cannot be changed to an Accu-Chek or OneTouch product. Based on the policy and the information we have, the request is denied. The	You do not meet the requirements of your plan. Your plan covers the requested test strips when you cannot be switched to an Accu-Chek or OneTouch product. Your request has been denied based on the information we have. [Short Description: Therapy can be switched]

These criteria apply to the following:			
✓ ACF	✓ BC	☐ MMT	✓ Aetna FI ACF
✓ ACFC	✓ BCC	☐ Marketplace (MF)	✓ Aetna FI ACFC
✓ SF	✓ VF	☐ Aetna SG ACA (Aetna Health Exchanges)	☐ Aetna FI SOO
✓ SFC	✓ VFC	☐ Aetna IVL	

			information provided to us indicates that you can be changed to an Accu-Chek or OneTouch product. [Short Description: Therapy can be switched]	
2.	Go to 3	Go to 4		
3.	Approve, 12 months	Deny	Coverage for this product is denied for the following reason(s). We reviewed the information we received about your condition and circumstances. We used the policy (INSERT CRITERIA NAME) when making this decision. The policy states that a Contour product may be approved when the doctor provides documentation that the member has a MiniMed insulin pump or OmniPod Dash insulin pump. Based on the policy and the information we have, the request is denied. The information provided to us indicates that you are requesting Contour test strips but your doctor did not provide documentation that you are using a MiniMed insulin pump or OmniPod Dash insulin pump. [Short Description: Contour, No documentation on MiniMed or OmniPod Dash]	You do not meet the requirements of your plan. Your plan covers this product if you have a MiniMed insulin pump or OmniPod Dash insulin pump that can only be used with a Contour product. Your request has been denied based on the information we have. [Short Description: Contour, No documentation on MiniMed or OmniPod Dash]
4.	Go to 5	Go to 6		
5.	Approve, 12 months	Deny	Coverage for this product is denied for the following reason(s). We reviewed the information we received about your condition and circumstances. We used the policy (INSERT CRITERIA NAME) when making this decision. The policy states that a Freestyle product may be approved when the member has an OmniPod insulin pump. Based on the policy and the information we have, the request is denied. The information provided to us indicates that you are requesting Freestyle test strips	You do not meet the requirements of your plan. Your plan covers this product if you have an OmniPod insulin pump that can only be used with a Freestyle product. Your request has been denied based on the information we have. [Short Description: Freestyle, Not using OmniPod]

These criteria apply to the following:			
✓ ACF	✓ BC	☐ MMT	✓ Aetna FI ACF
✓ ACFC	✓ BCC	☐ Marketplace (MF)	✓ Aetna FI ACFC
✓ SF	✓ VF	☐ Aetna SG ACA (Aetna Health Exchanges)	☐ Aetna FI SOO
✓ SFC	✓ VFC	☐ Aetna IVL	

			but are not using an OmniPod insulin pump. [Short Description: Freestyle, Not using OmniPod]	
6.	Approve, 12 months	Deny	Coverage for this product is denied for the following reason(s). We reviewed the information we received about your condition and circumstances. We used the policy (INSERT CRITERIA NAME) when making this decision. The policy states that the requested product may be approved when the member has an insulin pump which cannot be used with Accu-Chek or OneTouch products. Based on the policy and the information we have, the request is denied. The information provided to us indicates that you are not using an insulin pump which cannot be used with Accu-Chek or OneTouch products. [Short Description: Not using an incompatible pump]	You do not meet the requirements of your plan. Your plan covers this product if you have an insulin pump that cannot be used with Accu-Chek or OneTouch products. Your request has been denied based on the information we have. [Short Description: Not using an incompatible pump]

PRIOR AUTHORIZATION CRITERIA

DRUG CLASS	**TESTOSTERONE PRODUCTS**
BRAND NAME (generic)	
	ANDRODERM (testosterone transdermal patch)
	ANDROGEL (testosterone topical gel)
	DELATESTRYL (testosterone enanthate injection)
	DEPO-TESTOSTERONE (testosterone cypionate injection)
	FORTESTA (testosterone topical gel)
	JATENZO (testosterone undecanoate oral)
	KYZATREX (testosterone undecanoate oral)
	NATESTO (testosterone nasal gel)
	TESTIM (testosterone topical gel)
	TESTOPEL (testosterone propionate implant pellets)
	(testosterone topical solution)
	TLANDO (testosterone undecanoate oral)
	VOGELXO (testosterone topical gel)
	XYOSTED (testosterone enanthate)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

POLICY

FDA-APPROVED INDICATIONS

Androderm, AndroGel, Fortesta, Natesto, Testim, testosterone topical solution, Vogelxo

Topical, buccal, nasal, implant, and injectable testosterone products are indicated for replacement therapy in adult males for conditions associated with a deficiency or absence of endogenous testosterone.

Primary hypogonadism (congenital or acquired) - testicular failure due to conditions such as cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, orchiectomy, Klinefelter Syndrome, chemotherapy, or toxic damage from alcohol or heavy metals. These men usually have low serum testosterone concentrations and gonadotropins (FSH, LH) above the normal range.

Hypogonadotropic hypogonadism (congenital or acquired) - gonadotropin or luteinizing hormone-releasing hormone (LHRH) deficiency or pituitary-hypothalamic injury from tumors, trauma, or radiation. These men have low testosterone serum concentrations but have gonadotropins in the normal or low range.

Limitations of Use

Safety and efficacy of topical, buccal, nasal, implant, and injectable testosterone products in men with "age-related hypogonadism" (also referred to as "late-onset hypogonadism") have not been established.

Safety and efficacy of topical, buccal, nasal, implant, and injectable testosterone products in males less than 18 years old have not been established.

Topical testosterone products may have different doses, strengths or application instructions that may result in different systemic exposure.

Testosterone Enanthate Injection

Males

Testosterone Enanthate Injection (generic Delatestryl) is indicated for replacement therapy in conditions associated with a deficiency or absence of endogenous testosterone.

Primary hypogonadism (congenital or acquired) - testicular failure due to cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, or orchiectomy.

Hypogonadotropic hypogonadism (congenital or acquired) - gonadotropin or luteinizing hormone-releasing hormone (LHRH) deficiency, or pituitary-hypothalamic injury from tumors, trauma, or radiation. (Appropriate adrenal cortical and thyroid hormone replacement therapy are still necessary, however, and are actually of primary importance).

If the above conditions occur prior to puberty, androgen replacement therapy will be needed during the adolescent years for development of secondary sexual characteristics. Prolonged androgen treatment will be required to maintain sexual characteristics in these and other males who develop testosterone deficiency after puberty.

Safety and efficacy of Testosterone Enanthate Injection (generic Delatestryl) in men with "age-related hypogonadism" (also referred to as "late-onset hypogonadism") have not been established.

Delayed puberty - Testosterone Enanthate Injection (generic Delatestryl) may be used to stimulate puberty in carefully selected males with clearly delayed puberty. These patients usually have a familial pattern of delayed puberty that is not secondary to a pathological disorder; puberty is expected to occur spontaneously at a relatively late date. Brief treatment with conservative doses may occasionally be justified in these patients if they do not respond to psychological support. The potential adverse effect on bone maturation should be discussed with the patient and parents prior to androgen administration. An X-ray of the hand and wrist to determine bone age should be obtained every six months to assess the effect of treatment on the epiphyseal centers.

Females

Metastatic Mammary Cancer - Testosterone Enanthate Injection (generic Delatestryl) may be used secondarily in women with advancing inoperable metastatic (skeletal) mammary cancer who are one to five years postmenopausal. Primary goals of therapy in these women include ablation of the ovaries. Other methods of counteracting estrogen activity are adrenalectomy, hypophysectomy, and/or anti-estrogen therapy. This treatment has also been used in pre-menopausal

women with breast cancer who have benefited from oophorectomy and are considered to a have a hormone-responsive tumor. Judgment concerning androgen therapy should be made by an oncologist with expertise in this field.

Depo-Testosterone
Depo-Testosterone Injection is indicated for replacement therapy in the male in conditions associated with symptoms of deficiency or absence of endogenous testosterone.
Primary hypogonadism (congenital or acquired) - testicular failure due to cryptorchidism, bilateral torsion, orchitis, vanishing testes syndrome; or orchiectomy.
Hypogonadotropic hypogonadism (congenital or acquired) - gonadotropic or LHRH deficiency, or pituitary- hypothalamic injury from tumors, trauma or radiation.
Safety and efficacy of Depo-Testosterone (testosterone cypionate) in men with "age-related hypogonadism" (also referred to as "late-onset hypogonadism") have not been established.

Jatenzo, Kyzatrex, Tlando
Testosterone Undecanoate is an androgen indicated for testosterone replacement therapy in adult males for conditions associated with a deficiency or absence of endogenous testosterone:
Primary hypogonadism (congenital or acquired) - testicular failure due to conditions such as cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, orchiectomy, Klinefelter Syndrome, chemotherapy, or toxic damage from alcohol or heavy metals. These men usually have low serum testosterone concentrations and gonadotropins (follicle stimulating hormone (FSH), luteinizing hormone (LH)) above the normal range.
Hypogonadotropic hypogonadism (congenital or acquired) - gonadotropin or luteinizing hormone-releasing hormone (LHRH) deficiency or pituitary-hypothalamic injury from tumors, trauma, or radiation. These men have low testosterone serum concentrations but have gonadotropins in the normal or low range.

Limitations of Use
Safety and efficacy of Testosterone Undecanoate in males less than 18 years old have not been established.

Testopel
Males
Androgens are indicated for replacement therapy in conditions associated with a deficiency or absence of endogenous testosterone.
Primary hypogonadism (congenital or acquired) - testicular failure due to cryptorchidism, bilateral torsion, orchitis, vanishing testes syndrome; or orchiectomy.
Hypogonadotropic hypogonadism (congenital or acquired) - gonadotropic LHRH deficiency, or pituitary - hypothalamic injury from tumors, trauma or radiation.
If the above conditions occur prior to puberty, androgen replacement therapy will be needed during the adolescent years for development of secondary sex characteristics. Prolonged androgen treatment will be required to maintain sexual characteristics in these and other males who develop testosterone deficiency after puberty.
Safety and efficacy of Testopel (testosterone pellets) in men with "age-related hypogonadism" (also referred to as "late-onset hypogonadism") have not been established.
Androgens may be used to stimulate puberty in carefully selected males with clearly delayed puberty. These patients usually have a familial pattern of delayed puberty that is not secondary to a pathological disorder; puberty is expected to occur spontaneously at a relatively late date. Brief treatment with conservative doses may occasionally be justified in these patients if they do not respond to psychological support. The potential adverse effect on bone maturation should be discussed with the patient and parents prior to androgen administration. An x-ray of the hand and wrist to determine bone age should be taken every 6 months to assess the effect of treatment on epiphyseal centers.

Xyosted
Xyosted (testosterone enanthate) injection is an androgen indicated for testosterone replacement therapy in adult males for conditions associated with a deficiency or absence of endogenous testosterone:

- Primary hypogonadism (congenital or acquired): testicular failure due to cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, orchiectomy, Klinefelter's syndrome, chemotherapy, or toxic damage from alcohol or heavy metals. These men usually have low serum testosterone concentrations and gonadotropins (follicle-stimulating hormone [FSH], luteinizing hormone [LH]) above the normal range.

- Hypogonadotropic hypogonadism (congenital or acquired): gonadotropin or luteinizing hormone-releasing hormone (LHRH) deficiency or pituitary-hypothalamic injury from tumors, trauma, or radiation. These men have low testosterone serum concentrations but have gonadotropins in the low or normal range.

Limitations of Use
- Safety and efficacy of Xyosted in males less than 18 years of age have not been established.

Compendial Uses
Gender Dysphoria[16-17,20-23]

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is NOT being prescribed for age-related hypogonadism

AND

- The requested drug is being prescribed for primary or hypogonadotropic hypogonadism
  AND
  - Before the start of testosterone therapy, the patient has at least two confirmed low morning testosterone levels according to current practice guidelines or your standard lab reference values
    OR
  - For continuation of testosterone therapy: before the patient started testosterone therapy, the patient had a confirmed low morning testosterone level according to current practice guidelines or your standard lab reference values

OR

- The requested drug is being prescribed for gender dysphoria in a patient who is able to make an informed decision to engage in hormone therapy
  AND
  - For patients less than 18 years of age, the requested drug is prescribed by or in consultation with a provider specialized in the care of transgender youth (e.g., pediatric endocrinologist, family or internal medicine physician, obstetrician-gynecologist), that has collaborated care with a mental health provider
    AND
  - The patient's comorbid conditions are reasonably controlled
    AND
  - The patient has been educated on any contraindications and side effects to therapy
    AND
  - Before the start of therapy, the patient has been informed of fertility preservation options

OR

- Testosterone enanthate injection (generic Delatestryl) is being prescribed for inoperable metastatic breast cancer in a patient who is 1 to 5 years postmenopausal AND the patient had an incomplete response to other therapy for metastatic breast cancer

OR

- Testosterone enanthate injection (generic Delatestryl) is being prescribed for a premenopausal patient with breast cancer who has benefited from oophorectomy and is considered to a have a hormone-responsive tumor

OR

- Testosterone enanthate injection (generic Delatestryl) or testosterone propionate implant pellets (Testopel) is being prescribed for delayed puberty

REFERENCES

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3. Androgel 1.62% [package insert]. North Chicago, IL: Abbvie Inc; November 2020.
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Reference number(s)
2368-A

SPECIALTY GUIDELINE MANAGEMENT

THALOMID (thalidomide)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
1. Thalomid in combination with dexamethasone is indicated for the treatment of patients with newly diagnosed multiple myeloma (MM).
2. Erythema Nodosum Leprosum (ENL)
   a. Acute treatment of the cutaneous manifestations of moderate to severe ENL.
   b. Maintenance therapy for prevention and suppression of the cutaneous manifestations of ENL. recurrence

   Limitations of Use: Thalomid is not indicated as monotherapy for ENL treatment in the presence of moderate to severe neuritis.

B. Compendial Uses
1. Multiple Myeloma
2. Myelofibrosis-associated anemia
3. Multicentric Castleman disease
4. Aphthous stomatitis
5. Kaposi sarcoma
6. Chronic graft-versus-host disease
7. Crohn's disease
8. Histiocytic neoplasms
   i. Langerhans cell histiocytosis
   ii. Rosai-Dorfman disease

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Multiple Myeloma
Authorization of 12 months may be granted for treatment of multiple myeloma.

B. Myelofibrosis-associated Anemia
Authorization of 12 months may be granted for treatment of myelofibrosis-associated anemia when all of the following criteria are met:
1. The requested medication will be given in combination with prednisone
2. The member has serum erythropoietin (EPO) levels of either of the following:
   a. 500 mU/mL or greater
   b. Less than 500 mU/mL and no response or loss of response to erythropoiesis-stimulating agents

C. Erythema Nodosum Leprosum
Authorization of 12 months may be granted for treatment and prevention of erythema nodosum leprosum.

D. Crohn's Disease
Authorization of 12 months may be granted for treatment of Crohn's disease.

E. Kaposi Sarcoma
Authorization of 12 months may be granted for treatment of Kaposi sarcoma as subsequent therapy.

F. Chronic Graft-versus-Host Disease
Authorization of 12 months may be granted for treatment of chronic graft-versus-host disease.

G. Multicentric Castleman Disease
Authorization of 12 months may be granted for treatment of multicentric Castleman disease.

H. Aphthous Stomatitis
Authorization of 12 months may be granted for treatment of AIDS-related aphthous stomatitis and recurrent aphthous stomatitis in immunocompromised members.

I. Histiocytic Neoplasms
Authorization of 12 months may be granted for treatment of histiocytic neoplasms, including Langerhans cell histiocytosis and Rosai-Dorfman disease, as a single agent.

III. CONTINUATION OF THERAPY

A. Multiple Myeloma, Multicentric Castleman Disease, Histiocytic Neoplasms, and Kaposi sarcoma
Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for multiple myeloma, multicentric Castleman Disease, histiocytic neoplasms, or Kaposi sarcoma when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

B. All Other Indications
Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II, other than multiple myeloma, multicentric Castleman disease, histiocytic neoplasms, or Kaposi sarcoma, who have improvement in symptoms and no unacceptable toxicity.

IV. REFERENCES

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Reference number(s)
2635-A

SPECIALTY GUIDELINE MANAGEMENT

TIBSOVO (ivosidenib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Newly Diagnosed Acute Myeloid Leukemia
   Tibsovo is indicated in combination with azacitidine or as monotherapy for the treatment of newly-diagnosed acute myeloid leukemia (AML) with a susceptible isocitrate dehydrogenase-1 (IDH1) mutation as detected by an FDA-approved test in adult patients who are ≥ 75 years old or who have comorbidities that preclude use of intensive induction chemotherapy.

2. Relapsed or Refractory Acute Myeloid Leukemia
   Tibsovo is indicated for the treatment of adult patients with relapsed or refractory acute myeloid leukemia (AML) with a susceptible isocitrate dehydrogenase-1 (IDH1) mutation as detected by an FDA-approved test.

3. Locally Advanced or Metastatic Cholangiocarcinoma
   Tibsovo is indicated for the treatment of adult patients with previously treated, locally advanced or metastatic cholangiocarcinoma with an isocitrate dehydrogenase-1 (IDH1) mutation as detected by an FDA-approved test.

B. Compendial Uses

1. AML with an IDH1 mutation
2. Cholangiocarcinoma with an IDH1 mutation
3. Conventional (grades 1-3) or dedifferentiated chondrosarcoma with a susceptible IDH-1 mutation

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: medical record documentation of isocitrate dehydrogenase-1 (IDH1) mutation

III. CRITERIA FOR INITIAL APPROVAL

A. Acute Myeloid Leukemia (AML)

1. Authorization of 12 months may be granted for treatment of newly diagnosed AML with a susceptible IDH1 mutation when any of the following criteria is met:
   a. Member is 75 years of age or older and the requested medication will be used as a single agent or in combination with azacitidine
   b. Member has comorbidities that preclude the use of intensive induction chemotherapy and the requested medication will be used as a single agent or in combination with azacitidine
   c. Member is 60 years of age or older, declines intensive induction chemotherapy, and the requested medication will be used as a single agent

2. Authorization of 12 months may be granted for post-induction therapy for AML with a susceptible IDH1 mutation when all of the following criteria is met:
   a. The requested medication will be used as a single-agent
   b. Member is 60 years of age or older
   c. Member has experienced response to Tibsovo therapy

3. Authorization of 12 months may be granted for treatment of relapsed or refractory AML with a susceptible IDH1 mutation as a single agent.

B. Cholangiocarcinoma
Authorization of 12 months may be granted for subsequent treatment of unresectable, locally advanced or metastatic cholangiocarcinoma as a single agent in members with an IDH1 mutation.

C. Chondrosarcoma
Authorization of 12 months may be granted for treatment of conventional (grades 1-3) or dedifferentiated chondrosarcoma in members with a susceptible IDH1 mutation.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

V. REFERENCES

1. Tibsovo [package insert]. Boston, MA: Servier Pharmaceuticals LLC; May 2022.
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Reference number(s)
2991-A

SPECIALTY GUIDELINE MANAGEMENT

THIOLA (tiopronin)
THIOLA EC (tiopronin delayed release tablets)
tiopronin

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Thiola and Thiola EC are indicated, in combination with high fluid intake, alkali, and diet modification, for the prevention of cystine stone formation in adult and pediatric patients 20 kg and greater with severe homozygous cystinuria who are not responsive to these measures alone.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
A. Initial requests:
   1. Genetic testing results showing mutations in both alleles of the SLC3A1 or SLC7A9 genes; and
   2. Lab results documenting baseline urinary cystine levels.
B. Continuation of therapy requests: lab results documenting a decrease in urinary cystine levels compared to baseline.

III. CRITERIA FOR INITIAL APPROVAL

Cystinuria
Authorization of 12 months may be granted for prevention of cystine stone formation in a member with severe homozygous cystinuria (biallelic mutations/variants in the SLC3A1 or the SLC7A9 gene) when all of the following criteria are met:
A. Diagnosis of homozygous cystinuria (biallelic mutations/variants in the SLC3A1 or the SLC7A9 gene) was confirmed by genetic testing showing mutations in both alleles of the SLC3A1 or SLC7A9 genes.
B. The requested medication is being used as an adjunct to high fluid intake, alkali, and diet modification.
C. The member has elevated urinary cysteine levels at baseline.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment of severe cystinuria in members requesting reauthorization who have experienced a decrease in urinary cystine levels compared to pretreatment baseline.

V. REFERENCES

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Reference number(s)
1887-A

SPECIALTY GUIDELINE MANAGEMENT

tobramycin inhalation solution/TOBI
TOBI Podhaler (tobramycin inhalation powder)
Bethkis (tobramycin inhalation solution)
Kitabis Pak (tobramycin inhalation solution)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication
Management of cystic fibrosis in patients with *Pseudomonas aeruginosa*

B. Compendial Use
Pseudomonas aeruginosa lower respiratory tract infection in patients with non-cystic fibrosis bronchiectasis

All other indications are considered experimental/investigational and are not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Cystic Fibrosis
Authorization of 12 months may be granted for members 2 years of age and older with cystic fibrosis when *Pseudomonas aeruginosa* is present in airway cultures OR the member has a history of *Pseudomonas aeruginosa* infection or colonization in the airways.

B. Bronchiectasis (Non-Cystic Fibrosis)
Authorization of 12 months may be granted for members with non-cystic fibrosis bronchiectasis when *Pseudomonas aeruginosa* is present in airway cultures OR the member has a history of *Pseudomonas aeruginosa* infection or colonization in the airways.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II who are experiencing benefit from therapy as evidenced by disease stability or disease improvement.

IV. REFERENCES

1. Tobramycin inhalation solution [package insert]. Sellersville, PA: Teva Pharmaceuticals USA; April 2020.
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3. TOBI Podhaler [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; July 2020.
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Reference number
2181-A

SPECIALTY GUIDELINE MANAGEMENT

SAMSCA (tolvaptan)
tolvaptan (generic)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Treatment of clinically significant hypervolemic and euvolemic hyponatremia (serum sodium <125 mEq/L or less marked hyponatremia that is symptomatic and has resisted correction with fluid restriction), including patients with heart failure and Syndrome of Inappropriate Antidiuretic Hormone (SIADH)

Important Limitations
Patients requiring intervention to raise serum sodium urgently to prevent or to treat serious neurological symptoms should not be treated with Samsca/tolvaptan. It has not been established that raising serum sodium with Samsca/tolvaptan provides a symptomatic benefit to patients.

All other indications are considered experimental/investigational and are not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Hypervolemic/Euvolemic Hyponatremia
Authorization of 30 days may be granted for members prescribed the requested drug when all of the following criteria are met:
A. Therapy was initiated (or re-initiated) in the hospital, for hypervolemic or euvolemic hyponatremia; and
B. Serum sodium was less than 125 mEq/L or serum sodium was less than 135 mEq/L with symptoms (e.g., nausea, vomiting, headache, lethargy, confusion) at the time of therapy initiation; and
C. The member will not receive the requested drug continually for greater than 30 days.

III. REFERENCES

1. Samsca [package insert]. Rockville, MD: Otsuka America Pharmaceutical, Inc.; April 2021.
2. Tolvaptan [package insert]. Parsippany, NJ: Ascend Laboratories, LLC; May 2020.
3. Hoorn EJ, Zietse R. Diagnosis and treatment of hyponatremia: Compilation of the guidelines. *J Am Soc Nephol.* 2017; 28(5):1340-1349.

Reference number
2156-A

SPECIALTY GUIDELINE MANAGEMENT

TREMFYA (guselkumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

1. Treatment of adult patients with moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy
2. Treatment of adult patients with active psoriatic arthritis

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

A. Plaque psoriasis
   1. Initial requests:
      i. Chart notes or medical record documentation of affected area(s) and body surface area (BSA) affected.
      ii. Chart notes, medical record documentation, or claims history supporting previous medications tried (if applicable), including response to therapy. If therapy is not advisable, documentation of clinical reason to avoid therapy.
   2. Continuation requests: Chart notes or medical record documentation of decreased body surface area (BSA) affected and/or improvement in signs and symptoms.

B. Psoriatic arthritis: For continuation requests: Chart notes or medical record documentation supporting positive clinical response.

III. CRITERIA FOR INITIAL APPROVAL

A. Moderate to severe plaque psoriasis (PsO)

1. Authorization of 12 months may be granted for members who have previously received Otezla or a biologic indicated for the treatment of moderate to severe plaque psoriasis.

2. Authorization of 12 months may be granted for treatment of moderate to severe plaque psoriasis in members when any of the following criteria is met:
   i. Crucial body areas (e.g., hands, feet, face, neck, scalp, genitals/groin, intertriginous areas) are affected.
   ii. At least 10% of the body surface area (BSA) is affected.
   iii. At least 3% of body surface area (BSA) is affected and the member meets any of the following criteria:

a. Member has had an inadequate response or intolerance to either phototherapy (e.g., UVB, PUVA) or pharmacologic treatment with methotrexate, cyclosporine or acitretin.
b. Member has a clinical reason to avoid pharmacologic treatment with methotrexate, cyclosporine and acitretin (see Appendix).

B. Active psoriatic arthritis (PsA)
Authorization of 12 months may be granted for treatment of active psoriatic arthritis.

IV. CONTINUATION OF THERAPY

A. Moderate to severe plaque psoriasis (PsO)
Authorization of 12 months may be granted for all members (including new members) who are using the requested medication for moderate to severe plaque psoriasis and who achieve or maintain positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition when any of the following is met:
1. Reduction in body surface area (BSA) affected from baseline
2. Improvement in signs and symptoms from baseline (e.g., itching, redness, flaking, scaling, burning, cracking, pain)

B. Active psoriatic arthritis (PsA)
Authorization of 12 months may be granted for all members (including new members) who are using the requested medication for active psoriatic arthritis and who achieve or maintain positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition when there is improvement in any of the following from baseline:
1. Number of swollen joints
2. Number of tender joints
3. Dactylitis
4. Enthesitis
5. Skin and/or nail involvement

V. OTHER

For all indications: Member has had a documented negative TB test (which can include a tuberculosis skin test [PPD], an interferon-release assay [IGRA], or a chest x-ray)* within 6 months of initiating therapy for persons who are naïve to biologic DMARDs or targeted synthetic DMARDs associated with an increased risk of TB.

* If the screening testing for TB is positive, there must be further testing to confirm there is no active disease. Do not administer the requested medication to members with active TB infection. If there is latent disease, TB treatment must be started before initiation of the requested medication.

For all indications: Member cannot use the requested medication concomitantly with any other biologic DMARD or targeted synthetic DMARD.

VI. DOSAGE AND ADMINISTRATION

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

VII. APPENDIX

Examples of Clinical Reasons to Avoid Pharmacologic Treatment with Methotrexate, Cyclosporine or Acitretin

1. Clinical diagnosis of alcohol use disorder, alcoholic liver disease or other chronic liver disease
2. Breastfeeding
3. Drug interaction
4. Cannot be used due to risk of treatment-related toxicity
5. Pregnancy or currently planning pregnancy
6. Significant comorbidity prohibits use of systemic agents (examples include liver or kidney disease, blood dyscrasias, uncontrolled hypertension)

VIII. REFERENCES

1. Tremfya [package insert]. Horsham, PA: Janssen Biotech, Inc.; July 2020.
2. Menter A, Korman NJ, Elmets CA, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis. Section 4: Guidelines of care for the management and treatment of psoriasis with traditional systemic agents. *J Am Acad Dermatol.* 2009;61:451-485.
3. Menter A, Korman NJ, Elmets CA, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis. Section 6: Guidelines of care for the treatment of psoriasis and psoriatic arthritis: case-based presentations and evidence-based conclusions. *J Am Acad Dermatol*. 2011;65(1):137-174.
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PRIOR AUTHORIZATION CRITERIA

DRUG CLASS	**TOPICAL RETINOIDS**
BRAND NAME (generic)	
	ALTRENO (tretinoin)
	ATRALIN (tretinoin)
	AVITA (tretinoin)
	RETIN-A (tretinoin)
	RETIN-A MICRO (tretinoin)
	TWYNEO (tretinoin/benzoyl peroxide)
	VELTIN (clindamycin/tretinoin)
	ZIANA (clindamycin/tretinoin)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

POLICY

FDA-APPROVED INDICATIONS

Atralin, Avita, Retin-A
Atralin, Avita, and Retin-A are indicated for topical application in the treatment of acne vulgaris. The safety and efficacy of this product in the treatment of other disorders have not been established.

Altreno (tretinoin) lotion 0.05%, Twyneo
Altreno (tretinoin) lotion 0.05% and Twyneo are indicated for the topical treatment of acne vulgaris in patients 9 years of age and older.

Retin-A Micro
Retin-A Micro is indicated for topical application in the treatment of acne vulgaris.

Veltin, Ziana
Veltin and Ziana are indicated for the topical treatment of acne vulgaris in patients 12 years and older.

Compendial Uses
Keratosis follicularis (Darier's disease, Darier-White disease) [12,15-17]

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has a diagnosis of acne vulgaris

OR

- The patient has a diagnosis of keratosis follicularis (Darier's disease, Darier-White disease)

REFERENCES

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2. Atralin [package insert]. Bridgewater, NJ: Valeant Pharmaceuticals North America LLC; July 2016.
3. Avita Cream [package insert]. Morgantown, WV: Mylan Pharmaceuticals Inc.; June 2018.
4. Avita Gel [package insert]. Morgantown, WV: Mylan Pharmaceuticals Inc.; January 2018.
5. Refissa [package insert]. Irvine, CA: ZO Skin Health, Inc.; April 2020.
6. Renova [package insert]. Bridgewater, NJ: Bausch Health US, LLC; September 2019.
7. Retin-A [package insert]. Bridgewater, NJ: Bausch Health US, LLC; September 2019.
8. Retin-A Micro [package insert]. Bridgewater, NJ: Valeant Pharmaceuticals North America LLC; October 2017.
9. Twyneo [package insert]. Fort Worth, TX: Galderma Laboratories, L.P.; July 2021.
10. Veltin [package insert]. Malvern, PA: Almirall, LLC; June 2019.
11. Ziana [package insert]. Bridgewater, NJ: Valeant Pharmaceuticals North America LLC; March 2017.
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STEP THERAPY CRITERIA

BRAND NAME
(generic)

TREXIMET
(sumatriptan/naproxen)

Status: CVS Caremark Criteria
Type: Initial Step Therapy; Post Step Therapy Prior Authorization

POLICY

FDA-APPROVED INDICATIONS
Treximet is indicated for the acute treatment of migraine with or without aura in adults and pediatric patients 12 years of age and older.

Limitations of Use:
Use only if a clear diagnosis of migraine headache has been established. If a patient has no response to the first migraine attack treated with Treximet, reconsider the diagnosis of migraine before Treximet is administered to treat any subsequent attacks.
Treximet is not indicated for the prevention of migraine attacks.
Safety and effectiveness of Treximet have not been established for cluster headache.

INITIAL STEP THERAPY*
**Include Rx and OTC products unless otherwise stated.*

If the patient has filled a prescription for at least a 30-day supply of generic sumatriptan AND generic naproxen within the past 120 days under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit. If the patient does not meet the initial step therapy criteria, then the claim will reject with a message indicating that a prior authorization (PA) is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

COVERAGE CRITERIA
The requested drug will be covered with prior authorization when the following criteria are met:
- The patient has a diagnosis of migraine headache

AND
- The patient has tried and experienced an inadequate treatment response or intolerance to THREE 5-HT1 agonists (triptans)

AND
- The patient has tried sumatriptan taken with naproxen

REFERENCES

1. Treximet [package insert]. Morristown, NJ: Pernix Therapeutics, LLC; April 2021.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, Ohio: UpToDate, Inc.; 2022; Accessed June 1, 2022.
3. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed June 1, 2022.
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5. Oskoui M, Pringsheim T, Holler-Managen Y, et al. Practice guideline update: Acute treatment of migraine in children and adolescents: Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology and the American Headache Society. *Neurology* 2019;93:487-499.

Reference number(s)
3374-A

SPECIALTY GUIDELINE MANAGEMENT

TRIKAFTA (elexacaftor/tezacaftor/ivacaftor)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Trikafta is indicated for the treatment of cystic fibrosis (CF) in patients aged 6 years and older who have at least one *F508del* mutation in the cystic fibrosis transmembrane conductance regulator *(CFTR)* gene or a mutation in the *CFTR* gene that is responsive based on *in vitro* data.

If the patient's genotype is unknown, an FDA-cleared CF mutation test should be used to confirm the presence of at least one *F508del* mutation or a mutation that is responsive based on in vitro data.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: genetic testing report confirming the presence of the appropriate *CFTR* gene mutation.

III. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with a pulmonologist.

IV. CRITERIA FOR INITIAL APPROVAL

Cystic Fibrosis
Authorization of 12 months may be granted for treatment of cystic fibrosis when all of the following criteria are met:
A. Genetic testing was conducted to detect a mutation in the *CFTR* gene.
B. The member has one of the following mutations in the *CFTR* gene: A46D, A120T, A234D, A349V, A455E, A554E, A1006E, A1067T, D110E, D110H, D192G, D443Y, D443Y;G576A;R668C, D579G, D614G, D836Y, D924N, D979V, D1152H, D1270N, E56K, E60K, E92K, E116K, E193K, E403D, E474K, E588V, E822K, F191V, F311del, F311L, F508C, F508C;S1251N, F508del, F575Y, F1016S, F1052V, F1074L, F1099L, G27R, G85E, G126D, G178E, G178R, G194R, G194V, G314E, G463V, G480C, G551D, G551S, G576A, G576A;R668C, G622D, G628R, G970D, G1061R, G1069R, G1244E, G1249R, G1349D, H139R, H199Y, H939R, H1054D, H1085P, H1085R, H1375P, I148T, I175V, I336K, I502T, I601F, I618T, I807M, I980K, I1027T, I1139V, I1269N, I1366N, K1060T, L15P, L165S, L206W, L320V, L346P, L453S, L967S, L997F, L1077P, L1324P, L1335P, L1480P, M152V, M265R, M952I, M952T, M1101K, P5L, P67L, P205S, P574H, Q98R, Q237E, Q237H, Q359R, Q1291R, R31L, R74Q, R74W, R74W;D1270N, R74W;V201M,

R74W;V201M;D1270N, R75Q, R117C, R117G, R117H, R117L, R117P, R170H, R258G, R334L, R334Q, R347H, R347L, R347P, R352Q, R352W, R553Q, R668C, R751L, R792G, R933G, R1066H, R1070Q, R1070W, R1162L, R1283M, R1283S, S13F, S341P, S364P, S492F, S549N, S549R, S589N, S737F, S912L, S945L, S977F, S1159F, S1159P, S1251N, S1255P, T338I, T1036N, T1053I, V201M, V232D, V456A, V456F, V562I, V754M, V1153E, V1240G, V1293G, W361R, W1098C, W1282R, Y109N, Y161D, Y161S, Y563N, Y1014C, Y1032C, 3141del9, 546insCTA.

C. The member is at least 6 years of age.
D. Trikafta will not be used in combination with other medications containing ivacaftor.

V. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section IV who are experiencing benefit from therapy as evidenced by disease stability or disease improvement (e.g., improvement in FEV1 from baseline).

VI. REFERENCES

1. Trikafta [package insert]. Boston, MA: Vertex Pharmaceuticals Inc; June 2021.

Reference number(s)
3151-A

SPECIALTY GUIDELINE MANAGEMENT

TURALIO (pexidartinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication
Turalio is indicated for the treatment of adult patients with symptomatic tenosynovial giant cell tumor (TGCT) associated with severe morbidity or functional limitations and not amenable to improvement with surgery.

B. Compendial Uses
1. Pigmented villonodular synovitis (PVNS)
2. Histiocytic Neoplasms:
    a. Erdheim-Chester Disease (ECD)
    b. Langerhans Cell Histiocytosis (LCH)
    c. Rosai-Dorfman Disease (RDD)

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: Documentation of the presence of colony stimulating factor 1 receptor (CSF1R) mutation (where applicable).

III. CRITERIA FOR INITIAL APPROVAL

A. Pigmented Villonodular Synovitis/Tenosynovial Giant Cell Tumor (PVNS/TGCT)
Authorization of 12 months may be granted for the treatment of pigmented villonodular synovitis (PVNS)/ tenosynovial giant cell tumor (TGCT) as a single agent.

B. Histiocytic Neoplasms
Authorization of 12 months may be granted for any of the following histiocytic neoplasm subtypes as a single agent in members with a CSF1R mutation:
1. Symptomatic or relapsed/refractor Erdheim-Chester Disease (ECD)
2. Symptomatic or relapsed/refractory Rosai-Dorfman Disease (RDD)
3. Langerhans Cell Histiocytosis (LCH)

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

V. REFERENCES

1. Turalio [package insert]. Basking Ridge, NJ: Daiichi Sankyo, Inc.; October 2021.
2. The NCCN Drugs & Biologics Compendium® © 2022 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed February 16, 2022.

Reference number
1826-A

SPECIALTY GUIDELINE MANAGEMENT

TYMLOS (abaloparatide)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

A. Treatment of postmenopausal women with osteoporosis at high risk for fracture (defined as history of osteoporotic fracture or multiple risk factors for fracture), or patients who have failed or are intolerant to other available osteoporosis therapy.
B. Treatment to increase bone density in men with osteoporosis at high risk for fracture (defined as a history of osteoporotic fracture or multiple risk factors for fracture), or patients who have failed or are intolerant to other available osteoporosis therapy.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: Supporting chart notes or medical record indicating a history of fractures, T-score, and FRAX fracture probability as applicable to section III.

III. CRITERIA FOR INITIAL APPROVAL

A. Postmenopausal osteoporosis

Authorization of an initial total of 12 months may be granted to postmenopausal members with osteoporosis when ANY of the following criteria are met:

1. Member has a history of fragility fractures
2. Member has a pre-treatment T-score less than or equal to -2.5 OR member has osteopenia (i.e., pre-treatment T-score greater than -2.5 and less than -1) with a high pre-treatment FRAX fracture probability (See Appendix B) and meets ANY of the following criteria:
    i. Member has indicators of very high fracture risk (e.g., advanced age, frailty, glucocorticoid use, very low T-scores [less than or equal to -3], or increased fall risk)
    ii. Member has failed prior treatment with or is intolerant to previous injectable osteoporosis therapy (e.g., zoledronic acid [Reclast], denosumab [Prolia])
    iii. Member has had an oral bisphosphonate trial of at least 1-year duration or there is a clinical reason to avoid treatment with an oral bisphosphonate (See Appendix A)

B. Osteoporosis in men

Authorization of an initial total of 12 months may be granted to male members with osteoporosis when ANY of the following criteria are met:

1. Member has a history of an osteoporotic vertebral or hip fracture
2. Member meets BOTH of the following criteria:
   i. Member has a pre-treatment T-score less than or equal to -2.5 OR member has osteopenia (i.e., pre-treatment T-score greater than -2.5 and less than -1) with a high pre-treatment FRAX fracture probability (See Appendix B)
   ii. Member has had an oral OR injectable bisphosphonate trial of at least 1-year duration OR there is a clinical reason to avoid treatment with a bisphosphonate (See Appendix A)

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for all members (including new members) who are currently receiving the requested medication through a previously authorized pharmacy or medical benefit, who have not experienced clinically significant adverse events during therapy.

V. OTHER

The cumulative duration of parathyroid hormone analogs (teriparatide and abaloparatide) will not exceed a total of 24 months in the member's lifetime.

VI. APPENDICES

Appendix A. Clinical reasons to avoid oral bisphosphonate therapy

- Presence of anatomic or functional esophageal abnormalities that might delay transit of the tablet (e.g., achalasia, stricture, or dysmotility)
- Active upper gastrointestinal problem (e.g., dysphagia, gastritis, duodenitis, erosive esophagitis, ulcers)
- Presence of documented or potential gastrointestinal malabsorption (e.g., gastric bypass procedures, celiac disease, Crohn's disease, infiltrative disorders, etc.)
- Inability to stand or sit upright for at least 30 to 60 minutes
- Inability to take oral bisphosphonate at least 30 to 60 minutes before first food, drink, or medication of the day
- Renal insufficiency (creatinine clearance < 35 mL/min)
- History of intolerance to an oral bisphosphonate

Appendix B. WHO Fracture Risk Assessment Tool

- High FRAX fracture probability: 10-year major osteoporotic fracture risk ≥ 20% or hip fracture risk ≥ 3%
- 10-year probability; calculation tool available at: https:// www.shef.ac.uk/FRAX
- The estimated risk score generated with FRAX should be multiplied by 1.15 for major osteoporotic fracture (including fractures of the spine [clinical], hip, wrist, or humerus) and 1.2 for hip fracture if glucocorticoid treatment is greater than 7.5 mg (prednisone equivalent) per day

VII. REFERENCES

1. Tymlos [package insert]. Waltham, MA: Radius Health, Inc. December 2022.
2. Bisphosphonates. *Drug Facts and Comparisons.* Facts & Comparisons [database online]. St. Louis, MO: Wolters Kluwer Health Inc; September 1, 2022. Accessed October 10, 2022.

3. Miller PD, Hattersley G, Riis BJ, et al. Effect of Abalaoparatide Vs Placebo on New Vertebral Fractures in Postmenopausal Women with Osteoporosis: A Randomized Clinical Trial. *JAMA*. 2016; 316 (7): 722:733.
4. Camacho PM, Petak SM, Binkley N, et al. American Association of Clinical Endocrinologists and American College of Endocrinology Clinical Practice Guidelines for the Diagnosis and Treatment of Postmenopausal Osteoporosis 2020. *Endocr Pract*. 2020 ;26 (Suppl 1):1-46.
5. FRAX® Fracture Risk Assessment Tool. © Centre for Metabolic Bone Diseases, University of Sheffield, UK. Available at: https://www.shef.ac.uk/FRAX. Accessed October 10, 2022.
6. Ensrud KE, Crandall CJ. Osteoporosis. *Ann Intern Med*. 2017;167(03): ITC17–ITC32.
7. Eastell R, Rosen CJ, Black DM, et al. Pharmacological Management of Osteoporosis in Postmenopausal Women: An Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab*. 2019; 104:1595-1622.
8. Carey, John. What is failure of bisphosphonate therapy for osteoporosis. Cleve Clinic J Med. 2005; 72:1033-1039.
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10. Watts NB, Adler RA, Bilezikian JP, et al. Osteoporosis in men : an Endocrine Society clinical practice guideline. *J Clin Endocr Metab*. 2012;97(6):1802-1822.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME*
(generic)

TYRVAYA
(varenicline nasal spray solution)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization with Quantity Limit ***Ref # 5023-C***

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS
Tyrvaya (varenicline solution) nasal spray is indicated for the treatment of the signs and symptoms of dry eye disease.

COVERAGE CRITERIA
The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for dry eye disease

Quantity Limits apply.

RATIONALE
The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Tyrvaya (varenicline solution) nasal spray is indicated for the treatment of the signs and symptoms of dry eye disease.[1]

Dosage for Tyrvaya is one spray in each nostril twice a day, 4 sprays per day total. Tyrava is available in cartons containing two nasal spray bottles, each containing 60 sprays per bottle, equivalent to a 30 day supply with one spray in each nostril twice daily.[1] Therefore, the limit for Tyrvaya containers will be set at 2 nasal spray bottles per month.

REFERENCES

1. Tyrvaya [package insert]. Princeton, NJ: Oyster Point Pharma, Inc,; October 2021.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2021; Accessed October 29, 2021.

Written by:	UM Development (DS)
Date Written:	10/2021
Revised:	
Reviewed:	Medical Affairs: (CHART) 11/04/2021 External Review: 12/2021

CRITERIA FOR APPROVAL

1	Is the requested drug being prescribed for dry eye disease? [If no, then no further questions.]	Yes	No
2	Does the patient require more than the plan allowance of 4 sprays per day of the requested drug? [RPh Note: If yes, then deny and enter a partial approval for 2 nasal spray bottles (1 carton) per 25 days or 6 nasal spray bottles (3 cartons) per 75 days of Tyrvaya.]	Yes	No

Mapping Instructions			
	Yes	**No**	**DENIAL REASONS – DO NOT USE FOR MEDICARE PART D**
1.	Go to 2	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have dry eye disease. Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]
2.	Deny	Approve, 12 months, 2 nasal spray bottles (1 carton) per 25 days * or 6 nasal spray bottles (3 cartons) per 75 days *	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 2 nasal spray bottles (1 carton)/month of the requested drug and strength. Your request has been partially approved. You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity]

**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*

Reference number(s)
1650-A

SPECIALTY GUIDELINE MANAGEMENT

Tyvaso (treprostinil inhalation solution)
Tyvaso DPI (treprostinil inhalation powder)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

A. Treatment of Pulmonary arterial hypertension (PAH; World Health Organization [WHO] Group 1) to improve exercise ability. Studies establishing effectiveness predominately included patients with New York Heart Association (NYHA) Functional Class III symptoms and etiologies of idiopathic or heritable PAH or PAH associated with connective tissue diseases.
B. Treatment of Pulmonary hypertension associated with interstitial lung disease (PH-ILD; WHO Group 3) to improve exercise ability. The study establishing effectiveness predominately included patients with etiologies of idiopathic interstitial pneumonia (IIP) inclusive of idiopathic pulmonary fibrosis (IPF), combined pulmonary fibrosis and emphysema (CPFE), and WHO Group 3 connective tissue disease.

All other indications are considered experimental/investigational and not medically necessary.

II. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with a pulmonologist or cardiologist.

III. CRITERIA FOR INITIAL APPROVAL

Pulmonary Hypertension (PH)

Authorization of 12 months may be granted for treatment of PH when both of the following criteria are met:

A. Member has either of the following:
    1. WHO Group 1 class of pulmonary hypertension (refer to Appendix)
    2. Pulmonary hypertension associated with interstitial lung disease (WHO Group 3)
B. PH was confirmed by either criterion (1) or criterion (2) below:
    1. Pretreatment right heart catheterization with all of the following results:
        i. Mean pulmonary arterial pressure (mPAP) > 20 mmHg
        ii. Pulmonary capillary wedge pressure (PCWP) ≤ 15 mmHg
        iii. Pulmonary vascular resistance (PVR) ≥ 3 Wood units in adult patients or pulmonary vascular resistance index (PVRI) ≥ 3 Wood units x m^2 in pediatric patients
    2. For infants less than one year of age, PH was confirmed by Doppler echocardiogram if right heart catheterization cannot be performed.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for members with an indication listed in Section III who are currently receiving the requested medication through a paid pharmacy or medical benefit, and who are experiencing benefit from therapy as evidenced by disease stability or disease improvement.

V. APPENDIX

WHO Classification of Pulmonary Hypertension

1 PAH

1.1 Idiopathic (PAH)
1.2 Heritable PAH
1.3 Drug- and toxin-induced PAH
1.4. PAH associated with:
- 1.4.1 Connective tissue diseases
- 1.4.2 HIV infection
- 1.4.3 Portal hypertension
- 1.4.4 Congenital heart diseases
- 1.4.5 Schistosomiasis

1.5 PAH long-term responders to calcium channel blockers
1.6 PAH with overt features of venous/capillaries (PVOD/PCH) involvement
1.7 Persistent PH of the newborn syndrome

2 PH due to left heart disease

2.1 PH due to heart failure with preserved LVEF
2.2 PH due to heart failure with reduced LVEF
2.3 Valvular heart disease
2.4 Congenital/acquired cardiovascular conditions leading to post-capillary PH

3 PH due to lung diseases and/or hypoxia

3.1 Obstructive lung disease
3.2 Restrictive lung disease
3.3 Other lung disease with mixed restrictive/obstructive pattern
3.4 Hypoxia without lung disease
3.5 Developmental lung disorders

4 PH due to pulmonary artery obstruction

4.1 Chronic thromboembolic PH
4.2 Other pulmonary artery obstructions
- 4.2.1 Sarcoma (high or intermediate grade) or angiosarcoma
- 4.2.2 Other malignant tumors
  - Renal carcinoma
  - Uterine carcinoma
  - Germ cell tumours of the testis
  - Other tumours
- 4.2.3 Non-malignant tumours
  - Uterine leiomyoma
- 4.2.4 Arteritis without connective tissue disease
- 4.2.5 Congenital pulmonary artery stenosis
- 4.2.6 Parasites
  - Hydatidosis

5 PH with unclear and/or multifactorial mechanisms

5.1 Hematologic disorders: Chronic hemolytic anemia, myeloproliferative disorders

5.2 Systemic and metabolic disorders: Pulmonary Langerhans cell histiocytosis, Gaucher disease, glycogen storage disease, neurofibromatosis, sarcoidosis
5.3 Others: chronic renal failure with or without hemodialysis, fibrosing mediastinitis
5.4 Complex congenital heart disease

VI. REFERENCES

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2. Tyvaso DPI [package insert]. Research Triangle Park, NC: United Therapeutics Corp.; June 2023.
3. Chin KM, Rubin LJ. Pulmonary arterial hypertension. *J Am Coll Cardiol*. 2008;51(16):1527-1538.
4. McLaughlin VV, Archer SL, Badesch DB, et al. ACCF/AHA 2009 expert consensus document on pulmonary hypertension a report of the American College of Cardiology Foundation Task Force on Expert Consensus Documents and the American Heart Association developed in collaboration with the American College of Chest Physicians, American Thoracic Society, Inc., and the Pulmonary Hypertension Association. *J Am Coll Cardiol*. 2009;53(17):1573-1619.
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7. Barst RJ, Gibbs SR, Ghofrani HA, et al. Updated evidence-based treatment algorithm in pulmonary arterial hypertension. *J Am Coll Cardiol.* 2009;54:S78-S84.
8. Taichman DB, Ornelas J, Chung L, et al. Pharmacologic therapy for pulmonary arterial hypertension in adults. CHEST guideline and expert panel report. *Chest*. 2014;46(2):449-475.
9. Abman SH, Hansmann G, Archer SL, et al. Pediatric pulmonary hypertension: guidelines from the American Heart Association and American Thoracic Society. *Circulation*. 2015;132(21):2037-99.
10. Klinger JR, Elliott CG, Levine DJ, et al. Therapy for Pulmonary Arterial Hypertension in Adults: Update of the CHEST Guidelines and Expert Panel Report. *Chest*. 2019:155(3): 565-586.
11. Galie N, McLaughlin VV, Rubin LJ, Simonneau G. An overview of the 6th World Symposium on Pulmonary Hypertension. *Eur Respir J.* 2019; 53: 1802148; DOI: 10.1183/13993003.02148-2018. Published 24 January 2019.
12. Simonneau G, Montani D, Celermajer DS, et al. Haemodynamic definitions and updated clinical classification of pulmonary hypertension. *Eur Respir J.* 2019;53:1801913; doi:10.1183/13993003.01913-2018.

Reference number(s)
4501-A

SPECIALTY GUIDELINE MANAGEMENT

UKONIQ (umbralisib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. Marginal Zone Lymphoma (MZL)
      Ukoniq is indicated for the treatment of adult patients with relapsed or refractory MZL who have received at least one prior anti-CD20-based regimen.

   2. Follicular Lymphoma (FL)
      Ukoniq is indicated for the treatment of adult patients with relapsed or refractory FL who have received at least three prior lines of systemic therapy.

B. Compendial Uses
   1. Marginal zone lymphoma
   2. Follicular lymphoma

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Marginal Zone Lymphoma (MZL)
Authorization of 12 months may be granted for treatment of relapsed, refractory, progressive MZL in members who have received at least one prior anti-CD20-based regimen (e.g., rituximab, obinutuzumab) when the requested medication is used as a single agent.

B. Follicular Lymphoma (FL)
Authorization of 12 months may be granted for treatment of relapsed, refractory, or progressive FL as third-line and subsequent therapy when the requested medication is used as a single agent.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

IV. REFERENCES

1. Ukoniq [package insert]. Edison, NJ: TG Therapeutics, Inc.; February 2021.

2. The NCCN Drugs & Biologics Compendium® © 2022 National Comprehensive Cancer Network, Inc. Available at: https://www.nccn.org. Accessed March 8, 2022.

STEP THERAPY CRITERIA

DRUG CLASS	**XANTHINE OXIDASE INHIBITORS**
BRAND NAME*	
(generic)	
	ULORIC
	(febuxostat)
Status: CVS Caremark Criteria	
Type: Initial Step Therapy; Post Step Therapy Prior Authorization	***Ref # 540-D***

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Uloric is a xanthine oxidase (XO) inhibitor indicated for the chronic management of hyperuricemia in adult patients with gout who have an inadequate response to a maximally titrated dose of allopurinol, who are intolerant to allopurinol, or for whom treatment with allopurinol is not advisable.

For the safe and effective use of allopurinol, see allopurinol prescribing information.

Limitations of Use

Uloric is not recommended for the treatment of asymptomatic hyperuricemia.

INITIAL STEP THERAPY LOGIC

If the patient has filled a prescription for at least a 30-day supply of allopurinol within the past 180 days under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit. If the patient does not meet the initial step therapy logic criteria, then the claim will reject with a message indicating that a prior authorization (PA) is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for the chronic management of hyperuricemia in an adult patient with gout

AND

- The patient has experienced an inadequate treatment response to a maximally titrated dose of allopurinol

OR

- The patient has experienced an intolerance to allopurinol

OR

- The patient has a contraindication that would prohibit a trial of allopurinol

RATIONALE

If the patient has filled a prescription for at least a 30-day supply of allopurinol within the past 180 days under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit.

If the patient does not meet the initial step therapy criteria, then prior authorization is required.

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Uloric is a xanthine oxidase inhibitor indicated for

the chronic management of hyperuricemia in adult patients with gout who have an inadequate response to a maximally titrated dose of allopurinol, who are intolerant to allopurinol, or for whom treatment with allopurinol is not advisable.[1-3]

In a cardiovascular (CV) outcome study, gout patients with established CV disease treated with Uloric had a higher rate of CV death compared to those treated with allopurinol. The randomized, double-blind, allopurinol-controlled, non-inferiority study was conducted to evaluate the risk of major adverse cardiovascular events (MACE) in patients with gout who were treated with Uloric. The patients who were enrolled in the study had a history of major CV disease, cerebrovascular disease, or diabetes mellitus with microvascular and/or macrovascular disease. While Uloric was non-inferior to allopurinol for the primary endpoint of MACE, there was a significant increase in CV deaths in patients treated with Uloric compared to patients treated with allopurinol. Because of the increased risk of CV death, Uloric should only be used in patients who have an inadequate response to a maximally titrated dose of allopurinol, who are intolerant to allopurinol, or for whom treatment with allopurinol is not advisable.[1] Additionally, the 2020 American College of Rheumatology guideline for the management of gout strongly recommends treatment with allopurinol as the preferred first-line agent, over all other urate-lowering therapies, for all patients (including those with moderate-to-severe Chronic Kidney Disease [stage ≥3]).[4] Therefore, coverage will be provided when the patient has experienced an inadequate treatment response to a maximally titrated dose of allopurinol, has experienced an intolerance to allopurinol, or has a contraindication that would prohibit a trial of allopurinol.

REFERENCES

1. Uloric [package insert]. Lexington, Massachusetts: Takeda Pharmaceuticals America, Inc.; August 2020.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, Ohio: UpToDate, Inc.; 2021; Accessed October 6, 2021.
3. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed October 6, 2021.
4. FitzGerald JD, Dalbeth N, Mikuls T, et al. 2020 American College of Rheumatology Guideline for the Management of Gout. *Arthritis Care Res*. 2020;72(6):744-760.

Written by:	UM Development (SE)
Date Written:	11/2009
Revised:	(CY) 09/2010 (made standard), 01/2011(added CI question); (CT) 04/2011 (no longer MDC-1/new MDC-2 was developed); (MS) 09/2011, 11/2011, 01/2012 (removed theophylline as contraindication to match current PI), 06/2012, 10/2012 (extended duration); (CT) 06/2013; (MS) 12/2013; (CF) 12/2014 (no grids needed), 12/2015, 06/2015 (no clinical changes); (MS) 12/2016 (removed contraindication question due to lack of denials), (SF) 12/2017; (RP) 11/2018 (no clinical changes); (KC) 11/2019; (CJM) 11/2020 (no clinical changes); (MRS) 11/2021 (updated document title)
Reviewed:	Medical Affairs (WLF) 11/2009; (KP) 09/2010, 01/2011, 09/2011, 11/2011, 01/2012, 06/2012; (LCB) 06/2013, 12/2013; (DHR) 12/2014; (AN) 12/2016, (DC) 12/2017; (CHART) 11/27/2019, 12/3/2020, 12/02/2021 External Review: 12/2009, 12/2010, 02/2011, 03/2012, 10/2012, 08/2013, 04/2014, 04/2015, 02/2016, 02/2017, 02/2018, 02/2019, 02/2020, 02/2021, 02/2022

CRITERIA FOR APPROVAL

1	Is the requested drug being prescribed for the chronic management of hyperuricemia in an adult patient with gout? [If no, then no further questions.]	Yes	No
2	Has the patient experienced an inadequate treatment response to a maximally titrated dose of allopurinol? [If yes, then no further questions.]	Yes	No
3	Has the patient experienced an intolerance to allopurinol? [If yes, then no further questions.]	Yes	No
4	Does the patient have a contraindication that would prohibit a trial of allopurinol?	Yes	No

Mapping Instructions			
	Yes	**No**	**DENIAL REASONS – DO NOT USE FOR MEDICARE PART D**
1.	Go to 2	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you meet all of these conditions: - You are an adult - You have high uric acid levels in your blood - You have gout Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]
2.	Approve, 36 months	Go to 3	
3.	Approve, 36 months	Go to 4	
4.	Approve, 36 months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have tried allopurinol and it did not work for you, or you cannot use it. Your request has been denied based on the information we have. [Short Description: No trial of allopurinol]

Reference number(s)
1645-A

SPECIALTY GUIDELINE MANAGEMENT

Uptravi (selexipag)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Uptravi is indicated for the treatment of pulmonary arterial hypertension (PAH, World Health Organization [WHO] Group I) to delay disease progression and reduce the risk of hospitalization for PAH. Effectiveness of Uptravi tablets was established in a long-term study in PAH patients with WHO Functional Class II-III symptoms. Patients had idiopathic and heritable PAH, PAH associated with connective tissue disease, PAH associated with congenital heart disease with repaired shunts.

All other indications are considered experimental/investigational and not medically necessary.

II. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with a pulmonologist or cardiologist.

III. CRITERIA FOR INITIAL APPROVAL

Pulmonary Arterial Hypertension (PAH)
Authorization of 12 months may be granted for treatment of PAH when ALL of the following criteria are met:
A. Member has PAH defined as WHO Group 1 class of pulmonary hypertension (refer to Appendix).
B. PAH was confirmed by either criterion (1) or criterion (2) below:
    1. Pretreatment right heart catheterization with all of the following results:
        i. Mean pulmonary arterial pressure (mPAP) > 20 mmHg
        ii. Pulmonary capillary wedge pressure (PCWP) ≤ 15 mmHg
        iii. Pulmonary vascular resistance (PVR) ≥ 3 Wood units in adult patients or pulmonary vascular resistance index (PVRI) ≥ 3 Wood units x m^2 in pediatric patients
    2. For infants less than one year of age, PAH was confirmed by Doppler echocardiogram if right heart catheterization cannot be performed.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for members with an indication listed in Section III who are currently receiving the requested medication through a paid pharmacy or medical benefit, and who are experiencing benefit from therapy as evidenced by disease stability or disease improvement.

V. APPENDIX

WHO Classification of Pulmonary Hypertension

1 PAH

1.1 Idiopathic (PAH)
1.2 Heritable PAH
1.3 Drug- and toxin-induced PAH
1.4. PAH associated with:
- 1.4.1 Connective tissue diseases
- 1.4.2 HIV infection
- 1.4.3 Portal hypertension
- 1.4.4 Congenital heart diseases
- 1.4.5 Schistosomiasis

1.5 PAH long-term responders to calcium channel blockers
1.6 PAH with overt features of venous/capillaries (PVOD/PCH) involvement
1.7 Persistent PH of the newborn syndrome

2 PH due to left heart disease

2.1 PH due to heart failure with preserved LVEF
2.2 PH due to heart failure with reduced LVEF
2.3 Valvular heart disease
2.4 Congenital/acquired cardiovascular conditions leading to post-capillary PH

3 PH due to lung diseases and/or hypoxia

3.1 Obstructive lung disease
3.2 Restrictive lung disease
3.3 Other lung disease with mixed restrictive/obstructive pattern
3.4 Hypoxia without lung disease
3.5 Developmental lung disorders

4 PH due to pulmonary artery obstruction

4.1 Chronic thromboembolic PH
4.2 Other pulmonary artery obstructions
- 4.2.1 Sarcoma (high or intermediate grade) or angiosarcoma
- 4.2.2 Other malignant tumors
  - Renal carcinoma
  - Uterine carcinoma
  - Germ cell tumours of the testis
  - Other tumours
- 4.2.3 Non-malignant tumours
  - Uterine leiomyoma
- 4.2.4 Arteritis without connective tissue disease
- 4.2.5 Congenital pulmonary artery stenosis
- 4.2.6 Parasites
  - Hydatidosis

5 PH with unclear and/or multifactorial mechanisms

5.1 Hematologic disorders: Chronic hemolytic anemia, myeloproliferative disorders
5.2 Systemic and metabolic disorders: Pulmonary Langerhans cell histiocytosis, Gaucher disease, glycogen storage disease, neurofibromatosis, sarcoidosis
5.3 Others: chronic renal failure with or without hemodialysis, fibrosing mediastinitis
5.4 Complex congenital heart disease

VI. REFERENCES

1. Uptravi [package insert]. Titusville, NJ: Actelion Pharmaceuticals US, Inc.; July 2022.

2. Sitbon O, Channick R, Chin K, et al. Selexipag for the treatment of pulmonary arterial hypertension. *N Engl J Med*. 2015;373:2522-33.
3. Rubin LJ; American College of Chest Physicians. Diagnosis and management of pulmonary arterial hypertension: ACCP evidence-based clinical practice guidelines. *Chest*. 2004;126(1 Suppl):7S-10S.
4. McLaughlin V, et al. ACCF/AHA 2009 Expert Consensus Document on Pulmonary Hypertension. *J Am Coll Cardiol*. 2009;53:1573-1619.
5. Klinger JR, Elliott CG, Levine DJ, et al. Therapy for Pulmonary Arterial Hypertension in Adults: Update of the CHEST Guidelines and Expert Panel Report. *Chest*. 2019:155(3): 565-586.
6. Galie N, McLaughlin VV, Rubin LJ, Simonneau G. An overview of the 6th World Symposium on Pulmonary Hypertension. *Eur Respir J.* 2019; 53: 1802148; DOI: 10.1183/13993003.02148-2018. Published 24 January 2019.
7. Simonneau G, Montani D, Celermajer DS, et al. Haemodynamic definitions and updated clinical classification of pulmonary hypertension. *Eur Respir J.* 2019;53:1801913; doi:10.1183/13993003.01913-2018.
8. Abman SH, Hansmann G, Archer SL, et al. Pediatric pulmonary hypertension: guidelines from the American Heart Association and American Thoracic Society. *Circulation*. 2015;132(21):2037-99.

Reference number
1862-A

SPECIALTY GUIDELINE MANAGEMENT

VALCHLOR (mechlorethamine gel)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication
Valchlor is indicated for the topical treatment of Stage IA and IB mycosis fungoides-type cutaneous T-cell lymphoma in patients who have received prior skin-directed therapy.

B. Compendial Uses
1. Chronic or smoldering adult T-cell leukemia/lymphoma (ATLL)
2. Mycosis fungoides/Sezary syndrome (MF/SS)
3. Primary cutaneous B-cell lymphoma:
   a. Primary cutaneous marginal zone lymphoma
   b. Primary cutaneous follicle center lymphoma
4. Lymphomatoid papulosis (LyP)
5. Histiocytic Neoplasms
   a. Langerhans Cell Histiocytosis

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Mycosis Fungoides/Sezary Syndrome (MF/SS)
Authorization of 12 months may be granted for the treatment of mycosis fungoides or Sezary syndrome.

B. Adult T-cell leukemia/lymphoma (ATLL)
Authorization of 12 months may be granted for the treatment of chronic or smoldering adult T-cell leukemia/lymphoma (ATLL).

C. Primary cutaneous B-cell lymphoma
Authorization of 12 months may be granted for the treatment of primary cutaneous marginal zone or follicle center lymphoma.

D. Lymphomatoid Papulosis (LyP)
Authorization of 12 months may be granted for the treatment of lymphomatoid papulosis (LyP).

E. Histiocytic Neoplasms
Authorization of 12 months may be granted for the treatment of Langerhans cell histiocytosis with isolated skin disease.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

IV. REFERENCES

1. Valchlor [package insert]. Iselin, NJ: Helsinn Therapeutics, Inc.; January 2020.
2. The NCCN Drugs & Biologics Compendium® © 2022 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed January 3, 2022.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME*
(generic)

VALTOCO
(diazepam nasal spray)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization with Quantity Limit ***Ref # 3517-C***

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Valtoco is indicated for the acute treatment of intermittent, stereotypic episodes of frequent seizure activity (i.e., seizure clusters, acute repetitive seizures) that are distinct from a patient's usual seizure pattern in patients with epilepsy 6 years of age and older.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for the acute treatment of intermittent, stereotypic episodes of frequent seizure activity (i.e., seizure clusters, acute repetitive seizures) that are distinct from the patient's usual seizure pattern in a patient with epilepsy

AND

- The patient is 6 years of age or older

Quantity Limits apply.
**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*

RATIONALE

Valtoco is indicated for the acute treatment of intermittent, stereotypic episodes of frequent seizure activity (i.e., seizure clusters, acute repetitive seizures) that are distinct from a patient's usual seizure pattern in patients with epilepsy 6 years of age and older. Prior to treatment, healthcare professionals should instruct the individual administering Valtoco on how to identify seizure clusters and use the product appropriately.[1-3]

The recommended dose of Valtoco nasal spray is 0.2 mg/kg or 0.3 mg/kg, depending on the patient's age and weight. The following table provides the acceptable weight ranges for each dose and age category, such that patients will receive between 90% and 180% of the calculated recommended dose.[1]

Recommended Valtoco Dosage for Adults and Pediatric Patients 6 Years of Age and Older[1]

Dose Based on Age and Weight		Administration		
6 to 11 Years of Age (0.3 mg/kg)	**12 Years of Age and Older (0.2 mg/kg)**	**Dose (mg)**	**Number of Nasal Spray Devices**	**Number of Sprays**
Weight (kg)	**Weight (kg)**			
10 to 18	14 to 27	5	One 5 mg device	One spray in one nostril
19 to 37	28 to 50	10	One 10 mg device	One spray in one nostril
38 to 55	51 to 75	15	Two 7.5 mg devices	One spray in each nostril
56 to 74	76 and up	20	Two 10 mg devices	One spray in each nostril

A second dose of Valtoco, when required, may be administered after at least 4 hours after the initial dose. If the second dose is to be administered, use a new blister pack of Valtoco. Do not use more than 2 doses of Valtoco to treat a single

episode. It is recommended that Valtoco be used to treat no more than one episode every five days and no more than five episodes per month.[1]

Valtoco is available in 5 mg, 7.5 mg, and 10 mg strengths. Valtoco is supplied and packed in doses of 5 mg, 10 mg, 15 mg, or 20 mg cartons.[1]

Available Packaging Configurations[1]

Description	Contents
5 mg carton	2 individual blister packs, each containing one 5 mg nasal spray device
10 mg carton	2 individual blister packs, each containing one 10 mg nasal spray device
15 mg carton	2 individual blister packs, each containing two 7.5 mg nasal spray devices
20 mg carton	2 individual blister packs, each containing two 10 mg nasal spray devices

Each blister pack contains enough Valtoco to administer one dose of the prescribed quantity. Each carton contains two blister packs, which is enough to treat one to two episodes.[1] Because it is not recommended to treat more than 5 episodes per month and each episode could require up to 2 doses, the limit will be set at 10 blister packs (5 cartons) per month.

REFERENCES

1. Valtoco [package insert]. San Diego, CA: Neurelis, Inc.; February 2022.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2022; Accessed April 7, 2022.
3. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed April 7, 2022.

Written by: UM Development (DS)
Date Written: 01/2020
Revised: 05/2020 (no clinical changes), 05/2021 (no clinical changes), (DFW) 05/2022 (no clinical changes)
Reviewed: Medical Affairs (CHART) 02/06/2020, 05/28/2020, 05/27/2021, 05/26/2022
External Review: 04/2020, 10/2020, 08/2021, 08/2022

CRITERIA FOR APPROVAL

1	Is the requested drug being prescribed for the acute treatment of intermittent, stereotypic episodes of frequent seizure activity (i.e., seizure clusters, acute repetitive seizures) that are distinct from the patient's usual seizure pattern in a patient with epilepsy? [If yes, go to 2. If no, then no further questions.]	Yes	No
2	Is the patient 6 years of age or older? [If yes, go to 3. If no, then no further questions.]	Yes	No
3	Does the patient require more than the plan allowance of 10 blister packs (5 cartons) per month? [No further questions] [RPh Note: If yes, then deny and enter a partial approval for 10 blister packs (5 cartons) / 25 days or 30 blister packs (15 cartons) / 75 days of Valtoco.] [Note: Coverage is provided up to an amount sufficient for treating up to five episodes per month at the maximum dose of the requested drug.]	Yes	No

Mapping Instructions

	Yes	No	DENIAL REASONS
1.	Go to 2	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you meet all of the following: - You have epilepsy - The requested drug is being used for the acute treatment of intermittent, stereotypic episodes of frequent seizure activity (i.e., seizure clusters, acute repetitive seizures) that are distinct from your usual seizure pattern Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]
2.	Go to 3	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you are 6 years of age or older. Your request has been denied based on the information we have. [Short Description: No approvable age]
3.	Deny	Approve, 12 Months, 10 blister packs (5 cartons)/25 days or 30 blister packs (15 cartons)/75 days	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 5 cartons per month of the requested drug and strength. Your request has been partially approved. You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity]

QUANTITY LIMIT CRITERIA

BRAND NAME*
(generic)

FIRVANQ
(vancomycin)

VANCOCIN
(vancomycin capsules)

Status: CVS Caremark Criteria
Type: Quantity Limit ***Ref # 2559-H***

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Vancocin

Vancocin is indicated for the treatment of *Clostridioides difficile*-associated diarrhea. Vancocin is also used for the treatment of enterocolitis caused by *Staphylococcus aureus* (including methicillin-resistant strains) in adult and pediatric patients less than 18 years of age.

Limitations of Use

- Parenteral administration of vancomycin is not effective for the above infections; therefore, Vancocin must be given orally for these infections.
- Orally administered Vancocin is not effective for other types of infections.

To reduce the development of drug-resistant bacteria and maintain the effectiveness of Vancocin and other antibacterial drugs, Vancocin should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

Firvanq

Firvanq is indicated for the treatment of *Clostridium difficile*-associated diarrhea in adults and pediatric patients less than 18 years of age.
Firvanq is also indicated for the treatment of enterocolitis caused by *Staphylococcus aureus* (including methicillin-resistant strains) in adults and pediatric patients less than 18 years of age.

Important Limitations of Use

- Parenteral administration of vancomycin is not effective for the above infections; therefore, vancomycin must be given orally for these infections.
- Orally administered vancomycin hydrochloride is not effective for treatment of other types of infections.

To reduce the development of drug-resistant bacteria and maintain the effectiveness of Firvanq and other antibacterial drugs, Firvanq should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

RATIONALE

Vancocin capsules and Firvanq powder for oral solution are both indicated for the treatment of *C. difficil*e-associated

diarrhea.[1-4] The American College of Gastroenterology last published guidelines on the diagnosis, treatment and prevention of Clostridium difficile infection (CDI) in 2013. Since that publication, there was a change in the taxonomic classification in 2016, with the organism assigned to a new genus and now called Clostridioides difficile. The US Centers for Disease Control and Prevention has adopted the new nomenclature, which has become standard throughout the scientific literature.[7] Vancocin capsules and Firvanq powder for oral solution are also used for the treatment of enterocolitis caused by *Staphylococcus aureus* (including methicillin-resistant strains). Parenteral administration of vancomycin is not effective for the above infections; therefore, vancomycin must be given orally for these infections. Orally administered vancomycin is not effective for other types of infections. To reduce the development of drug-resistant bacteria and maintain the effectiveness of Firvanq, Vancocin capsules, and other antibacterial drugs, Firvanq and Vancocin capsules should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.[1-4]

The recommended dose of Vancocin and Firvanq for adults with *C. difficile*-associated diarrhea is 125 mg given four times daily for ten days. The recommended total daily dosage of Vancocin and Firvanq for adults with staphylococcal enterocolitis is 500 mg to 2 grams given in three or four divided doses for seven to ten days. For both *C. difficile*-associated diarrhea and staphylococcal enterocolitis in pediatric patients, the usual daily dosage of Firvanq and Vancocin is 40 mg/kg given in three or four divided doses for seven to ten days. The total daily dosage should not exceed 2 grams. Vancocin 125 mg and 250 mg capsules are available as two blister packs with ten capsules each, for a total of 20 capsules per carton. Firvanq is available as 25 mg/mL reconstituted to 150 mL or 300 mL and 50 mg/mL reconstituted to 150 mL or 300 mL.[1-4]

The Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA) 2021 Focused Update Guideline of the Management of *Clostridioides difficile* infection in adults recommends a dosage for vancomycin of 125 mg taken orally four times a day for 10 days for an initial CDI episode and first recurrent episode of CDI. For a second or subsequent recurrence, a vancomycin dosing of 125 mg taken orally four times a day for 10 days, followed by rifaximin 400 mg three times daily for 20 days is recommended. Alternatively, a tapered/pulsed vancomycin regimen (e.g., 125 mg four times daily for 10-14 days, 2 times daily for 7 days, once daily for 7 days, and then every 2 to 3 days for 2 to 8 weeks) can be given for both a first CDI recurrence and a second or subsequent CDI recurrence. For fulminant CDI, vancomycin 500 mg four times daily by mouth or nasogastric tube is recommended.[6] The American College of Gastroenterology (ACG) Clinical Guideline: Prevention, Diagnosis and Treatment of *Clostridioides difficile* Infections recommends oral vancomycin 125 mg four times daily for 10 days for the treatment of initial episodes of nonsevere CDI and initial episodes of severe CDI in adult patients. The ACG guideline suggests tapering/pulsed-dose vancomycin for adult patients experiencing a first recurrence of CDI and 500 mg of oral vancomycin every 6 hours for 48-72 hours in adult patients with fulminant CDI.[7]

The Infectious Disease Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA) 2017 Clinical Practice Guideline for *Clostridium difficile* Infection in Adults and Children recommends an oral vancomycin dose of 10 mg/kg//dose four times daily for 10 days (maximum of 125 mg four times daily) for an initial episode of non-severe CDI and a first recurrence of non-severe CDI in children. For a second or subsequent recurrence of CDI in children, the guideline recommends oral vancomycin 10 mg/kg/dose four times daily for 10 days (maximum of 500 mg four times daily) followed by rifaximin for 20 days. Alternatively, oral vancomycin in a tapered and pulsed regimen (10 mg/kg/dose with max of 125 mg 4 times per day for 10–14 days, then 10 mg/kg with max of 125 mg 2 times per day for a week, then 10 mg/kg with max of 125 mg once per day for a week, and then 10 mg/kg with max of 125 mg every 2 or 3 days for 2–8 weeks) can be given for a second or subsequent recurrence of CDI in children. For an initial episode of severe/fulminant CDI in children, an oral vancomycin dose of 10 mg/kg/dose four times daily for 10 days (up to a maximum of 500 mg four times daily) is given with or without metronidazole.[5]

The quantity limit will be 80 Vancocin capsules OR 450 mL Firvanq solution to accommodate a 10 day standard course of vancomycin for CDI or 10 days of treatment for staphylococcal enterocolitis. The maximum dose for staphylococcal enterocolitis is 2 grams given in three or four divided doses for ten days, which equates to 80 units of the 250 mg oral capsules and 400 mL of the 50 mg/mL oral solution. The initial limit of 450 mL of Firvanq is reflective of the available package sizes for the 50 mg/mL oral solution (150 mL or 300 mL). The maximum pulse dose for CDI is 125 mg four times per day for 14 days, two times per day for a week, once per day for one week, and then every two days for eight weeks, which is equal to a total of 13,125 mg. The maximum pulse dose equates to 105 units of the 125 mg oral capsules, 262.5

mL of the 50 mg/mL oral solution or 525 mL of the 25 mg/mL oral solution. All pulse treatment courses using the 125 mg capsules, or the 25 mg/mL solution can be fulfilled in two or less fills based on the initial quantity limits. A full pulse regimen can be met with one fill of the 50 mg/mL oral solution. For a maximum pulse dose using the 25 mg/mL solution or the 125 mg capsules, the quantity limit will cover at least 4 weeks of therapy before a refill is required. Since quantity limits are set at every 10 days, patients will have 2-3 weeks to obtain a refill to finish the pulse treatment.

Recurrent *Clostridium difficile* infection (rCDI) is generally defined as the recurrence of diarrhea and a confirmatory positive test (NAAT or EIA) within 8 weeks after treatment of an initial episode of CDI. Approximately 20% of patients will experience an initial recurrence, and rates of further recurrences continue to go up significantly after each one. Another course of antibiotics is generally required for the treatment of a first recurrence of CDI.[7] Therefore, no limit has been placed on the number of fills per year.

If the patient is requesting more than the initial quantity limit, then the claim will reject with a message indicating that quantity limits are exceeded.

REFERENCES

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Written by:	UM Development (ES/JK/JH)
Date Written:	04/2018
Revised:	(CF) 02/2019 (no clinical changes); (KC) 12/2019 (no clinical changes), 11/2020 (no clinical changes), (DFW) 11/2021 (no clinical changes)
Reviewed:	Medical Affairs (AN) 04/2018; (CHART) 01/02/20, (CHART) 12/03/20, (CHART) 12/02/2021 External Review: 06/2018, 04/2019, 04/2020, 04/2021, 02/2022

LIMIT CRITERIA

Limits should accumulate across all drugs and strengths up to highest quantity listed depending on the order the claims are processed. Accumulation does not apply if limit is coded for daily dose.

Drug	Limit*
Firvanq (vancomycin) powder for oral solution (all strengths)	450 mL / 10 days
Vancocin (vancomycin) capsules (all strengths)	80 capsules / 10 days

This drug is indicated for short-term acute use.

Reference number(s)
6096-A

SPECIALTY GUIDELINE MANAGEMENT

VANFLYTA (quizartinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Acute Myeloid Leukemia
Vanflyta in combination with standard cytarabine and anthracycline induction and cytarabine consolidation, and as maintenance monotherapy following consolidation chemotherapy, for the treatment of adult patients with newly diagnosed acute myeloid leukemia (AML) that is FLT3 internal tandem duplication (ITD)-positive as detected by an FDA-approved test.

Limitations of Use:
Vanflyta is not indicated as maintenance monotherapy following allogeneic hematopoietic stem cell transplantation (HSCT); improvement in overall survival with Vanflyta in this setting has not been demonstrated.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: medical record documentation of FLT3 internal tandem duplication (ITD) mutation.

III. CRITERIA FOR INITIAL APPROVAL

Acute Myeloid Leukemia (AML)
Authorization of 12 months may be granted for treatment of newly diagnosed acute myeloid leukemia (AML) that is FLT3 internal tandem duplication (ITD)-positive when the requested medication is not being used as single agent maintenance therapy following hematopoietic stem cell transplantation (HSCT).

IV. CONTINUATION OF THERAPY

Authorization of 12 months (for up to 36 months maintenance therapy) may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

V. REFERENCES

1. Vanflyta [package insert]. Basking Ridge, NJ: Daiichi Sankyo, Inc.; July 2023.

Reference number(s)
2901-A

SUPPLEMENTAL SPECIALTY PA

VEMLIDY (tenofovir alafenamide)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Treatment of chronic hepatitis B virus (HBV) infection in adults with compensated liver disease.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Chronic hepatitis B virus infection
Authorization of 6 months may be granted for treatment of chronic hepatitis B virus (HBV) when all of the following criteria are met:
A. Member is HIV-1 negative
B. Member has compensated liver disease as evidenced by:
   1. No evidence of ascites, hepatic encephalopathy, or variceal bleeding
   2. INR < 1.5× ULN
   3. Total bilirubin < 2.5× ULN
   4. Albumin > 3.0 g/dL

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for chronic HBV who achieve or maintain positive clinical response (e.g., decreased HBV DNA level, ALT normalization, HBsAg and/or HBeAg loss and seroconversion) and are HIV-1 negative.

IV. REFERENCES

1. Vemlidy [package insert]. Foster City, CA: Gilead Sciences, Inc.; September 2021.

Reference number(s)
2374-A

SPECIALTY GUIDELINE MANAGEMENT

VENCLEXTA (venetoclax)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
1. Venclexta is indicated for the treatment of adult patients with chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL).
2. Venclexta is indicated in combination with azacitidine, or decitabine, or low-dose cytarabine for the treatment of newly-diagnosed acute myeloid leukemia (AML) in adults who are age 75 years or older, or who have comorbidities that preclude use of intensive induction chemotherapy.

B. Compendial Uses
1. Mantle cell lymphoma (MCL)
2. Acute myeloid leukemia (AML)
3. Blastic plasmacytoid dendritic cell neoplasm (BPDCN)
4. Multiple myeloma (MM) with translocation t(11;14).
5. Systemic light chain amyloidosis (SLCA) with translocation t(11;14).
6. Waldenström Macroglobulinemia/Lymphoplasmacytic Lymphoma (WM/LPL)

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: Documentation of the presence of translocation t(11,14) and TP53-mutation (where applicable).

III. CRITERIA FOR INITIAL APPROVAL

A. Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (CLL/SLL)
Authorization of 12 months may be granted for treatment of chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) when used as monotherapy, in combination with rituximab (Rituxan), or in combination with obinutuzumab (Gazyva).

B. Newly-diagnosed Acute Myeloid Leukemia (AML)
Authorization of 12 months may be granted for treatment of newly-diagnosed acute myeloid leukemia (AML) when one of the following criteria is met:
1. Used in combination with decitabine, azacitidine, or low-dose cytarabine and member meets any of the following:
   a. The member is 75 years of age or older.
   b. The member has comorbidities that preclude treatment with intensive induction chemotherapy.

c. The member is 60 years of age or older and is a candidate for intensive remission induction therapy with unfavorable-risk cytogenetics.
d. The member is 60 years of age or older and is not a candidate for intensive remission induction therapy or declines intensive therapy.
e. The member is 60 years of age or older and will use Venclexta as post-induction therapy following response to a Venclexta-based regimen.

2. Used in combination with azacitidine in a member less than 60 years of age for alternative induction treatment with unfavorable risk genetics and TP53-mutation.

C. Relapsed or Refractory Acute Myeloid Leukemia (AML)
Authorization of 12 months may be granted for treatment of relapsed or refractory acute myeloid leukemia in combination with azacitidine, decitabine or low-dose cytarabine.

D. Mantle Cell Lymphoma (MCL)
Authorization of 12 months may be granted for subsequent treatment of mantle cell lymphoma as a single agent or in combination with rituximab or ibrutinib.

E. Blastic Plasmacytoid Dendritic Cell Neoplasm (BPDCN)
Authorization of 12 months may be granted for BPDCN in combination with azacitidine, decitabine or low-dose cytarabine.

F. Multiple Myeloma (MM)
Authorization of 12 months may be granted for treatment of relapsed or progressive multiple myeloma in combination with dexamethasone in members with translocation t(11;14).

G. Systemic light chain amyloidosis (SLCA)
Authorization of 12 months may be granted for treatment of relapsed or refractory systemic light chain amyloidosis with translocation t(11;14) as a single agent or in combination with dexamethasone.

H. Waldenström Macroglobulinemia/Lymphoplasmacytic Lymphoma (WM/LPL)
Authorization of 12 months may be granted for subsequent treatment of Waldenström Macroglobulinemia/Lymphoplasmacytic Lymphoma as a single agent.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III when there is no evidence of unacceptable toxicity or disease progression while on the current regimen. For members with CLL/SLL who will use Venclexta with Rituxan, Venclexta will not be used longer than 24 months from cycle 1 day 1 of Rituxan initiation. For members with CLL/SLL who will use Venclexta with Gazyva, Venclexta will not be used longer than 12 cycles.

V. REFERENCES

1. Venclexta® [package insert]. North Chicago, IL: AbbVie Inc.; December 2021.
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Reference number(s)
1648-A

SPECIALTY GUIDELINE MANAGEMENT

Ventavis (iloprost inhalation solution)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Ventavis is indicated for the treatment of pulmonary arterial hypertension (PAH) (World Health Organization [WHO] Group 1) to improve a composite endpoint consisting of exercise tolerance, symptoms (New York Heart Association [NYHA] Class), and lack of deterioration. Studies establishing effectiveness included predominately patients with NYHA Functional Class III-IV symptoms and etiologies of idiopathic or heritable PAH or PAH associated with connective tissue diseases.

All other indications are considered experimental/investigational and not medically necessary.

II. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with a pulmonologist or cardiologist.

III. CRITERIA FOR INITIAL APPROVAL

Pulmonary Arterial Hypertension (PAH)
Authorization of 12 months may be granted for treatment of PAH when ALL of the following criteria are met:
A. Member has PAH defined as WHO Group 1 class of pulmonary hypertension (refer to Appendix).
B. PAH was confirmed by either criterion (1) or criterion (2) below:
    1. Pretreatment right heart catheterization with all of the following results:
        i. Mean pulmonary arterial pressure (mPAP) > 20 mmHg
        ii. Pulmonary capillary wedge pressure (PCWP) ≤ 15 mmHg
        iii. Pulmonary vascular resistance (PVR) ≥ 3 Wood units in adult patients or pulmonary vascular resistance index (PVRI) ≥ 3 Wood units x m^2 in pediatric patients
    2. For infants less than one year of age, PAH was confirmed by Doppler echocardiogram if right heart catheterization cannot be performed.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for members with an indication listed in Section III who are currently receiving the requested medication through a paid pharmacy or medical benefit, and who are experiencing benefit from therapy as evidenced by disease stability or disease improvement.

V. APPENDIX

WHO Classification of Pulmonary Hypertension

1 PAH

1.1 Idiopathic (PAH)
1.2 Heritable PAH
1.3 Drug- and toxin-induced PAH
1.4. PAH associated with:
- 1.4.1 Connective tissue diseases
- 1.4.2 HIV infection
- 1.4.3 Portal hypertension
- 1.4.4 Congenital heart diseases
- 1.4.5 Schistosomiasis

1.5 PAH long-term responders to calcium channel blockers
1.6 PAH with overt features of venous/capillaries (PVOD/PCH) involvement
1.7 Persistent PH of the newborn syndrome

2 PH due to left heart disease

2.1 PH due to heart failure with preserved LVEF
2.2 PH due to heart failure with reduced LVEF
2.3 Valvular heart disease
2.4 Congenital/acquired cardiovascular conditions leading to post-capillary PH

3 PH due to lung diseases and/or hypoxia

3.1 Obstructive lung disease
3.2 Restrictive lung disease
3.3 Other lung disease with mixed restrictive/obstructive pattern
3.4 Hypoxia without lung disease
3.5 Developmental lung disorders

4 PH due to pulmonary artery obstruction

4.1 Chronic thromboembolic PH
4.2 Other pulmonary artery obstructions
- 4.2.1 Sarcoma (high or intermediate grade) or angiosarcoma
- 4.2.2 Other malignant tumors
  - Renal carcinoma
  - Uterine carcinoma
  - Germ cell tumours of the testis
  - Other tumours
- 4.2.3 Non-malignant tumours
  - Uterine leiomyoma
- 4.2.4 Arteritis without connective tissue disease
- 4.2.5 Congenital pulmonary artery stenosis
- 4.2.6 Parasites
  - Hydatidosis

5 PH with unclear and/or multifactorial mechanisms

5.1 Hematologic disorders: Chronic hemolytic anemia, myeloproliferative disorders
5.2 Systemic and metabolic disorders: Pulmonary Langerhans cell histiocytosis, Gaucher disease, glycogen storage disease, neurofibromatosis, sarcoidosis
5.3 Others: chronic renal failure with or without hemodialysis, fibrosing mediastinitis
5.4 Complex congenital heart disease

VI. REFERENCES

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PRIOR AUTHORIZATION CRITERIA

BRAND NAME
(generic)

VERQUVO
(vericiguat)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

POLICY

FDA-APPROVED INDICATIONS

Verquvo is indicated to reduce the risk of cardiovascular death and heart failure (HF) hospitalization following a hospitalization for heart failure or need for outpatient IV diuretics, in adults with symptomatic chronic HF and ejection fraction less than 45%.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed to reduce the risk of cardiovascular death and heart failure hospitalization in an adult patient with symptomatic chronic heart failure

AND

- The patient has a left ventricular ejection fraction (LVEF) less than 45 percent. Documentation is required for approval.

AND

- The patient is currently receiving optimal therapy for heart failure management (e.g., angiotensin-converting enzyme inhibitor [ACEI], angiotensin II receptor blocker [ARB], angiotensin receptor-neprilysin inhibitor [ARNI], beta-blocker, sodium-glucose co-transporter-2 inhibitor [SGLT2I], mineralocorticoid receptor antagonist [MRA])

AND

- If the request is not for continuation of therapy, the patient has had any of the following: A) Hospitalization for heart failure within the past 6 months, B) Use of outpatient intravenous (IV) diuretics for heart failure within the past 3 months

REFERENCES

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3. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed June 20, 2022.
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PRIOR AUTHORIZATION CRITERIA

BRAND NAME
(generic)

VFEND
(voriconazole)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

POLICY

FDA-APPROVED INDICATIONS
Invasive Aspergillosis
Vfend is indicated in adults and pediatric patients (2 years of age and older) for the treatment of invasive aspergillosis (IA). In clinical trials, the majority of isolates recovered were *Aspergillus fumigatus*. There was a small number of cases of culture-proven disease due to species of *Aspergillus* other than *A. fumigatus*.
Candidemia in Non-neutropenic Patients and Other Deep Tissue Candida Infections
Vfend is indicated in adults and pediatric patients (2 years of age and older) for the treatment of candidemia in non-neutropenic patients and the following *Candida* infections: disseminated infections in skin and infections in abdomen, kidney, bladder wall, and wounds.
Esophageal Candidiasis
Vfend is indicated in adults and pediatric patients (2 years of age and older) for the treatment of esophageal candidiasis (EC) in adults and pediatric patients 2 years of age and older.
Scedosporiosis and Fusariosis
Vfend is indicated for the treatment of serious fungal infections caused by *Scedosporium apiospermum* (asexual form of *Pseudallescheria boydii*) and *Fusarium spp*. including *Fusarium solani*, in adults and pediatric patients (2 years of age and older) intolerant of, or refractory to, other therapy.

Specimens for fungal culture and other relevant laboratory studies (including histopathology) should be obtained prior to therapy to isolate and identify causative organism(s). Therapy may be instituted before the results of the cultures and other laboratory studies are known. However, once these results become available, antifungal therapy should be adjusted accordingly.

Compendial Uses
Febrile Neutropenia, Empiric Antifungal Therapy, High-Risk Patients[2,3,6,8]
Invasive Aspergillosis, Prophylaxis, High-Risk Patients[3,6]
Mycosis, Due to *Scedosporium prolificans*[3]
Oropharyngeal Candidiasis[2,3,5]
Pulmonary Aspergillosis, Chronic[3,6]

COVERAGE CRITERIA
The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for any of the following: A) treatment of invasive aspergillosis (including invasive pulmonary aspergillosis), B) serious fungal infection caused by Scedosporium apiospermum and Fusarium species, C) prophylaxis of invasive aspergillosis in a high-risk patient, D) chronic pulmonary aspergillosis, E) empiric antifungal therapy for febrile neutropenia in a high-risk patient, F) mycosis due to Scedosporium prolificans

OR

The requested drug is being prescribed for any of the following: A) candidemia in a non-neutropenic patient, B) disseminated Candida infection in the skin, C) Candida infection in the abdomen, kidney, bladder wall, or wounds, D) esophageal candidiasis, E) oropharyngeal candidiasis

AND

- The patient has experienced an inadequate treatment response to an alternative antifungal therapy

OR

- The patient has experienced an intolerance to an alternative antifungal therapy

OR

- The patient has a contraindication that would prohibit a trial of an alternative antifungal therapy

AND

- The patient will use the requested drug orally or intravenously

AND

- If the request is for voriconazole powder for oral suspension, the patient meets one of the following: A) has difficulty swallowing solid oral dosage forms (e.g., tablets), B) requires a dose that cannot be obtained using the commercially available tablets

REFERENCES

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Reference number(s)
2143-A, 2682-A

SPECIALTY GUIDELINE MANAGEMENT

VIEKIRA PAK
(ombitasvir/paritaprevir/ritonavir/dasabuvir)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Viekira Pak is indicated for the treatment of adult patients with chronic hepatitis C virus (HCV):
A. genotype 1b without cirrhosis or with compensated cirrhosis
B. genotype 1a without cirrhosis or with compensated cirrhosis for use in combination with ribavirin (RBV)

All other indications are considered experimental/investigational and not medically necessary.

II. EXCLUSIONS

Coverage will not be provided for members with decompensated cirrhosis/moderate or severe hepatic impairment (Child Turcotte Pugh Class B or C).

Note: When the requested drug is being used in a combination therapy regimen, exclusions to the other antiviral drugs also apply.

III. CRITERIA FOR INITIAL APPROVAL

A. Chronic hepatitis C virus infection, in combination with ribavirin
Note: Members with mixed genotype 1 infection or unknown genotype 1 subtype should follow the criteria for approval for genotype 1a infection.

1. Genotype 1a infection
i. Authorization of up to 12 weeks total may be granted for members without cirrhosis who are either of the following:
   a. Treatment-naïve
   b. Failed prior treatment with peginterferon alfa (PEG-IFN) and RBV
ii. Authorization of up to 24 weeks total may be granted for members with compensated cirrhosis who are either of the following:
   a. Treatment-naïve
   b. Failed prior treatment with PEG-IFN and RBV

2. Recurrent HCV infection post liver transplantation
Authorization of up to 24 weeks total may be granted for members with recurrent HCV infection post liver transplantation who meet all of the following criteria:
i. Genotype 1 infection (irrespective of subtype)
ii. Metavir fibrosis score of 2 or lower

B. Chronic hepatitis C virus infection, without ribavirin
Genotype 1b infection
Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who are either of the following:
1. Treatment-naïve
2. Failed prior treatment with PEG-IFN and RBV

C. HCV and HIV coinfection
Authorization may be granted for members with HCV and HIV coinfection when the criteria for approval of the requested regimen in section A or B above are met.

IV. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

V. REFERENCES

1. Viekira Pak [package insert]. North Chicago, IL: AbbVie Inc.; December 2019.

Reference number
1770-A

SPECIALTY GUIDELINE MANAGEMENT

SABRIL (vigabatrin) tablets and powder for oral solution
VIGADRONE (vigabatrin) powder for oral solution
vigabatrin tablets and powder for oral solution

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

A. Infantile spasms: Monotherapy for pediatric patients with infantile spasms one month to two years of age for whom the potential benefits outweigh the potential risk of vision loss.
B. Complex Partial Seizures: Adjunctive therapy for adults and pediatric patients two years of age and older with refractory complex partial seizures who have inadequately responded to several alternative treatments and for whom the potential benefits outweigh the risk of vision loss. Vigabatrin products are not indicated as a first line agent for complex partial seizures.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Infantile Spasms
Authorization of 4 weeks may be granted for treatment of infantile spasms in members less than 2 years of age.

B. Complex Partial Seizures
Authorization of 3 months may be granted for treatment of complex partial seizures when member has had an inadequate response to at least two alternative treatments for complex partial seizures.

III. CONTINUATION OF THERAPY

A. Infantile Spasms
Authorization of 6 months may be granted for members requesting vigabatrin for continuation of therapy when member has shown substantial clinical benefit from vigabatrin therapy.

B. Complex Partial Seizures
Authorization of 12 months may be granted for members requesting vigabatrin for continuation of therapy when member has shown substantial clinical benefit from vigabatrin therapy.

IV. REFERENCES

1. Sabril [package insert]. Deerfield, IL: Lundbeck Inc.; October 2021.

2. Vigabatrin for oral solution [package insert]. Chestnut Ridge, NY: Par Pharmaceutical; October 2021.
3. Vigadrone [package insert]. Maple grove, MN: Upsher-Smith Laboratories, LLC; February 2020.
4. Livingston JH, Beaumont D, Arzimanoglou A, et al: Vigabatrin in the treatment of epilepsy in children. *Br J Clin Pharmacol*. 1989; 27:109S-112S.
5. Luna D, Dulac O, Pajot N, et al: Vigabatrin in the treatment of childhood epilepsies: a single-blind placebo-controlled study. *Epilepsia.* 1989; 30:430-437.
6. Pellock JM, Hrachovy R, Shinnar S, et al. Infantile spasms: A U.S. consensus report. *Epilepsia*. 2010:51:2175-2189.
7. Go CY, Mackay MT, Weiss SK, et al. Evidence-based guideline update: Medical treatment of infantile spasms: Report of the Guideline Development Subcommittee of the American Academy of Neurology and the Practice Committee of the Child Neurology Society. *Neurology.* 2012; 78:1974-1980.
8. Hancock EC, Osborne JP, Edwards SW. Treatment of infantile spasms. *Cochrane Database Syst Rev*. 2013;6:CD001770.
9. Riikonen R. Recent advances in the pharmacotherapy of infantile spasms. *CNS Drugs* 2014; 28:279-290.
10. Pavone P, Striano P, Falsaperla R, et al. Infantile spasms syndrome, West Syndrome and related phenotypes: what we know in 2013. *Brain & Development*. 2014; 739-751.
11. Willmore LJ, Abelson MB, Ben-Menachem E, Pellock JM, Shields WD. Vigabatrin: 2008 Update. *Epilepsia.* 2009; 50(2):163-173.
12. Faught E. Vigabatrin therapy for refractory complex partial seizures: review of clinical trial experience in the United States. *Acta Neurol Scand*. 2011; 124(Suppl.192):29-35.

STEP THERAPY CRITERIA

DRUG CLASS	**VITAMIN D ANALOGS TOPICAL**
BRAND NAME (generic)	
	(calcipotriene topical scalp solution)
	CALCITRENE (calcipotriene ointment)
	DOVONEX (calcipotriene cream)
	ENSTILAR (calcipotriene/betamethasone dipropionate foam)
	SORILUX (calcipotriene foam)
	TACLONEX (calcipotriene/betamethasone dipropionate ointment, suspension)
	VECTICAL (calcitriol ointment)
	WYNZORA (calcipotriene/betamethasone dipropionate cream)

Status: CVS Caremark Criteria
Type: Initial Step Therapy with Quantity Limit;
Post Step Therapy Prior Authorization with Quantity Limit

POLICY

FDA-APPROVED INDICATIONS

Calcipotriene Topical Scalp Solution
Calcipotriene Topical Solution, 0.005% (Scalp Solution) is indicated for the topical treatment of chronic, moderately severe psoriasis of the scalp. The safety and effectiveness of topical calcipotriene in dermatoses other than psoriasis have not been established.

Calcitrene
Calcitrene (calcipotriene) ointment, 0.005% is indicated for the treatment of plaque psoriasis in adults. The safety and effectiveness of topical calcipotriene in dermatoses other than psoriasis have not been established.

Dovonex
Dovonex (calcipotriene) Cream, 0.005%, is indicated for the treatment of plaque psoriasis. The safety and effectiveness of topical calcipotriene in dermatoses other than psoriasis have not been established.

Enstilar
Enstilar (calcipotriene and betamethasone dipropionate) Foam is indicated for the topical treatment of plaque psoriasis in patients 12 years of age and older.

Sorilux
Sorilux foam is indicated for the topical treatment of plaque psoriasis of the scalp and body in patients 4 years of age and older.

Taclonex Ointment
Taclonex Ointment is indicated for the topical treatment of plaque psoriasis in patients 12 years of age and older.

Taclonex Topical Suspension
Taclonex Topical Suspension is indicated for the topical treatment of plaque psoriasis of the scalp and body in patients 12 years and older.

Vectical
Vectical Ointment is indicated for the topical treatment of mild to moderate plaque psoriasis in adults and pediatric patients 2 years and older.

Limitations of Use
Vectical Ointment should not be applied to the eyes, lips, or facial skin.

Wynzora
Wynzora Cream is indicated for the topical treatment of plaque psoriasis in patients 18 years of age and older.

INITIAL STEP THERAPY with QUANTITY LIMIT*
***Include Rx and OTC products unless otherwise stated.*

If the patient has filled a prescription for at least a 30-day supply of a topical steroid within the past 180 days under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit. If the patient does not meet the initial step therapy criteria or exceeds the initial quantity limit, then the claim will reject with a message indicating that a prior authorization (PA) is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

**If the patient meets the initial step therapy criteria, then the initial limit criteria will apply. If the patient is requesting more than the initial quantity limit the claim will reject with a message indicating that a PA is required.

****INITIAL LIMIT CRITERIA**
Limits do not accumulate together; patient is allowed the maximum limit for each drug and strength

Drug	1 Month Limit*	3 Month Limit*
Calcipotriene Topical Scalp Solution 0.005%	60 mL / 25 days	180 mL / 75 days
Calcitrene (calcipotriene) Topical Ointment 0.005%	60 g / 25 days	180 g / 75 days
Dovonex (calcipotriene) Cream 0.005%	60 g / 25 days	180 g / 75 days
Enstilar (calcipotriene/betamethasone diproprionate) Foam 0.005%/0.064%	60 g / 25 days	180 g / 75 days
Sorilux (calcipotriene) Foam 0.005%	60 g / 25 days	180 g / 75 days
Taclonex (calcipotriene/betamethasone diproprionate) Ointment 0.005%/0.064%	60 g / 25 days	180 g / 75 days

Taclonex (calcipotriene/betamethasone diproprionate) Suspension 0.005%/0.064%	60 g / 25 days	180 g / 75 days
Vectical (calcitriol) Ointment 3 mcg/g	100 g / 25 days	300 g / 75 days
Wynzora (calcipotriene/betamethasone diproprionate) Cream 0.005%/0.064%	60 g / 25 days	180 g / 75 days

**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for the treatment of psoriasis
  AND
- The patient has experienced an inadequate treatment response, intolerance, or the patient has a contraindication to a topical steroid
  AND
  - If additional quantities are being requested, then Vectical is being prescribed to treat a body surface area that requires more than 100 grams per month
    OR
  - If additional quantities are being requested, then Calcipotriene Topical Scalp Solution, Calcitrene Topical Ointment, Dovonex Cream, Enstilar Foam, Sorilux Foam, Taclonex Ointment, Taclonex Suspension, or Wynzora Cream is being prescribed to treat a body surface area that requires more than 60 units per month

Quantity limits apply.

POST LIMIT QUANTITY

Drug	1 Month Limit*	3 Month Limit*
Calcipotriene Topical Scalp Solution 0.005%	120 mL / 25 days	360 mL / 75 days
Calcitrene (calcipotriene) Topical Ointment 0.005%	120 g / 25 days	360 g / 75 days
Dovonex (calcipotriene) Cream 0.005%	120 g / 25 days	360 g / 75 days
Enstilar (calcipotriene/betamethasone diproprionate) Foam 0.005%/0.064%	120 g / 25 days	360 g / 75 days
Sorilux (calcipotriene) Foam 0.005%	120 g / 25 days	360 g / 75 days
Taclonex (calcipotriene/betamethasone diproprionate) Ointment 0.005%/0.064%	120 g / 25 days	360 g / 75 days
Taclonex (calcipotriene/betamethasone diproprionate) Suspension 0.005%/0.064%	120 g / 25 days	360 g / 75 days
Vectical (calcitriol) Ointment 3 mcg/g	200 g / 25 days	600 g / 75 days
Wynzora (calcipotriene/betamethasone diproprionate) Cream 0.005%/0.064%	120 g / 25 days	360 g / 75 days

**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*

REFERENCES

1. Calcipotriene Topical Scalp Solution [package insert]. Bridgewater, NJ: Amneal Pharmaceuticals LLC; December 2018.
2. Calcitrene Ointment [package insert]. Hawthorne, NY: Taro Pharmaceuticals U.S.A., Inc.; November 2011.
3. Dovonex Cream [package insert]. Madison, NJ: LEO Pharma Inc.; June 2017.
4. Enstilar Foam [package insert]. Madison, NJ: LEO Pharma Inc.; August 2021.
5. Sorilux [package insert].Greenville, NC: Mayne Pharma.; November 2019.
6. Taclonex Ointment [package insert]. Madison, NJ: LEO Pharma Inc.; March 2020.
7. Taclonex Topical Suspension [package insert]. Madison, NJ: LEO Pharma Inc.; August 2020.
8. Vectical Ointment [package insert]. Fort Worth, Texas: Galderma Laboratories, L.P.; September 2021.
9. Wynzora Cream [package insert]. Charleston, SC; EPI Health, LLC..; December 2021.
10. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2022; Accessed May 2, 2022.
11. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed May 2, 2022.
12. Elmets C, Korman, N, Farley Prater E, et al. Joint AAD-NPF Guidelines of care for the management and treatment of psoriasis with topical therapy and alternative medicine modalities for psoriasis severity measures. *J Am Acad Dermatol* 2020; 84:432-470.
13. Eichenfield L, Tom W, Berger T, et al. Guidelines of care for the management of atopic dermatitis: Section 2. Management and treatment of atopic dermatitis with topical therapies. *J Am Acad Dermatol* 2014; 71:116-32.

Reference number(s)
2799-A

SPECIALTY GUIDELINE MANAGEMENT

VITRAKVI (larotrectinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Vitrakvi is indicated for the treatment of adult and pediatric patients with solid tumors that:
1. have a neurotrophic receptor tyrosine kinase (NTRK) gene fusion without a known acquired resistance mutation,
2. are metastatic or where surgical resection is likely to result in severe morbidity, and
3. have no satisfactory alternative treatments or that have progressed following treatment.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: Chart documentation indicating a NTRK gene fusion status.

III. CRITERIA FOR INITIAL APPROVAL

Solid tumors with a NTRK gene fusion
Authorization of 12 months may be granted for treatment of solid tumors that have a NTRK gene fusion without a known acquired resistance mutation, as demonstrated by laboratory testing (e.g., next-generation sequencing [NGS] or fluorescence in situ hybridization [FISH]).

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

V. REFERENCES

1. Vitrakvi [package insert]. Whippany, NJ: Bayer HealthCare Pharmaceuticals Inc.; December 2022.
2. The NCCN Drugs & Biologics Compendium® © 2023 National Comprehensive Cancer Network, Inc. Available at: https://www.nccn.org. Accessed August 22, 2023.

Reference number(s)
2770-A

SPECIALTY GUIDELINE MANAGEMENT

VIZIMPRO (dacomitinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Vizimpro is indicated for the first-line treatment of patients with metastatic non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) exon 19 deletion or exon 21 L858R substitution mutations as detected by an FDA-approved test.

Compendial Uses
NSCLC, recurrent, advanced or metastatic sensitizing EGFR mutation-positive

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: For NSCLC, EGFR mutation testing results.

III. CRITERIA FOR INITIAL APPROVAL

Non-small cell lung cancer (NSCLC)
Authorization of 12 months may be granted for treatment of recurrent, advanced or metastatic NSCLC when the member has sensitizing EGFR mutation-positive disease as a single agent.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for EGFR positive NSCLC when either of the following criteria are met:
1. There is no evidence of unacceptable toxicity or disease progression while on the current regimen.
2. Disease is T790M negative and there is no evidence of unacceptable toxicity.

V. REFERENCES

1. Vizimpro [package insert]. New York, NY: Pfizer, Inc.; December 2020.
2. The NCCN Drugs & Biologics Compendium 2022 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed March 4, 2022.

3. Wu YL, Cheng Y, Zhou X, et al. Dacomitinib versus gefitinib as first-line treatment for patients with *EGFR*-mutation-positive non-small-cell lung cancer (ARCHER 1050): a randomised, open-label, phase 3 trial. *Lancet Oncology*. 2017; 18:1454-66.

QUANTITY LIMIT CRITERIA

DRUG CLASS **TOPICAL NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDs)**

BRAND NAME
(generic)

(diclofenac sodium topical gel 1%)

VOLTAREN GEL (OTC)
(diclofenac sodium topical gel 1%)

Status: CVS Caremark® Criteria
Type: Quantity Limit

POLICY

FDA-APPROVED INDICATIONS

Diclofenac sodium topical gel, 1%

Diclofenac sodium topical gel is indicated for the relief of the pain of osteoarthritis of joints amenable to topical treatment, such as the knees and those of the hands.

- Diclofenac sodium topical gel has not been evaluated for use on the spine, hip, or shoulder.

Voltaren Gel (OTC)

Voltaren Arthritis Pain is for the temporary relief of arthritis pain ONLY in the following areas:

- hand, wrist, elbow (upper body areas)
- foot, ankle, knee (lower body areas)

This product may take up to 7 days to work for arthritis pain; it is not for immediate relief. If no relief in 7 days, stop use.

INITIAL LIMIT QUANTITY

Drug	1 Month Limit*	3 Month Limit*
(diclofenac sodium topical gel, 1%)	300 grams / 25 days	900 grams / 75 days
Voltaren Gel (OTC) (diclofenac sodium topical gel, 1%)	300 grams / 25 days	900 grams / 75 days

**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*

REFERENCES

1. Diclofenac sodium topical gel, 1% gel [package insert]. Durham, NC: Encube Ethicals, Inc.; February 2020.
2. Voltaren Gel (OTC) [package insert]. Warren, NJ: GSK Consumer Healthcare; 2021.
3. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Waltham, MA: UpToDate, Inc.; 2023. https://online.lexi.com. Accessed April 25, 2023.
4. Micromedex (electronic version). Merative, Ann Arbor, Michigan, USA. Available at: https://www.micromedexsolutions.com/ (cited 04/25/2023).

Reference number(s)
5258-A

SPECIALTY GUIDELINE MANAGEMENT

VONJO (pacritinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Vonjo is indicated for the treatment of adults with intermediate or high-risk primary or secondary (post-polycythemia vera or post-essential thrombocythemia) myelofibrosis (MF) with a platelet count below 50 × 10^9/L.

Compendial Uses
1. Symptomatic low-risk MF with a platelet count <50 × 10^9/L
2. Symptomatic high-risk MF with a platelet count ≥50 × 10^9/L
3. Symptomatic accelerated phase or blast phase myelofibrosis/acute myeloid leukemia

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: pretreatment platelet count.

III. CRITERIA FOR INITIAL APPROVAL

Myelofibrosis/Acute Myeloid Leukemia
Authorization of 12 months may be granted for the treatment myelofibrosis/acute myeloid leukemia when any of the following criteria are met:
1. Member has a platelet count of <50 × 10^9/L and any of the following:
   a. Symptomatic low-risk MF and has failed treatment with ruxolitinib, peginterferon alfa-2a, or hydroxyurea
   b. Intermediate or high-risk primary or secondary (post-polycythemia vera or post-essential thrombocythemia) MF
2. Member has a platelet count of ≥50 × 10^9/L, symptomatic disease (e.g., splenomegaly and other disease-related symptoms) and any of the following:
   a. High-risk MF and is a candidate for transplant
   b. High-risk MF, is not a candidate for transplant, and has failed one prior JAK inhibitor (e.g., ruxolitinib or fedratinib)
   c. High-risk MF-associated anemia and is not a candidate for transplant
3. Member has symptomatic accelerated phase or blast phase myelofibrosis/acute myeloid leukemia

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III when there is no evidence of unacceptable toxicity and there has been an improvement in symptoms while on the current regimen.

V. REFERENCES

1. Vonjo [package insert]. Seattle, WA: CTI BioPharma Corp.; February 2022.
2. The NCCN Drugs & Biologics Compendium® © 2022 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed May 3, 2022.

Reference number(s)
2176-A, 2683-A

SPECIALTY GUIDELINE MANAGEMENT

VOSEVI (sofosbuvir/velpatasvir/voxilaprevir)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Vosevi is indicated for the treatment of adult patients with chronic hepatitis C virus (HCV) infection without cirrhosis or with compensated cirrhosis (Child-Pugh A) who have:

A. Genotype 1, 2, 3, 4, 5, or 6 infection and have previously been treated with an HCV regimen containing an NS5A inhibitor
B. Genotype 1a or 3 infection and have previously been treated with an HCV regimen containing sofosbuvir without an NS5A inhibitor
   Additional benefit of Vosevi over sofosbuvir/velpatasvir was not shown in adults with genotype 1b, 2, 4, 5, or 6 infection previously treated with sofosbuvir without an NS5A inhibitor.

All other indications are considered experimental/investigational and not medically necessary.

II. EXCLUSIONS

Coverage will not be provided for members with decompensated cirrhosis/moderate or severe hepatic impairment (Child Turcotte Pugh Class B or C).

Note: When the requested drug is being used in a combination therapy regimen, exclusions to the other antiviral drugs also apply.

III. CRITERIA FOR INITIAL APPROVAL

A. Hepatitis C virus infection, without ribavirin

1. Genotype 1a, 1b, and 2 infection

i. Authorization of up to 12 weeks total may be granted for members who failed prior treatment with a sofosbuvir-containing regimen.
ii. Authorization of up to 12 weeks total may be granted for members who failed prior treatment with an HCV NS5A inhibitor-containing regimen (except glecaprevir/pibrentasvir [Mavyret]).
iii. Authorization of up to 12 weeks total may be granted for members without cirrhosis who failed initial treatment with glecaprevir/pibrentasvir (Mavyret).

2. Genotype 3 infection

i. Authorization of up to 12 weeks total may be granted for members without cirrhosis who failed prior treatment with any direct-acting antiviral regimen (eg, NS5A- or sofosbuvir-containing regimen), including glecaprevir/pibrentasvir [Mavyret]).

ii. Authorization of up to 12 weeks total may be granted for members with compensated cirrhosis who are treatment naïve and have the Y93H substitution associated with velpatasvir resistance.

3. Genotype 4, 5, or 6 infection

i. Authorization of up to 12 weeks total may be granted for members who failed prior treatment with any direct-acting antiviral regimen (eg, NS5A- or sofosbuvir-containing regimen except glecaprevir/pibrentasvir [Mavyret]).

ii. Authorization of up to 12 weeks total may be granted for members without cirrhosis who failed initial treatment with glecaprevir/pibrentasvir (Mavyret).

4. Recurrent HCV infection post liver transplantation

Authorization of up to 12 weeks total may be granted for members with recurrent HCV genotype 1, 2, 3, 4, 5 or 6 infection who failed prior treatment with any direct-acting antiviral regimen (eg, NS5A- or sofosbuvir-containing regimen).

5. Kidney transplant recipients

Authorization of up to 12 weeks total may be granted for members who have genotype 1, 2, 3, 4, 5 or 6 infection and failed prior treatment with any direct-acting antiviral regimen (eg, NS5A- or sofosbuvir-containing regimen).

B. Hepatitis C virus infection, in combination with ribavirin

1. Genotype 3 infection

Authorization of up to 12 weeks total may be granted for members with compensated cirrhosis who failed prior treatment with any direct-acting antiviral regimen (eg, NS5A- or sofosbuvir-containing regimen), including glecaprevir/pibrentasvir [Mavyret]).

2. Direct-acting antiviral treatment failure

Genotype 1, 2, 3, 4, 5, or 6 infection

i. Authorization of up to 12 weeks total may be granted for members with compensated cirrhosis who failed initial treatment with glecaprevir/pibrentasvir (Mavyret).

ii. Authorization of up to 24 weeks total may be granted for members with or without compensated cirrhosis who failed initial treatment with sofosbuvir/velpatasvir/voxilaprevir (Vosevi).

3. Recurrent HCV infection post liver transplantation

Authorization of up to 12 weeks total may be granted for members with recurrent HCV genotype 1, 2, 3, 4, 5 or 6 infection who failed prior treatment with any direct-acting antiviral regimen (eg, NS5A- or sofosbuvir-containing regimen).

4. Kidney transplant recipients

Authorization of up to 12 weeks total may be granted for members who have genotype 1, 2, 3, 4, 5 or 6 infection and failed prior treatment with any direct-acting antiviral regimen (eg, NS5A- or sofosbuvir-containing regimen).

C. HCV and HIV Coinfection

Authorization may be granted for members with HCV and HIV coinfection when the criteria for approval of the requested regimen in Section A or B above are met.

IV. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

V. REFERENCES

1. Vosevi [package insert]. Foster City, CA: Gilead Sciences, Inc.; November 2019.
2. AASLD/IDSA/IAS–USA. Recommendations for testing, managing, and treating hepatitis C. https://www.hcvguidelines.org. Last changes made September 29, 2021. Accessed October 15, 2021.

Reference number
2009-A

SPECIALTY GUIDELINE MANAGEMENT

VOTRIENT (pazopanib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
1. Treatment of adults with advanced renal cell carcinoma (RCC)
2. Treatment of adults with advanced soft tissue sarcoma (STS) who have received prior chemotherapy

Limitations of Use: The efficacy of Votrient for the treatment of patients with adipocytic STS or gastrointestinal stromal tumors has not been demonstrated.

B. Compendial Uses
1. Relapsed or stage IV renal cell carcinoma
2. Uterine sarcoma
3. Gastrointestinal stromal tumors (GIST)
4. Soft tissue sarcoma that is not an adipocytic sarcoma
5. Medullary, papillary, Hürthle cell, or follicular thyroid carcinoma
6. Bone cancer of one of the following subtypes:
   a. Chordoma
   b. Chondrosarcoma
   c. Osteosarcoma

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Renal Cell Carcinoma

Authorization of 12 months may be granted when either the following criteria are met:
1. The requested medication will be used as a single agent for treatment of advanced, relapsed, or stage IV renal cell carcinoma.
2. The requested medication will be used for treatment of von Hippel-Lindau (VHL)-associated renal cell carcinoma.

B. Gastrointestinal Stromal Tumors

Authorization of 12 months may be granted for treatment of GIST when any of the following criteria are met:
1. The requested medication will be used as a single agent for treatment of unresectable, recurrent/progressive, or metastatic GIST after the member has failed at least four FDA-approved therapies (e.g., imatinib, sunitinib, regorafenib and ripretinib).

2. The requested medication will be used for treatment of unresectable succinate dehydrogenase (SDH)-deficient GIST as a single agent.
3. The requested medication will be used for palliation of symptoms if previously tolerated and effective.

C. Soft Tissue Sarcoma

Authorization of 12 months may be granted for treatment of soft tissue sarcoma, excluding adipocytic sarcoma and GIST (see specific criteria for GIST) when either of the following criteria are met:

1. The requested medication will be used as a single agent
2. The requested medication will be used for treatment of angiosarcoma and the requested medication will be used in combination with gemcitabine

D. Uterine Sarcoma

Authorization of 12 months may be granted as a single agent for subsequent treatment of recurrent or metastatic uterine sarcoma.

E. Papillary, Hürthle Cell, or Follicular Thyroid Carcinoma

Authorization of 12 months may be granted for treatment of progressive and/or symptomatic papillary, Hürthle cell, or follicular thyroid carcinoma not amenable to radioactive iodine (RAI) therapy.

F. Medullary Thyroid Carcinoma

Authorization of 12 months may be granted for treatment of recurrent or metastatic medullary thyroid carcinoma when either of the following criteria are met:

1. Member has an intolerance or contraindication to FDA approved systemic therapy options (e.g., cabozantinib [Cometriq], vandetanib [Caprelsa]); OR
2. Member has disease progression while on FDA approved systemic therapy options (e.g., cabozantinib [Cometriq], vandetanib [Caprelsa]).

G. Bone cancer

Authorization of 12 months may be granted for treatment of one of the following subtypes of bone cancer:

1. Chordoma
2. Chondrosarcoma
3. Osteosarcoma

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

IV. REFERENCES

1. Votrient [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; December 2021.
2. The NCCN Drugs & Biologics Compendium® © 2022 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed May 3, 2022.
3. Ganjoo KN, Villalobos VM, Kamaya A, et al. A multicenter phase II study of pazopanib in patients with advanced gastrointestinal stromal tumors (GIST) following failure of at least imatinib and sunitinib. *Ann Oncol* 2014;25(1):236-40.
4. van der Graaf WT, Blay JY, Chawla SP, et al. Pazopanib for metastatic soft-tissue sarcoma (PALETTE): a randomised, double blind, placebo-controlled phase 3 trial. *Lancet*. 2012;379(9829):1879-1886.

5. Nakano K, Motoi N, Inagaki L, et al. Differences in the responses to pazopanib and the prognoses of soft tissue sarcomas by their histological eligibility for the PALETTE study. *Jpn J Clin Oncol.* 2015;45(5):449-455.
6. Lipplaa A, Dijkstra S, Gelderblom H. Efficacy of pazopanib and sunitinib in advanced axial chordoma: a single reference centre case series. *Clin Sarcoma Res*. 2016;6:19.
7. Jones RL, Katz D, Loggers ET, et al. Clinical benefit of antiangiogenic therapy in advanced and metastatic chondrosarcoma. *Med Oncol*. 2017;34:167.
8. Safwat A, Boysen A, Lücke A, et al. Pazopanib in metastatic osteosarcoma: Significant clinical response in three consecutive patients. *Acta Oncol.*;53(10):1451-1454.

Reference number(s)
5922-A

SPECIALTY GUIDELINE MANAGEMENT

VOWST (fecal microbiota spores, live-brpk)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Vowst is indicated to prevent the recurrence of Clostridioides difficile infection (CDI) in individuals 18 years of age and older following antibacterial treatment for recurrent CDI (rCDI).

Limitations of Use
Vowst is not indicated for the treatment of CDI.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
A. Medical records, chart notes, and/or lab test results documenting the following:
   1. Recurrent CDI infection
   2. Stool test confirming the presence of *C.difficile* toxin or toxigenic *C. difficile*

III. EXCLUSIONS

Coverage will not be provided for members requesting Vowst for the treatment of CDI.

IV. CRITERIA FOR INITIAL APPROVAL

Prevention of recurrence of Clostridioides difficile infection (CDI)[1]
Authorization of 30 days for a one-time treatment may be granted for prevention of CDI when all of the following criteria are met:
A. Member is 18 years of age and older
B. Member has had three or more episodes of CDI within the past 12 months (including the most recent episode).
C. Member has a recent episode of recurrent CDI with all of the following:
   1. At least 3 unformed stools per day for 2 consecutive days
   2. Stool test confirming the presence of *C.difficile* toxin or toxigenic *C. difficile*
   3. An adequate clinical response (e.g., resolution of symptoms) following standard of care antibiotic therapy (e.g., vancomycin, fidaxomicin).

V. REFERENCES

1. Vowst [package insert]. Cambridge, MA: Seres Therapeutics Inc; April 2023.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME
(generic)

VUITY
(pilocarpine hydrochloride ophthalmic solution)

Status: CVS Caremark® Criteria
Type: Initial Prior Authorization

POLICY

FDA-APPROVED INDICATIONS
Vuity is indicated for the treatment of presbyopia in adults.

COVERAGE CRITERIA
The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for the treatment of presbyopia in an adult patient

AND

- The patient has been receiving the requested drug for at least 30 days **AND**
- The patient has demonstrated improvement from baseline presbyopia including gaining 3 lines or more in mesopic, high contrast, binocular distance corrected near visual acuity (DCNVA), without losing more than 1 line (5 letters) of corrected distance visual acuity (CDVA) with the same refractive correction since starting this therapy
  [Documentation is required for approval]

OR

- The presbyopia impacts the patient's activities of daily living to the point where pharmacologic intervention is required
  [Documentation is required for approval]

Quantity Limits apply.
5 mL per 19 days* or 15 mL per 57 days*
**The duration of 19 days is used for a 25-day fill period and 57 days is used for a 75-day fill period to allow time for refill processing.*
For new starts, the mail limit will be the same as the retail limit.* ***The intent is for prescriptions of the requested drug to be filled one fill at a time for new starts, even if filled at mail order; there should be no 3-month supplies filled for new starts. *The duration of 19 days is used for a 25-day fill period and 57 days is used for a 75-day fill period to allow time for refill processing.*

REFERENCES

1. Vuity [package insert]. North Chicago, IL: AbbVie Inc.; March 2023.
2. Lexicomp Online, Lexi-Drugs Online, Hudson, Ohio: UpToDate, Inc.; 2022; Accessed September 21, 2022.
3. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed September 21, 2022.
4. AbbVie. U.S. Food and Drug Administration Approves VUITYTM (pilocarpine HCl ophthalmic solution) 1.25%, the First and Only Eye Drop to Treat Presbyopia (Age-Related Blurry Near Vision). October 29, 2021. Available at: https://news.abbvie.com/news/press-releases/us-food-and-drug-administration-approves-vuity-pilocarpine-hci-ophthalmic-solution-125-first-and-only-eye-drop-to-treat-presbyopia-age-related-blurry-near-vision.htm. Accessed October 4, 2022.
5. Chuck RS, Jacobs DS, Lee JK, et al. Refractive Errors & Refractive Surgery Preferred Practice Pattern. *Ophthalmology*. 2018;125(1):P1-P104.

6. Pharmacy Auditing and Dispensing Job Aid: Billing Other Dosage Forms. Centers for Medicare and Medicaid Services. December 2015.
7. Waring GO 4th, Price FW Jr, Wirta D, et al. Safety and Efficacy of AGN-190584 in Individuals With Presbyopia: The GEMINI 1 Phase 3 Randomized Clinical Trial. *JAMA Ophthalmol*. 2022;140(4):363-371.
8. Clinicaltrials.gov. Allergan. Phase 3 Efficacy Study of AGN-190584 in Participants with Presbyopia. Last Updated September 2021. Retrieved from: https://clinicaltrials.gov/ct2/show/NCT03857542?term=NCT03857542. Accessed October 4, 2022.
9. Clinicaltrials.gov. Allergan. Study to Assess Safety and Efficacy in Participants Age 40 to 55 with Presbyopia (Old Eye) Who Receive AGN-190584 in Both Eyes Twice Daily (Virgo). Last Updated: March 2023. Retrieved from: https://clinicaltrials.gov/ct2/show/NCT04983589. Accessed April 17, 2023.

Reference number(s)
3395-A

SPECIALTY GUIDELINE MANAGEMENT

VUMERITY (diroximel fumarate)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Vumerity is indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Relapsing forms of multiple sclerosis (MS)
Authorization of 12 months may be granted to members who have been diagnosed with a relapsing form of multiple sclerosis (including relapsing-remitting and secondary progressive disease for those who continue to experience relapse).

B. Clinically isolated syndrome
Authorization of 12 months may be granted to members for the treatment of clinically isolated syndrome.

III. CONTINUATION OF THERAPY

For all indications: Authorization of 12 months may be granted to members who are experiencing disease stability or improvement while receiving Vumerity.

IV. OTHER CRITERIA

Members will not use Vumerity concomitantly with other disease modifying multiple sclerosis agents (Note: Ampyra and Nuedexta are not disease modifying).

V. REFERENCES

1. Vumerity [package insert]. Cambridge, MA: Biogen; January 2021.

CVS caremark®

PRIOR AUTHORIZATION CRITERIA

BRAND NAME
(generic)

VYLEESI
(bremelanotide)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization with Quantity Limit

POLICY

FDA-APPROVED INDICATIONS
Vyleesi is indicated for the treatment of premenopausal women with acquired, generalized hypoactive sexual desire disorder (HSDD), as characterized by low sexual desire that causes marked distress or interpersonal difficulty and is NOT due to:
• A co-existing medical or psychiatric condition,
• Problems with the relationship, or
• The effects of a medication or drug substance.
Acquired HSDD refers to HSDD that develops in a patient who previously had no problems with sexual desire.
Generalized HSDD refers to HSDD that occurs regardless of the type of stimulation, situation or partner.

Limitations of Use
• Vyleesi is not indicated for the treatment of HSDD in postmenopausal women or in men.
• Vyleesi is not indicated to enhance sexual performance.

COVERAGE CRITERIA
The requested drug will be covered with prior authorization when the following criteria are met:

- The patient is premenopausal

AND

- The patient has a diagnosis of acquired, generalized hypoactive sexual desire disorder (HSDD)

AND

- Hypoactive sexual desire disorder (HSDD) is NOT caused by a co-existing medical or psychiatric condition, problems with the relationship, or the effects of a medication or drug substance

  AND

  - The diagnosis has been appropriately documented (i.e., evaluated by a complete clinical assessment, using Diagnostic and Statistical Manual of Mental Disorders (DSM) and interviews/questionnaires)

  OR

  - The request is for continuation of therapy

    AND

  - The patient has received at least an 8-week supply of the requested drug as a paid claim through a pharmacy benefit (excluding the use of samples or vouchers/coupons)

    AND

  - The patient has experienced an improvement in the symptoms of hypoactive sexual desire disorder (HSDD) since staring this therapy

Quantity Limits apply.
8 autoinjectors (2.4 mL)/ 25 days* or 24 autoinjectors (7.2 mL)/ 75 days*
**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*

REFERENCES

1. Vyleesi [package insert]. Cranbury, NJ: Palatin Technologies, Inc.; February 2021.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2022; Accessed November 21, 2022.
3. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed November 21, 2022.
4. American Psychiatric Association, Diagnostic and Statistical Manual of Mental Disorder, Fourth Edition, Text Revision. Washington, District of Columbia: American Psychiatric Association; 2000.
5. American Psychiatric Association, Diagnostic and Statistical Manual of Mental Disorder, Fifth Edition, Text Revison. Arlington, Virgina: American Psychiatric Association; 2022.

Reference number(s)
3076-A

SPECIALTY GUIDELINE MANAGEMENT

VYNDAQEL (tafamidis meglumine)
VYNDAMAX (tafamidis)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Vyndaqel and Vyndamax are transthyretin stabilizers indicated for the treatment of the cardiomyopathy of wild-type or hereditary transthyretin-mediated amyloidosis (ATTR-CM) in adults to reduce cardiovascular mortality and cardiovascular-related hospitalization.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
A. Echocardiography or cardiac magnetic resonance imaging results confirming cardiac involvement
B. For members with hereditary ATTR-CM: results confirming a mutation of the transthyretin (TTR) gene
C. For biopsy proven disease:
   1. Tissue biopsy confirming the presence of the transthyretin amyloid deposition
   2. Immunohistochemical analysis, mass spectrometry, tissue staining, or polarized light microscopy results confirming transthyretin precursor proteins
D. For technetium-labeled bone scintigraphy proven disease:
   1. A serum kappa/lambda free light chain ratio, serum protein immunofixation or urine protein immunofixation test result showing the absence of monoclonal proteins
   2. Scintigraphy tracing results confirming presence of amyloid deposits
E. For continuation of therapy: Medical record documentation confirming the member demonstrates a beneficial response to treatment (e.g., improvement in rate of disease progression as demonstrated by distance walked on the 6-minute walk test, the Kansas City Cardiomyopathy Questionnaire–Overall Summary (KCCQ-OS) score, cardiovascular-related hospitalizations, NYHA classification of heart failure, left ventricular stroke volume, NT-proBNP level)

III. CRITERIA FOR INITIAL APPROVAL

Cardiomyopathy of wild-type or hereditary transthyretin-mediated amyloidosis
Authorization of 12 months may be granted for treatment of cardiomyopathy of wild-type or hereditary transthyretin-mediated amyloidosis (ATTR-CM) when all of the following criteria are met:
A. The member exhibits clinical symptoms of cardiomyopathy and heart failure (e.g., dyspnea, fatigue, orthostatic hypotension, syncope, peripheral edema).

B. Cardiac involvement was confirmed by echocardiography or cardiac magnetic resonance imaging (e.g., end-diastolic interventricular septal wall thickness exceeding 12 mm).
C. The diagnosis is confirmed by one of the following:
    1. The member meets both of the following:
        i. Presence of transthyretin amyloid deposits on analysis of biopsy from cardiac or noncardiac sites.
        ii. Presence of transthyretin precursor proteins was confirmed by immunohistochemical analysis, mass spectrometry, tissue staining, or polarized light microscopy.
    2. The member meets both of the following:
        i. Positive technetium-labeled bone scintigraphy tracing.
        ii. Systemic light chain amyloidosis is ruled out by a test showing absence of monoclonal proteins (serum kappa/lambda free light chain ratio, serum protein immunofixation, or urine protein immunofixation).
D. For members with hereditary ATTR-CM, presence of a mutation of the TTR gene was confirmed.
E. The member is not a liver transplant recipient.
F. The requested medication will not be used in combination with inotersen (Tegsedi), patisiran (Onpattro), or vutrisiran (Amvuttra).

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for the continued treatment of ATTR-CM when all of the following criteria are met:
A. The member must meet all initial authorization criteria.
B. The member must have demonstrated a beneficial response to treatment with tafamidis therapy (e.g., improvement in rate of disease progression as demonstrated by distance walked on the 6-minute walk test, the Kansas City Cardiomyopathy Questionnaire–Overall Summary [KCCQ-OS] score, cardiovascular-related hospitalizations, NYHA classification of heart failure, left ventricular stroke volume, N-terminal B-type natriuretic peptide [NT-proBNP] level). Documentation from the medical record must be provided.

V. REFERENCES

1. Vyndaqel and Vyndamax [package insert]. New York, NY: Pfizer Labs; April 2023.
2. Maurer MS, Schwartz JH, Gundapaneni B, et al. Tafamidis treatment for patients with transthyretin amyloid cardiomyopathy. *N Engl J Med*. 2018 Sep 13; 379(11):1007-1016.
3. Maurer MS, Sabahat B, Thibaud D, et al. Expert consensus recommendations for the suspicion and diagnosis of transthyretin cardiac amyloidosis. *Circ Heart Fail*. 2019 Sep 4;12:9.
4. Ruberg FL, Grogan M, et al. Transthyretin amyloid cardiomyopathy. *J Am Coll Cardiol*. 2019;73:2872-91.
5. Yadav JD, Othee H, Chan KA, Man DC, Belliveau PP, Towle J. Transthyretin Amyloid Cardiomyopathy-Current and Future Therapies. *Ann Pharmacother*. 2021;55(12):1502-1514.

STEP THERAPY CRITERIA

DRUG CLASS	**HMG-COA REDUCTASE INHIBITOR (STATIN)**
BRAND NAME*	
(generic)	
	VYTORIN 10/80 MG STRENGTH ONLY (ezetimibe / simvastatin 10/80mg)
	ZOCOR 80 MG STRENGTH ONLY (simvastatin 80mg)
Status: CVS Caremark Criteria	
Type: Initial Step Therapy; Post Step Therapy Prior Authorization	***Ref # 981-D***

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Vytorin

Therapy with lipid-altering agents should be only one component of multiple risk factor intervention in individuals at significantly increased risk for atherosclerotic vascular disease due to hypercholesterolemia. Drug therapy is indicated as an adjunct to diet when the response to a diet restricted in saturated fat and cholesterol and other nonpharmacologic measures alone has been inadequate.

Primary Hyperlipidemia

Vytorin is indicated for the reduction of elevated total cholesterol (total-C), low-density lipoprotein cholesterol (LDL-C), apolipoprotein B (Apo B), triglycerides (TG), and non-high-density lipoprotein cholesterol (non-HDL-C), and to increase high-density lipoprotein cholesterol (HDL-C) in patients with primary (heterozygous familial and non-familial) hyperlipidemia or mixed hyperlipidemia.

Homozygous Familial Hypercholesterolemia (HoFH)

Vytorin is indicated for the reduction of elevated total-C and LDL-C in patients with homozygous familial hypercholesterolemia, as an adjunct to other lipid-lowering treatments (e.g., LDL apheresis) or if such treatments are unavailable.

Limitations of Use

No incremental benefit of Vytorin on cardiovascular morbidity and mortality over and above that demonstrated for simvastatin has been established. Vytorin has not been studied in Fredrickson type I, III, IV, and V dyslipidemias.

Zocor

Therapy with lipid-altering agents should be only one component of multiple risk factor intervention in individuals at significantly increased risk for atherosclerotic vascular disease due to hypercholesterolemia. Drug therapy is indicated as an adjunct to diet when the response to a diet restricted in saturated fat and cholesterol and other nonpharmacologic measures alone has been inadequate. In patients with coronary heart disease (CHD) or at high risk of CHD, Zocor can be started simultaneously with diet.

Reductions in Risk of CHD Mortality and Cardiovascular Events

In patients at high risk of coronary events because of existing coronary heart disease, diabetes, peripheral vessel disease, history of stroke or other cerebrovascular disease, Zocor is indicated to:

- Reduce the risk of total mortality by reducing CHD deaths.

- Reduce the risk of non-fatal myocardial infarction and stroke.
- Reduce the need for coronary and non-coronary revascularization procedures.

Hyperlipidemia
Zocor is indicated to:
- Reduce elevated total cholesterol (total-C), low-density lipoprotein cholesterol (LDL-C), apolipoprotein B (Apo B), and triglycerides (TG), and to increase high-density lipoprotein cholesterol (HDL-C) in patients with primary hyperlipidemia (Fredrickson type IIa, heterozygous familial and nonfamilial) or mixed dyslipidemia (Fredrickson type IIb).
- Reduce elevated TG in patients with hypertriglyceridemia (Fredrickson type IV hyperlipidemia).
- Reduce elevated TG and VLDL-C in patients with primary dysbetalipoproteinemia (Fredrickson type III hyperlipidemia).
- Reduce total-C and LDL-C in patients with homozygous familial hypercholesterolemia (HoFH) as an adjunct to other lipid-lowering treatments (e.g., LDL apheresis) or if such treatments are unavailable.

Adolescent Patients with Heterozygous Familial Hypercholesterolemia (HeFH)
Zocor is indicated as an adjunct to diet to reduce total-C, LDL-C, and Apo B levels in adolescent boys and girls who are at least one year post-menarche, 10-17 years of age, with HeFH, if after an adequate trial of diet therapy the following findings are present:
1. LDL cholesterol remains ≥190 mg/dL; or
2. LDL cholesterol remains ≥160 mg/dL and
   - There is a positive family history of premature cardiovascular disease (CVD) or
   - Two or more other CVD risk factors are present in the adolescent patient.

The minimum goal of treatment in pediatric and adolescent patients is to achieve a mean LDL-C <130 mg/dL. The optimal age at which to initiate lipid-lowering therapy to decrease the risk of symptomatic adulthood CAD has not been determined.

Limitations of Use
Zocor has not been studied in conditions where the major abnormality is elevation of chylomicrons (i.e., hyperlipidemia Fredrickson types I and V).

INITIAL STEP THERAPY
If the patient has filled a prescription for at least a 290 day supply of 10/80 mg strength of ezetimibe/simvastatin (Vytorin) or at least a 290 day supply of 80 mg strength of simvastatin (Zocor) within the past 365 days under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit. If the patient does not meet the initial step therapy criteria, then the claim will reject with a message indicating that a prior authorization (PA) is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

COVERAGE CRITERIA
The requested drug will be covered with prior authorization when the following criteria are met:
- The patient has been taking the 10/80 mg strength of ezetimibe/simvastatin (Vytorin) OR the 80 mg strength of simvastatin (Zocor) chronically for 12 months or more

RATIONALE
If the patient has filled a prescription for at least a 290 day supply of 10/80 mg strength of ezetimibe/simvastatin (Vytorin) or at least a 290 day supply of 80 mg strength of simvastatin (Zocor) within the past 365 days under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit. The use of 290 days is based on an 80% medication possession ratio (MPR).

If the patient does not meet the initial step therapy criteria, then prior authorization is required.

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Due to the increased risk of myopathy, including

rhabdomyolysis, particularly during the first year of treatment, use of the 80 mg dose of simvastatin (Zocor) or the 10/80 mg dose of ezetimibe/simvastatin (Vytorin) should be restricted to patients who have been taking 80 mg of simvastatin chronically (e.g., for 12 months or more) without evidence of muscle toxicity. Due to an increased risk of myopathy, including rhabdomyolysis, associated with 80 mg of simvastatin, patients unable to achieve their low-density lipoprotein cholesterol (LDL-C) goal utilizing the 40 mg dose of simvastatin (Zocor) or the 10/40 mg dose of ezetimibe/simvastatin (Vytorin) should not be titrated to the 80 mg dose of simvastatin (Zocor) or the 10/80 mg dose of ezetimibe/simvastatin (Vytorin), but should be placed on alternative LDL-C-lowering treatment(s) that provides greater LDL-C lowering.[1-4] Therefore, Vytorin 10/80 mg strength or simvastatin (Zocor) 80 mg strength will only be approved for continuation of therapy and not for new starts.

REFERENCES

1. Vytorin [package insert]. Whitehouse Station, NJ: Merck Sharp & Dohme Corp; May 2020.
2. Zocor [package insert]. Whitehouse Station, NJ: Merck & Dohme Corp September 2020.
3. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. http://online.lexi.com/. Accessed November 2020.
4. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. http://www.micromedexsolutions.com/. Accessed November 2020.

Written by: UM Development (JK)
Date Written: 04/2013
Revised: (PL) 11/2013; (CF) 11/2014, 11/2015 (no clinical changes); (KM) 11/2016 (no clinical changes); 11/2017 (no clinical changes), 11/2018; (DS) 11/2019 (no clinical changes), (ME) 11/2020 (no clinical changes)
Reviewed: Medical Affairs (WLF) 04/2013; (LCB) 11/2013; (KJC) 11/2014; (DNC) 11/2018; (CHART) 11/27/2019, (CHART) 12/3/20
External Review: 06/2013, 02/2014, 02/2015, 02/2016, 02/2017, 02/2018, 02/2019, 02/2020, 02/2021

CRITERIA FOR APPROVAL

1	Has the patient been taking the 10/80 mg strength of ezetimibe/simvastatin (Vytorin) OR the 80 mg strength of simvastatin (Zocor) chronically for 12 months or more?	Yes	No

Mapping Instructions			
	Yes	**No**	**DENIAL REASONS – DO NOT USE FOR MEDICARE PART D**
1.	Approve, 36 months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have been taking it for 12 months or more. Your request has been denied based on the information we have. [Short Description: New to therapy]

Reference number(s)
3176-A

SPECIALTY GUIDELINE MANAGEMENT

WAKIX (pitolisant)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Wakix is indicated for the treatment of excessive daytime sleepiness (EDS) or cataplexy in adult patients with narcolepsy.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

A. For initial requests, all of the following (if applicable):
   1. Documentation of a sleep lab evaluation.
   2. Chart notes, medical record documentation, or claims history supporting previous medications tried (if applicable), including response to therapy. If therapy is not advisable, documentation of clinical reason to avoid therapy.

B. For continuation requests, chart notes or medical record documentation supporting a beneficial response to therapy (e.g., decrease in daytime sleepiness, decrease in cataplexy episodes from baseline).

III. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with a sleep specialist (e.g., neurologist experienced with sleep disorders, physician certified in sleep medicine).

IV. CRITERIA FOR INITIAL APPROVAL

A. Excessive Daytime Sleepiness with Narcolepsy
Authorization of 12 months may be granted for treatment of excessive daytime sleepiness (EDS) in adult patients with narcolepsy when all of the following criteria are met:
1. The diagnosis of narcolepsy is confirmed by a sleep lab evaluation.
2. The member has experienced an inadequate treatment response, intolerance to armodafinil or modafinil OR the member has a contraindication to both armodafinil and modafinil.

B. Cataplexy with Narcolepsy
Authorization of 12 months may be granted for the treatment of cataplexy in adult patients with narcolepsy when all of the following criteria are met:
1. The diagnosis of narcolepsy is confirmed by a sleep lab evaluation.

2. The member experiences at least 3 cataplexy attacks per week.

V. CONTINUATION OF THERAPY

A. Excessive Daytime Sleepiness with Narcolepsy

Authorization of 12 months may be granted for continued treatment of excessive daytime sleepiness (EDS) with narcolepsy when the member has demonstrated beneficial response to treatment as defined by a decrease in symptoms of daytime sleepiness from baseline.

B. Cataplexy with Narcolepsy

Authorization of 12 months may be granted for continued treatment of cataplexy with narcolepsy when the member has demonstrated beneficial response to treatment as defined by a decrease in cataplexy episodes from baseline.

VI. REFERENCES

1. Wakix [package insert]. Plymouth Meeting, PA: Harmony Biosciences, LLC; December 2022.
2. Dauvilliers Y, Bassetti C, Lammers GJ, et al. Pitolisant versus placebo or modafinil in patients with narcolepsy: a double-blind, randomised trial. *Lancet Neurol*. 2013 Nov;12(11):1068-75. doi: 10.1016/S1474-4422(13)70225-4. Epub 2013 Oct 7. Accessed March 10, 2020.
3. Fronczek R, Middelkoop HA, van Dijk JG, Lammers GJ. Focusing on vigilance instead of sleepiness in the assessment of narcolepsy: high sensitivity of the Sustained Attention to Response Task (SART). *Sleep*. 2006 Feb;29(2):187-91. Accessed March 10, 2020.
4. Morgenthaler TI, Vishesh KK, Brown T, et al. Practice Parameters for the Treatment of Narcolepsy and other Hypersomnias of Central Origin. *Sleep* 2007;30(12):1705-11.
5. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. http://www.micromedexsolutions.com/. Accessed February 24, 2023.
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PRIOR AUTHORIZATION CRITERIA

DRUG CLASS	**WEIGHT LOSS MANAGEMENT**
BRAND NAME (generic)	**WEGOVY (semaglutide injection)**
Status: CVS Caremark Criteria	
Type: Initial Prior Authorization	

POLICY

FDA-APPROVED INDICATIONS

Wegovy is indicated as an adjunct to a reduced calorie diet and increased physical activity for chronic weight management in adults with an initial body mass index (BMI) of:

- 30 kg/m^2 or greater (obesity), or
- 27 kg/m^2 or greater (overweight) in the presence of at least one weight-related comorbid condition (e.g., hypertension, type 2 diabetes mellitus, or dyslipidemia)

Limitations of Use

- Wegovy contains semaglutide and should not be coadministered with other semaglutide-containing products or with any other GLP-1 receptor agonist.
- The safety and effectiveness of Wegovy in combination with other products intended for weight loss, including prescription drugs, over-the-counter drugs, and herbal preparations, have not been established.
- Wegovy has not been studied in patients with a history of pancreatitis

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has completed at least 3 months of therapy with the requested drug at a stable maintenance dose
  AND
  - The patient lost at least 5 percent of baseline body weight OR the patient has continued to maintain their initial 5 percent weight loss. Documentation is required for approval.

OR

- The requested drug will be used with a reduced calorie diet and increased physical activity for chronic weight management in an adult
  AND
- The patient has participated in a comprehensive weight management program that encourages behavioral modification, reduced calorie diet and increased physical activity with continuing follow-up for at least 6 months prior to using drug therapy
  AND
  - The patient has a body mass index (BMI) greater than or equal to 30 kilogram per square meter
    OR
  - The patient has a body mass index (BMI) greater than or equal to 27 kilogram per square meter AND has at least one weight related comorbid condition (e.g., hypertension, type 2 diabetes mellitus or dyslipidemia)

REFERENCES

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Reference number(s)
4898-A

SPECIALTY GUIDELINE MANAGEMENT

WELIREG (belzutifan)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Von Hippel-Lindau (VHL) Disease
Welireg is indicated for the treatment of adult patients with von Hippel-Lindau (VHL) disease who require therapy for associated renal cell carcinoma (RCC), central nervous system (CNS) hemangioblastomas, or pancreatic neuroendocrine tumors (pNET), not requiring immediate surgery.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: genetic testing confirming germline VHL alteration

III. CRITERIA FOR INITIAL APPROVAL

Von Hippel-Lindau (VHL) Disease
Authorization of 12 months may be granted for treatment of VHL disease when all of the following criteria are met:
A. Diagnosis has been confirmed by genetic testing
B. Member does not require immediate surgery
C. Requested medication is being used to treat any of the following VHL-associated tumors:
    1. Renal cell carcinoma (RCC), as a single agent
    2. Central nervous system (CNS) hemangioblastomas, as a single agent
    3. Pancreatic neuroendocrine tumors (pNET)

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

V. REFERENCES

1. Welireg [package insert]. Rahway, NJ: Merck Sharp & Dohme Corp.; May 2022.

2. The NCCN Drugs & Biologics Compendium® © 2023 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed August 22, 2023.
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Reference number(s)
1666-A

SPECIALTY GUIDELINE MANAGEMENT

XALKORI (crizotinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
1. Non-Small Cell Lung Cancer (NSCLC)
   Xalkori is indicated for the treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors are anaplastic lymphoma kinase (ALK) or ROS1-positive as detected by an FDA-approved test.
2. Anaplastic Large Cell Lymphoma (ALCL)
   Xalkori is indicated for the treatment of pediatric patients 1 year of age and older and young adults with relapsed or refractory, systemic anaplastic large cell lymphoma (ALCL) that is ALK-positive.
3. Inflammatory myofibroblastic tumor (IMT)
   Xalkori is indicated for the treatment of adult and pediatric patients 1 year of age and older with unresectable, recurrent, or refractory inflammatory myofibroblastic tumor (IMT) that is ALK-positive.

Limitations of Use: The safety and efficacy of Xalkori have not been established in older adults with relapsed or refractory, systemic ALK-positive ALCL.

B. Compendial Uses
1. Cutaneous Melanoma
2. NSCLC, recurrent, advanced or metastatic ALK rearrangement-positive or ROS1 rearrangement-positive tumors
3. NSCLC, recurrent, advanced or metastatic MET exon 14 skipping positive tumors
4. NSCLC with high-level MET amplification
5. Inflammatory myofibroblastic tumor (IMT) with ALK translocation
6. Anaplastic large cell lymphoma, relapsed or refractory ALK-positive
7. Histiocytic Neoplasms:
   a. Erdheim-Chester Disease (ECD)
   b. Langerhans Cell Histiocytosis (LCH)
   c. Rosai-Dorfman Disease

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: ALK mutation or translocation status, ROS-1 mutation status, MET exon 14 skipping mutation status, or high-level MET amplification status (where applicable).

III. CRITERIA FOR INITIAL APPROVAL

A. Non-Small Cell Lung Cancer (NSCLC)

Authorization of 12 months may be granted for treatment of NSCLC when the member meets any of the following criteria:

1. Member has recurrent, advanced or metastatic ALK-positive NSCLC and will be used as a single agent.
2. Member has recurrent, advanced or metastatic ROS1-positive NSCLC and will be used as a single agent.
3. Member has recurrent, advanced, or metastatic MET exon 14 skipping mutation-positive NSCLC and will be used as a single agent.
4. Member has NSCLC with high-level MET amplification.

B. Inflammatory Myofibroblastic Tumor (IMT)

Authorization of 12 months may be granted for treatment of ALK-positive IMT as a single agent when either of the following criteria are met:

1. The member has uterine sarcoma and the disease is advanced, recurrent, metastatic, or inoperable
2. The member has a soft tissue sarcoma (not including uterine sarcoma)

C. Anaplastic Large Cell Lymphoma (ALCL)

Authorization of 12 months may be granted for initial palliative therapy or for treatment of relapsed or refractory ALK-positive ALCL as a single agent.

D. Histiocytic Neoplasms

Authorization of 12 months may be granted for treatment of any of the following histiocytic neoplasm subtypes as a single agent in members with an ALK gene fusion:

1. Symptomatic or relapsed/refractory Erdheim-Chester Disease (ECD)
2. Symptomatic or relapsed/refractory Rosai-Dorfman Disease
3. Langerhans Cell Histiocytosis (LCH)

E. Cutaneous Melanoma

Authorization of 12 months may be granted for subsequent treatment of unresectable or metastatic cutaneous melanoma when all of the following criteria are met:

1. The disease is ROS1-positive
2. The member had disease progression, had an intolerance or has a projected risk of progression with BRAF-targeted therapy (e.g., dabrafenib, encorafenib)
3. The requested medication will be used as a single agent

IV. CONTINUATION OF THERAPY

A. ALK-positive Non-Small Cell Lung Cancer (NSCLC) and ROS1-positive Non-Small Cell Lung Cancer (NSCLC)

Authorization of 12 months may be granted for continued treatment of ALK-positive non-small cell lung cancer (NSCLC) and ROS1-positive non-small cell lung cancer (NSCLC) in members requesting reauthorization when there is no evidence of unacceptable toxicity while on the current regimen.

B. All Other Indications

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

V. REFERENCES

1. Xalkori [package insert]. New York, NY: Pfizer Inc.; July 2022.
2. The NCCN Drugs & Biologics Compendium 2023 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed March 4, 2023.

Reference number(s)
2011-A

SPECIALTY GUIDELINE MANAGEMENT

XELJANZ (tofacitinib tablets; oral solution)
XELJANZ XR (tofacitinib extended release tablets)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
1. Xeljanz/Xeljanz XR is indicated for the treatment of adult patients with moderately to severely active rheumatoid arthritis (RA) who have had an inadequate response or intolerance to one or more tumor necrosis factor (TNF) blockers.
2. Xeljanz/Xeljanz XR is indicated for the treatment of adult patients with active psoriatic arthritis (PsA) who have had an inadequate response or intolerance to one or more TNF blockers.
3. Xeljanz/Xeljanz XR is indicated for the treatment of adult patients with active ankylosing spondylitis (AS) who have had an inadequate response or intolerance to one or more TNF blockers.
4. Xeljanz/Xeljanz XR is indicated for the treatment of adult patients with moderately to severely active ulcerative colitis (UC) who have had an inadequate response or intolerance to one or more TNF blockers.
5. Xeljanz/Xeljanz Oral Solution is indicated for the treatment of active polyarticular course juvenile idiopathic arthritis (pcJIA) in patients 2 years of age and older who have had an inadequate response or intolerance to one or more TNF blockers.

B. Compendial Uses
1. Oligoarticular juvenile idiopathic arthritis
2. Immune checkpoint inhibitor related toxicity

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

A. Rheumatoid arthritis (RA)
1. For initial requests: Chart notes, medical record documentation, or claims history supporting previous medications tried, including response to therapy (if applicable).
2. For continuation requests: Chart notes or medical record documentation supporting positive clinical response.

B. Psoriatic arthritis (PsA)
1. For initial requests: Chart notes, medical record documentation, or claims history supporting previous medications tried, including response to therapy.

2. For continuation requests: Chart notes or medical record documentation supporting positive clinical response.

C. Ankylosing spondylitis (AS)
1. Initial requests: Chart notes, medical record documentation, or claims history supporting previous medications tried, including response to therapy (if applicable).
2. Continuation requests: Chart notes or medical record documentation supporting positive clinical response.

D. Ulcerative colitis (UC)
1. Initial requests:
   i. Chart notes, medical record documentation, or claims history supporting previous medications tried (if applicable), including response to therapy. If therapy is not advisable, documentation of clinical reason to avoid therapy.
   ii. Chart notes or medical record documentation of hospitalization due to acute, severe ulcerative colitis (if applicable).
2. Continuation requests: Chart notes or medical record documentation supporting positive clinical response to therapy or remission.

E. Articular juvenile idiopathic arthritis:
1. Initial requests: Chart notes, medical record documentation, or claims history supporting previous medications tried, including response to therapy (if applicable).
2. Continuation requests: Chart notes or medical record documentation supporting positive clinical response.

F. Immune checkpoint inhibitor-related toxicity: Chart notes, medical record documentation, or claims history supporting previous medications tried, including response to therapy or intolerance to therapy. If therapy is not advisable, documentation of clinical reason to avoid therapy.

III. CRITERIA FOR INITIAL APPROVAL

A. Moderately to severely active rheumatoid arthritis (RA)
1. Authorization of 12 months may be granted for treatment of moderately to severely active rheumatoid arthritis (RA) when the member has experienced an inadequate response or intolerance to at least one tumor necrosis factor (TNF) inhibitor.

2. Authorization of 12 months may be granted for members who have previously received a biologic (other than a TNF inhibitor) or targeted synthetic drug (e.g., Rinvoq, Olumiant) indicated for moderately to severely active RA.

B. Active psoriatic arthritis (PsA)
Authorization of 12 months may be granted for treatment of active psoriatic arthritis (PsA) when both of the following criteria are met:
1. The requested drug will be used in combination with a conventional synthetic drug.
2. The member has experienced an inadequate response or intolerance to at least one TNF inhibitor.

C. Active ankylosing spondylitis (AS)
1. Authorization of 12 months may be granted for treatment of active ankylosing spondylitis when the member has experienced an inadequate response or intolerance to at least one TNF inhibitor.

2. Authorization of 12 months may be granted for members who have previously received a biologic (other than a TNF inhibitor) or targeted synthetic drug (e.g., Rinvoq) indicated for active ankylosing spondylitis.

D. Moderately to severely active ulcerative colitis (UC)

1. Authorization of 12 months may be granted for the treatment of moderately to severely active UC when the member has had an inadequate response, intolerance, or contraindication to at least one TNF inhibitor.

2. Authorization of 12 months may be granted for members who have previously received a biologic (other than a TNF inhibitor) or targeted synthetic drug (e.g., Rinvoq) indicated for moderately to severely active ulcerative colitis.

3. Authorization of 12 months may be granted for members who have been hospitalized for acute, severe UC (e.g., continuous bleeding, severe toxic symptoms, including fever and anorexia).

E. Active articular juvenile idiopathic arthritis

1. Authorization of 12 months may be granted for treatment of active articular juvenile idiopathic arthritis when the member has experienced an inadequate response or intolerance to at least one TNF inhibitor.

2. Authorization of 12 months may be granted for members who have previously received a biologic (other than a TNF inhibitor) or targeted synthetic drug indicated for active articular juvenile idiopathic arthritis.

F. Immune checkpoint inhibitor-related toxicity

Authorization of 1 month may be granted for treatment of immune checkpoint inhibitor-related colitis when the member has experienced an inadequate response, intolerance, or contraindication to infliximab or vedolizumab.

IV. CONTINUATION OF THERAPY

A. Moderately to severely active rheumatoid arthritis (RA)

Authorization of 12 months may be granted for all members (including new members) who are using the requested medication for moderately to severely active rheumatoid arthritis and who achieve or maintain a positive clinical response as evidenced by disease activity improvement of at least 20% from baseline in tender joint count, swollen joint count, pain, or disability.

B. Active psoriatic arthritis (PsA)

Authorization of 12 months may be granted for all members (including new members) who are using the requested medication for active psoriatic arthritis and who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition when there is improvement in any of the following from baseline:

1. Number of swollen joints
2. Number of tender joints
3. Dactylitis
4. Enthesitis
5. Skin and/or nail involvement

C. Active ankylosing spondylitis (AS)
Authorization of 12 months may be granted for all members (including new members) who are using the requested medication for active ankylosing spondylitis and who achieve or maintain a positive clinical response with the requested medication as evidenced by low disease activity or improvement in signs and symptoms of the condition when there is improvement in any of the following from baseline:
1. Functional status
2. Total spinal pain
3. Inflammation (e.g., morning stiffness)

D. Moderately to severely active ulcerative colitis (UC)
1. Authorization of 12 months may be granted for all members (including new members) who are using the requested medication for moderately to severely active ulcerative colitis and who achieve or maintain remission.

2. Authorization of 12 months may be granted for all members (including new members) who are using the requested medication for moderately to severely active ulcerative colitis and who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition when there is improvement in any of the following from baseline:
   i. Stool frequency
   ii. Rectal bleeding
   iii. Urgency of defecation
   iv. C-reactive protein (CRP)
   v. Fecal calprotectin (FC)
   vi. Endoscopic appearance of the mucosa
   vii. Improvement on a disease activity scoring tool (e.g., Ulcerative Colitis Endoscopic Index of Severity [UCEIS], Mayo score)

E. Active articular juvenile idiopathic arthritis
Authorization of 12 months may be granted for all members (including new members) who are using the requested medication for active articular juvenile idiopathic arthritis and who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition when there is improvement in any of the following from baseline:
1. Number of joints with active arthritis (e.g., swelling, pain, limitation of motion)
2. Number of joints with limitation of movement
3. Functional ability

F. Immune checkpoint inhibitor-related toxicity
All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

V. OTHER

For all indications: Member has had a documented negative TB test (which can include a tuberculosis skin test [PPD], an interferon-release assay [IGRA], or a chest x-ray)* within 6 months of initiating therapy for persons who are naïve to biologic drugs or targeted synthetic drug associated with an increased risk of TB.

* If the screening testing for TB is positive, there must be further testing to confirm there is no active disease. Do not administer the requested drug to members with active TB infection. If there is latent disease, TB treatment must be started before initiation of the requested drug.

For all indications: Member cannot use the requested medication concomitantly with any other biologic drugs, targeted synthetic drugs, or potent immunosuppressants such as azathioprine or cyclosporine.

VI. DOSAGE AND ADMINISTRATION

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

VII. REFERENCES

1. Xeljanz/Xeljanz XR [package insert]. New York, NY: Pfizer, Inc.; December 2021.
2. Singh JA, Saag KG, Bridges SL Jr, et al. 2015 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. *Arthritis Rheumatol.* 2016;68(1)1-26.
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13. Fraenkel L, Bathon JM, England BR, et al. 2021 American College of Rheumatology guideline for the treatment of rheumatoid arthritis. *Arthrit Care Res*. 2021.
14. The NCCN Drugs & Biologics Compendium® © 2021 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed June 6, 2021.
15. Ward MM, Deodhar A, Gensler LS, et al. 2019 Update of the American College of Rheumatology/Spondylitis Association of America/Spondyloarthritis Research and Treatment Network Recommendations for the Treatment of Ankylosing Spondylitis and Nonradiographic Axial Spondyloarthritis. *Arthritis Rheumatol.* 2019;71(10):1599-1613. doi:10.1002/art.41042.

Reference number(s)
1993-A

SPECIALTY GUIDELINE MANAGEMENT

XELODA (capecitabine)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
1. Colorectal Cancer
   a. Xeloda is indicated as a single agent for adjuvant treatment in patients with Dukes' C colon cancer who have undergone complete resection of the primary tumor when treatment with fluoropyrimidine therapy alone is preferred.
   b. Xeloda is indicated as first-line treatment in patients with metastatic colorectal carcinoma when treatment with fluoropyrimidine therapy alone is preferred.
2. Breast Cancer
   a. Xeloda in combination with docetaxel is indicated for the treatment of patients with metastatic breast cancer after failure of prior anthracycline-containing chemotherapy.
   b. Xeloda monotherapy is also indicated for the treatment of patients with metastatic breast cancer resistant to both paclitaxel and an anthracycline-containing chemotherapy regimen or resistant to paclitaxel and for whom further anthracycline therapy is not indicated, for example, patients who have received cumulative doses of 400 mg/m^2 of doxorubicin or doxorubicin equivalents.

B. Compendial Uses
1. Ampullary Adenocarcinoma
2. Anal carcinoma
3. Breast cancer
4. Central nervous system (CNS) metastases from breast cancer
5. Colorectal Cancer (including anal adenocarcinoma and appendiceal adenocarcinoma)
6. Esophageal and esophagogastric junction cancer
7. Gastric cancer
8. Head and neck cancers (including very advanced head and neck cancer)
9. Hepatobiliary cancers (including extrahepatic and intra-hepatic cholangiocarcinoma and gallbladder cancer)
10. Occult primary tumors (cancer of unknown primary)
11. Ovarian cancer, fallopian tube cancer, and primary peritoneal cancer: Epithelial ovarian cancer, fallopian tube cancer, primary peritoneal cancer, mucinous cancer, carcinosarcoma (malignant mixed Mullerian tumors), clear cell carcinoma, grade 1 endometrioid carcinoma, low-grade serious carcinoma/ovarian borderline epithelial tumor
12. Pancreatic adenocarcinoma
13. Penile cancer
14. Neuroendocrine and adrenal tumors
15. Thymomas and Thymic Carcinomas
16. Gestational Trophoblastic Neoplasia
17. Small bowel adenocarcinoma
18. Squamous cell skin cancer

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Colorectal Cancer (CRC)

Authorization of 12 months may be granted for treatment of colorectal cancer, including anal adenocarcinoma and appendiceal adenocarcinoma, as a single agent or as a component of CAPEOX (capecitabine and oxaliplatin) regimen.

B. Breast Cancer

Authorization of 12 months may be granted for treatment of breast cancer in members when any of the following criteria are met:

1. Member has human epidermal growth factor receptor 2 (HER2) negative recurrent unresectable, or metastatic disease or member had no response to preoperative systemic therapy, as a single agent or in combination with docetaxel; or
2. Member has early-stage HER2 negative postoperative residual disease, as a single agent; or
3. Member has HER2 positive advanced, recurrent unresectable, or metastatic disease or member had no response to preoperative systemic therapy, and the requested medication will be used as subsequent therapy in combination with trastuzumab and tucatinib or in combination with a HER2 inhibitor (e.g., margetuximab-cmkb [Margenza], trastuzumab [Herceptin], lapatinib [Tykerb], neratinib [Nerlynx]); or
4. The requested medication will be used in combination with ixabepilone for treatment of metastatic or locally advanced disease; or
5. Member has triple negative disease and meets one of the following criteria:
   a. The requested medication will be used as adjuvant therapy; or
   b. The requested medication will be used as maintenance therapy following adjuvant chemotherapy
6. Member has brain metastases in breast cancer and the requested medication will be used as initial therapy or for recurrent or relapsed disease.

C. Neuroendocrine and Adrenal Tumors

Authorization of 12 months may be granted for treatment of ANY of the following:

1. Member has neuroendocrine tumors of the gastrointestinal tract, lung, or thymus (carcinoid tumors); or
2. Member has neuroendocrine and adrenal tumors of the pancreas, in combination with temozolomide or as a component of CAPEOX (capecitabine and oxaliplatin) regimen; or
3. Member has extrapulmonary poorly differentiated disease/large or small cell disease/mixed neuroendocrine-non-neuroendocrine neoplasm, in combination with temozolomide or with concurrent or sequential radiation; or
4. Member has well differentiated grade 3 neuroendocrine tumors, in combination with temozolomide or as a component of CAPEOX (capecitabine and oxaliplatin) regimen

D. Pancreatic Adenocarcinoma

Authorization of 12 months may be granted for treatment of pancreatic adenocarcinoma.

E. Esophageal and Esophagogastric Junction Cancers

Authorization of 12 months may be granted for treatment of esophageal and esophagogastric junction cancers.

F. Gastric Cancer

Authorization of 12 months may be granted for treatment of gastric cancer.

G. Hepatobiliary Cancers
Authorization of 12 months may be granted for treatment of hepatobiliary cancers (including extrahepatic and intrahepatic cholangiocarcinoma and gallbladder cancer).

H. Ovarian Cancer, Fallopian Tube Cancer, and Primary Peritoneal Cancer
Authorization of 12 months may be granted for treatment of ANY of the following:
1. As a single agent therapy for persistent or recurrent epithelial ovarian cancer, fallopian tube cancer, primary peritoneal cancer, carcinosarcoma (malignant mixed Mullerian tumors), clear cell carcinoma, or grade 1 endometrioid carcinoma; or
2. Member has low-grade serous carcinoma/borderline epithelial tumor and the requested medication will be used as a single agent for platinum-sensitive or platinum-resistant recurrence
3. Member has mucinous carcinoma and either of the following criteria are met:
    a. The requested medication will be used in combination with oxaliplatin as adjuvant treatment; or
    b. The requested medication will be used as a single agent or in combination with oxaliplatin for treatment of persistent or relapsed/recurrent disease.

I. Head and Neck Cancers
Authorization of 12 months may be granted for treatment of head and neck cancers (including very advanced head and neck cancer), as a single agent.

J. Occult Primary Tumors (cancer of unknown primary)
Authorization of 12 months may be granted for treatment of occult primary tumors, as a single agent or as a component of CAPEOX (capecitabine and oxaliplatin) regimen.

K. Penile Cancer
Authorization of 12 months may be granted for treatment of penile cancer, as a single agent.

L. Anal Carcinoma
Authorization of 12 months may be granted for treatment of anal carcinoma when any of the following criteria are met:
1. The requested drug will be used with concurrent chemoradiation in combination with mitomycin.
2. The requested drug will be used with radiation after primary treatment of metastatic disease, as a single agent.

M. Thymomas and Thymic Carcinomas
Authorization of 12 months may be granted for treatment of thymomas and thymic carcinomas in combination with gemcitabine.

N. Gestational Trophoblastic Neoplasia
Authorization of 12 months may be granted for treatment of gestational trophoblastic neoplasia, as a single agent.

O. Small Bowel Adenocarcinoma
Authorization of 12 months may be granted for treatment of small bowel adenocarcinoma.

P. Squamous Cell Skin Cancer
Authorization of 12 months may be granted for treatment of squamous cell skin cancer when all of the following criteria are met:
1. Disease is new regional disease, unresectable, inoperable or incompletely resected, locally advanced, recurrent, or metastatic
2. Member is ineligible for or has progressed on immune checkpoint inhibitors and clinical trials
3. The requested medication will be used as a single agent.

Q. Ampullary Adenocarcinoma
Authorization of 12 months may be granted for treatment of ampullary adenocarcinoma.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

IV. REFERENCES

1. Xeloda [package insert]. South San Francisco, CA: Genentech, Inc.; May 2021.
2. The NCCN Drugs & Biologics Compendium 2022 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed July 6, 2022.
3. Clinical Pharmacology powered by ClinicalKey [database online]. Tampa, FL. Elsevier; https://www.clinicalkey.com/pharmacology/ [available with subscription]. Accessed July 6, 2022.
4. Ixempra [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; January 2016.
5. Lexicomp [database online]. Hudson, OH: Lexi-Comp, Inc.; http://online.lexi.com/lco/action/index/dataset/complete_ashp [available with subscription]. Accessed July 6, 2022.
6. Micromedex Solutions [database online]. Ann Arbor, MI: Truven Health Analytics Inc. Updated periodically. www.micromedexsolutions.com [available with subscription]. Accessed July 6, 2022.
7. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Gestational Trophoblastic Neoplasia. Version 2.2021. https://www.nccn.org/professionals/physician_gls/pdf/gtn.pdf. Accessed July 14, 2021.
8. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Anal Carcinoma. Version 1.2022. https://www.nccn.org/professionals/physician_gls/pdf/anal.pdf. Accessed June 30, 2022.

PRIOR AUTHORIZATION CRITERIA

DRUG CLASS	**WEIGHT LOSS MANAGEMENT**
BRAND NAME (generic)	**XENICAL (orlistat)**

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

POLICY

FDA-APPROVED INDICATIONS

Xenical is indicated for obesity management including weight loss and weight maintenance when used in conjunction with a reduced-calorie diet. Xenical is also indicated to reduce the risk for weight regain after prior weight loss. Xenical is indicated for obese patients with an initial body mass index (BMI) $\geq$30 kg/m^2 or $\geq$27 kg/m^2 in the presence of other risk factors (e.g., hypertension, diabetes, dyslipidemia).

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has completed at least 6 months of therapy with the requested drug
  AND
  - The patient lost at least 5 percent of baseline bodyweight OR the patient has continued to maintain their initial 5 percent weight loss. Documentation is required for approval.

OR

- The requested drug will be used with a reduced calorie diet and increased physical activity for chronic weight management
  AND
- The patient has participated in a comprehensive weight management program that encourages behavioral modification, reduced calorie diet and increased physical activity with continuing follow-up for at least 6 months prior to using drug therapy
  AND
  - The patient has a body mass index (BMI) greater than or equal to 30 kilogram per square meter
    OR
  - The patient has a body mass index (BMI) greater than or equal to 27 kilogram per square meter AND has at least one weight related comorbid condition (e.g., hypertension, type 2 diabetes mellitus or dyslipidemia)

REFERENCES

1. Xenical [package insert]. Montgomery, AL: H2-Pharma, LLC; January 2018.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, Ohio: UpToDate, Inc.; 2022; Accessed May 26, 2022.
3. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com/. Accessed May 26, 2022.
4. National Heart, Lung, and Blood Institute. Goals of Weight Management/Treatment to Prevent Further Weight Gain. https://www.nhlbi.nih.gov/health/educational/wecan/portion/documents/CORESET3. Accessed May 26, 2022.

5. Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents. National Heart, Lung, and Blood Institute. NIH Publication No. 12-7486. October 2012. http://www.nhlbi.nih.gov/guidelines/cvd_ped/peds_guidelines_full.pdf. 141-159. Accessed May 17, 2022.
6. Pharmacological Management of Obesity: An Endocrine Society Clinical Practice Guideline. The Journal of Clinical Endocrinology & Metabolism, Volume 100, Issue 2, 1 February 2015, Pages 342–362. https://academic.oup.com/jcem/article/100/2/342/2813109. Accessed May 17, 2022.
7. Jensen MD, et al. 2013 AHA/ACC/TOS guideline for the management of overweight and obesity in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and The Obesity Society. *Circulation.* 2013; 129:S102–S138.
8. Torgerson JS, Boldrin MN, Hauptman J, et al. Xenical in the prevention of diabetes in obese subjects (XENDOS) study. A randomized study of orlistat as an adjunct to lifestyle changes for the prevention of type 2 diabetes in obese patients. *Diabetes Care* 2004; 27:155-161.

Reference number(s)
1670-A

SPECIALTY GUIDELINE MANAGEMENT

XERMELO (telotristat ethyl)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Xermelo is indicated for the treatment of carcinoid syndrome diarrhea in combination with somatostatin analog (SSA) therapy in adults inadequately controlled by SSA therapy.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Carcinoid syndrome diarrhea
Authorization of 3 months may be granted for the treatment of carcinoid syndrome diarrhea when both of the following criteria are met:
A. The member has had an inadequate response to somatostatin analog (SSA) therapy alone
B. Xermelo will be used in combination with SSA therapy

III. CONTINUATION OF THERAPY

Authorization of 6 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II when all of the following criteria are met:
A. The member is currently receiving the requested medication through a paid pharmacy or medical benefit
B. The member is receiving the requested medication in combination with SSA therapy
C. The member is experiencing benefit from therapy as evidenced by disease stability or disease improvement (e.g., reduction in the number of daily bowel movements).

IV. REFERENCES

1. Xermelo [package insert]. Deerfield, IL: TerSera Therapeutics LLC; October 2020.

QUANTITY LIMIT PRIOR AUTHORIZATION CRITERIA

BRAND NAME*
(generic)

XIFAXAN 200 MG ONLY
(rifaximin)

Status: CVS Caremark Criteria
Type: Quantity Limit; Post Limit Prior Authorization ***Ref # 3123-HJ***

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

To reduce the development of drug-resistant bacteria and maintain the effectiveness of Xifaxan and other antibacterial drugs, Xifaxan when used to treat infection should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

Travelers' Diarrhea

Xifaxan is indicated for the treatment of travelers' diarrhea (TD) caused by noninvasive strains of *Escherichia coli* in adults and pediatric patients 12 years of age and older.

Limitations of Use

Xifaxan should not be used in patients with diarrhea complicated by fever or blood in the stool or diarrhea due to pathogens other than *Escherichia coli*.

INITIAL QUANTITY LIMIT**

LIMIT CRITERIA

Drug	1 Month Limit*	3 Month Limit*
Xifaxan 200 mg (rifaximin)	9 tablets / 25 days	Does Not Apply**

**The duration of 25 days is used for a 30-day fill period to allow time for refill processing.*
***** These drugs are for short-term acute use; therefore, the mail limit will be the same as the retail limit. The intent is for prescriptions of the requested drug to be filled one month at a time, even if filled at mail order; there should be no 3 month supplies filled.***

**If the patient is requesting more than the initial quantity limit, the claim will reject with a message indicating that a prior authorization is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for the treatment of moderate to severe travelers' diarrhea caused by noninvasive strains of *Escherichia coli* in a patient 12 years of age or older
  AND
- The infection is proven or strongly suspected to be caused by susceptible bacteria based on culture and susceptibility OR local epidemiology and susceptibility patterns
  AND

- The patient requires additional quantities due to multiple occurrences of travelers' diarrhea in a one-month period [Note: If diarrhea worsens or persists for more than 24-48 hours after initiating rifaximin, the drug should be discontinued and an alternative anti-infective considered.]

Quantity Limits apply.

RATIONALE

The usual dose of Xifaxan for the treatment of travelers' diarrhea is one 200 mg tablet taken orally three times a day for three days.[1] Treatment with a higher rifaximin dose did not provide additional clinical benefit.[2] Initial quantity limits will be set to allow for one treatment course for travelers' diarrhea per month. Dosing for the other FDA-approved indications of irritable bowel syndrome with diarrhea and prevention of hepatic encephalopathy are for the 550 mg tablets only and will not be addressed in this criteria.

If the patient is requesting more than the initial quantity limit, the claim will reject with a message indicating that a prior authorization is required.

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Xifaxan is indicated for the treatment of travelers' diarrhea (TD) caused by noninvasive strains of *Escherichia coli* in adults and pediatric patients 12 years of age and older. Xifaxan should not be used in patients with diarrhea complicated by fever or blood in the stool or diarrhea due to pathogens other than *Escherichia coli*. If diarrhea symptoms worsen or persist for more than 24-48 hours after initiating rifaximin, the drug should be discontinued and an alternative anti-infective should be considered.[1-3]

According to the Centers for Disease Control and Prevention (CDC), antibiotic treatment is not recommended in patients with mild travelers' diarrhea. Antibiotics may be used to treat cases of moderate travelers' diarrhea and should be used to treat severe travelers' diarrhea. Rifaximin may be used for noninvasive travelers' diarrhea.[4] Therefore, rifaximin will be approved for patients with moderate to severe travelers' diarrhea.

Additional quantities beyond 9 tablets per month will be approved when Xifaxan 200 mg is being prescribed for travelers' diarrhea caused by noninvasive strains of *Escherichia coli* in patients 12 years of age or older and the patient requires additional quantities due to multiple occurrences of travelers' diarrhea in a one-month period. The post limit will allow 9 additional tablets per month to allow a second course of treatment (total of 18 tablets per month). Due to the acute nature of travelers' diarrhea, the approval duration will be for one month.

REFERENCES

1. Xifaxan [package insert]. Bridgewater, New Jersey: Salix Pharmaceuticals, Inc.; October 2020.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: UpToDate, Inc.; 2022; Accessed March 14, 2022.
3. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. https://www.micromedexsolutions.com. Accessed March 14, 2022.
4. Centers for Disease Control and Prevention. CDC Yellow Book 2020: Health Information for International Travel. New York: Oxford University Press; 2019. Chapter 2, Preparing International Travelers.

Written by:	UM Development (KC)
Date Written:	07/2019
Revised:	(NZ) 03/2020 (no clinical changes), 03/2021 (added susceptibility question and note); (MRS) 03/2022 (added severity to indication question)
Reviewed:	Medical Affairs (CHART) 08/08/2019, 03/26/20, 03/25/21, 03/31/2022 External Review: 08/2019, 06/2020, 06/2021, 06/2022

CRITERIA FOR APPROVAL

1	Is the requested drug being prescribed for the treatment of moderate to severe travelers' diarrhea caused by noninvasive strains of *Escherichia coli* in a patient 12 years of age or older? [If no, then no further questions.]	Yes	No
2	Is the infection proven or strongly suspected to be caused by susceptible bacteria based on culture and susceptibility information OR local epidemiology and susceptibility patterns? [If no, then no further questions.]	Yes	No
3	Does the patient require additional quantities due to multiple occurrences of travelers' diarrhea in a one-month period? [Note: If diarrhea worsens or persists for more than 24-48 hours after initiating rifaximin, the drug should be discontinued and an alternative anti-infective considered.] [If no, then no further questions.]	Yes	No
4	Does the patient require MORE than the plan allowance of 18 tablets (2 courses of treatment) in one month? [RPh Note: If yes, then deny and enter a partial approval for 18 tablets per 25 days of Xifaxan 200 mg for one month.]	Yes	No

Mapping Instructions			
	Yes	**No**	**DENIAL REASONS – DO NOT USE FOR MEDICARE PART D**
1.	Go to 2	Deny	You do not meet the requirements of your plan. Your plan covers additional quantities of this drug when you meet all of these conditions: - You have moderate to severe travelers' diarrhea - You are 12 years of age or older Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]
2.	Go to 3	Deny	You do not meet the requirements of your plan. Your plan covers additional quantities of this drug when all of these conditions apply: - You have travelers' diarrhea that is caused by a specific bacteria - The specific bacteria are susceptible to the drug. Your request has been denied based on the information we have. [Short Description: No confirmation of diagnosis.]
3.	Go to 4	Deny	You do not meet the requirements of your plan. Your plan covers additional quantities of this drug when you have travelers' diarrhea more than once in a month. Your request has been denied based on the information we have. [Short Description: No multiple occurrences of travelers' diarrhea]
4.	Deny	Approve, 1 month, see Post Limit Quantity Chart	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 18 tablets per month of the requested drug and strength. You have been approved for the maximum quantity that your plan covers for a duration of 1 month. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity]

POST LIMIT QUANTITY

Drug	1 Month Limit*	3 Month Limit*
Xifaxan 200 mg (rifaximin)	18 tablets / 25 days	Does Not Apply*

** The duration of 25 days is used for a 30-day fill period to allow time for refill processing.*
***** This drug is for short-term acute use; therefore, the mail limit will be the same as the retail limit. The intent is for prescriptions of the requested drug to be filled one month at a time, even if filled at mail order; there should be no 3 month supplies filled.***

QUANTITY LIMIT PRIOR AUTHORIZATION CRITERIA

BRAND NAME
(generic)

XIFAXAN 200 MG ONLY
(rifaximin)

Status: CVS Caremark® Criteria
Type: Quantity Limit; Post Limit Prior Authorization

POLICY

FDA-APPROVED INDICATIONS
To reduce the development of drug-resistant bacteria and maintain the effectiveness of Xifaxan and other antibacterial drugs, Xifaxan when used to treat infection should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.
Travelers' Diarrhea
Xifaxan is indicated for the treatment of travelers' diarrhea (TD) caused by noninvasive strains of *Escherichia coli* in adults and pediatric patients 12 years of age and older.
Limitations of Use
Xifaxan should not be used in patients with diarrhea complicated by fever or blood in the stool or diarrhea due to pathogens other than *Escherichia coli*.

INITIAL QUANTITY LIMIT**

INITIAL LIMIT QUANTITY

Drug	1 Month Limit*	3 Month Limit*
Xifaxan 200 mg (rifaximin)	9 tablets / 25 days	Does Not Apply*

**The duration of 25 days is used for a 30-day fill period to allow time for refill processing.*
**** These drugs are for short-term acute use; therefore, the mail limit will be the same as the retail limit. The intent is for prescriptions of the requested drug to be filled one month at a time, even if filled at mail order; there should be no 3 month supplies filled.***

**If the patient is requesting more than the initial quantity limit, the claim will reject with a message indicating that a prior authorization is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

COVERAGE CRITERIA
The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for the treatment of moderate to severe travelers' diarrhea (TD) caused by noninvasive strains of *Escherichia coli*

AND

- The patient is 12 years of age or older

AND

- The infection is proven or strongly suspected to be caused by susceptible bacteria based on culture and susceptibility information OR local epidemiology and susceptibility patterns

AND

- The patient requires additional quantities due to multiple occurrences of travelers' diarrhea (TD) in a one-month period [Note: If diarrhea worsens or persists for more than 24-48 hours after initiating rifaximin, the drug should be discontinued and an alternative anti-infective considered.]

Quantity Limits apply.

POST LIMIT QUANTITY

Drug	1 Month Limit*	3 Month Limit*
Xifaxan 200 mg (rifaximin)	18 tablets / 25 days	Does Not Apply*

** The duration of 25 days is used for a 30-day fill period to allow time for refill processing.*
**** This drug is for short-term acute use; therefore, the mail limit will be the same as the retail limit. The intent is for prescriptions of the requested drug to be filled one month at a time, even if filled at mail order; there should be no 3 month supplies filled.***

REFERENCES

1. Xifaxan [package insert]. Bridgewater, New Jersey: Salix Pharmaceuticals, Inc.; September 2022.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Waltham, MA: UpToDate, Inc.; 2023. https://online.lexi.com. Accessed March 7, 2023.
3. Micromedex (electronic version). Merative, Ann Arbor, Michigan, USA. Available at: https://www.micromedexsolutions.com/ (cited: 03/07/2023).
4. Centers for Disease Control and Prevention. CDC Yellow Book 2020: Health Information for International Travel. New York: Oxford University Press; 2019. Chapter 2, Preparing International Travelers.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME*
(generic)

XIIDRA
(lifitegrast)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization with Quantity Limit ***Ref # 1504-C***

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Xiidra (lifitegrast ophthalmic solution) 5% is indicated for the treatment of the signs and symptoms of dry eye disease (DED).

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for dry eye disease

Quantity Limits apply.

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Xiidra (lifitegrast ophthalmic solution) 5% is indicated for the treatment of the signs and symptoms of dry eye disease (DED).[1]

Dosage for Xiidra is one drop in each eye twice a day, 4 drops per day total. Xiidra is available as single-use container. Each container contains enough solution to deliver one drop in each eye.[1] Therefore, the limit for Xiidra containers will be set at 60 containers per month.

REFERENCES

1. Xiidra [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corp.; June 2020.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2021; Accessed October 5, 2021.
3. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed October 5, 2021.

Written by:	UM Development (MS)
Date Written:	07/2016
Revised:	11/2016 (no clinical changes), (DS) 11/2017 (no clinical changes), 10/2018 (no clinical changes), 10/2019 (removed MDC designation; no clinical changes), 03/2020 (added QLs), 10/2020 (no clinical changes; updated document title), 10/2021 (no clinical changes)
Reviewed:	Medical Affairs (ME) 07/2016; (CHART) 10/31/2019, 04/02/2020, 10/29/2020, 10/28/2021 External Review: 08/2016, 02/2017, 12/2017, 02/2019, 02/2020, 06/2020 (FYI), 12/2020, 12/2021

CRITERIA FOR APPROVAL

1	Is the requested drug being prescribed for dry eye disease? [If no, then no further questions.]	Yes	No
2	Does the patient require more than the plan allowance of 4 drops per day of the requested drug? [RPh Note: If yes, then deny and enter a partial approval for 60 containers per 25 days or 180 containers per 75 days of Xiidra.]	Yes	No

Mapping Instructions			
	Yes	**No**	**DENIAL REASONS – DO NOT USE FOR MEDICARE PART D**
1.	Go to 2	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have dry eye disease. Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]
2.	Deny	Approve, 12 months, 60 containers/25 days* or 180 containers/75 days*	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 60 containers/month of the requested drug and strength. Your request has been partially approved. You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity]

**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*

Reference number(s)
2807-A

SPECIALTY GUIDELINE MANAGEMENT

XOSPATA (gilteritinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
Xospata is indicated for the treatment of adult patients who have relapsed or refractory acute myeloid leukemia (AML) with a FMS-like tyrosine kinase 3 (FLT3) mutation as detected by an FDA-approved test.

B. Compendial Uses
1. Myeloid/lymphoid neoplasms with eosinophilia and FLT3 rearrangement in chronic phase
2. Myeloid, lymphoid, or mixed lineage neoplasms with eosinophilia and FLT3 rearrangement in blast phase

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: medical record documentation of FLT3 mutation

III. CRITERIA FOR INITIAL APPROVAL

A. Acute Myeloid Leukemia (AML)
Authorization of 12 months may be granted for the treatment of FLT3 mutation-positive relapsed or refractory AML when the requested medication is used as a single-agent.

B. Myeloid/Lymphoid Neoplasms with eosinophilia
Authorization of 12 months may be granted for the treatment of myeloid and/or lymphoid neoplasms with eosinophilia with a FLT3 rearrangement in the chronic phase or blast phase.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

V. REFERENCES

1. Xospata [package insert]. Northbrook, IL: Astellas Pharma US, Inc.; January 2022.

2. The NCCN Drugs & Biologics Compendium® 2022 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed January 05, 2022.

Reference number(s)
3119-A

SPECIALTY GUIDELINE MANAGEMENT

XPOVIO (selinexor)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
1. Xpovio is indicated in combination with bortezomib and dexamethasone for the treatment of adult patients with multiple myeloma who have received at least one prior therapy.

2. Xpovio is indicated in combination with dexamethasone for the treatment of adult patients with relapsed or refractory multiple myeloma who have received at least four prior therapies and whose disease is refractory to at least two proteasome inhibitors, at least two immunomodulatory agents, and an anti-CD38 monoclonal antibody.

3. Xpovio is indicated for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL), not otherwise specified, including DLBCL arising from follicular lymphoma, after at least 2 lines of systemic therapy.

B. Compendial Uses
1. Multiple myeloma
2. B-cell lymphomas

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Multiple Myeloma
Authorization of 12 months may be granted for the treatment of multiple myeloma in any of the following settings:
1. The requested medication will be used in combination with dexamethasone for relapsed, refractory, or progressive disease and all of the following are met:
    a. The member has received at least four prior therapy regimens
    b. The member is refractory to at least two proteasome inhibitors
    c. The member is refractory to at least two immunomodulatory agents
    d. The member is refractory to an anti-CD38 monoclonal antibody

2. The requested medication will be used for relapsed or progressive disease in combination with any of the following:
    a. Bortezomib and dexamethasone
    b. Daratumumab and dexamethasone

c. Carfilzomib and dexamethasone
d. Pomalidomide and dexamethasone, after member has received at least two prior therapies, including an immunomodulatory agent and a proteasome inhibitor

B. B-Cell Lymphomas

Authorization of 12 months may be granted for the treatment of B-cell lymphoma when all of the following criteria are met:

1. Member has partially responsive, progressive, relapsed, or refractory disease
2. Member has received at least 2 prior lines of systemic therapy (includes transplant or CAR T-cell therapy)
3. Member has one of the following B-cell lymphoma subtypes:
    a. AIDS-related diffuse large B-cell lymphoma (DLBCL)
    b. AIDS-related primary effusion lymphoma
    c. AIDS-related HHV8-positive DLBCL
    d. DLBCL, including transformed DLBCL arising from follicular lymphoma
    e. High-grade B-cell lymphoma

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

IV. REFERENCES

1. Xpovio [package insert]. Newton, MA: Karyopharm Therapeutics Inc.; July 2022.
2. The NCCN Drugs & Biologics Compendium® 2022 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed September 30, 2022.

Reference number(s)
1933-A

SPECIALTY GUIDELINE MANAGEMENT

XTANDI (enzalutamide)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
Xtandi is indicated for the treatment of patients with:
1. Castration-resistant prostate cancer (CRPC)
2. Metastatic castration-sensitive prostate cancer (mCSPC)

B. Compendial Use
Prostate Cancer

All other indications are considered experimental/investigational and not medically necessary.

II. EXCLUSIONS

Coverage will not be provided if the requested medication is used in combination with a second-generation oral anti-androgen (e.g., apalutamide [Erleada]) or an oral androgen metabolism inhibitor (e.g., abiraterone acetate [Zytiga]).

III. CRITERIA FOR INITIAL APPROVAL

A. Castration-resistant prostate cancer (CRPC)
Authorization of 12 months may be granted for the treatment of castration-resistant prostate cancer when the member has had a bilateral orchiectomy or will be using the requested medication in combination with a GnRH agonist or degarelix.

B. Metastatic castration-sensitive prostate cancer (mCSPC)
Authorization of 12 months may be granted for the treatment of metastatic castration-sensitive prostate cancer when the member has had a bilateral orchiectomy or will be using the requested medication in combination with a GnRH agonist or degarelix.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

V. REFERENCES

1. Xtandi [package insert]. Northbrook, IL: Astellas Pharma US, Inc.; September 2022.
2. The NCCN Drugs & Biologics Compendium™ © 2023 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed August 6, 2023.

Reference number(s)
3677-A

SPECIALTY GUIDELINE MANAGEMENT

XYREM (sodium oxybate)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Treatment of cataplexy or excessive daytime sleepiness (EDS) in patients 7 years of age and older with narcolepsy.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

A. For initial requests, all of the following (if applicable):
   1. Documentation of a sleep lab evaluation
   2. Chart notes, medical record documentation, or claims history supporting previous medications tried (if applicable), including response to therapy. If therapy is not advisable, documentation of clinical reason to avoid therapy

B. For continuation requests, chart notes or medical record documentation supporting a beneficial response to therapy (e.g., decrease in daytime sleepiness, decrease in cataplexy episodes from baseline)

III. PRESCRIBER RESTRICTION

This medication must be prescribed by or in consultation with a sleep specialist.

IV. CRITERIA FOR INITIAL APPROVAL

A. Excessive Daytime Sleepiness with Narcolepsy

Authorization of 12 months may be granted for treatment of excessive daytime sleepiness when all of the following criteria are met:

1. The diagnosis of narcolepsy is confirmed by a sleep lab evaluation
2. If the member is 7 years of age or older and less than 18 years of age:
   i. The member has experienced an inadequate treatment response or intolerance to at least one central nervous system (CNS) stimulant drug (e.g., amphetamine, dextroamphetamine, or methylphenidate) OR
   ii. The member has a contraindication to at least one central nervous system (CNS) stimulant drug (e.g., amphetamine, dextroamphetamine, or methylphenidate)
3. If the member is 18 years of age or older:
   i. The member has experienced an inadequate treatment response or intolerance to modafinil or armodafinil OR
   ii. The member has a contraindication to both modafinil and armodafinil

B. Cataplexy with Narcolepsy
Authorization of 12 months may be granted for treatment of cataplexy with narcolepsy when all of the following criteria are met:
1. The member is 7 years of age or older
2. The diagnosis of narcolepsy is confirmed by a sleep lab evaluation
3. The member has a baseline history of at least 14 cataplexy attacks in a typical 2-week period

V. CONTINUATION OF THERAPY

A. Cataplexy with Narcolepsy
Authorization of 12 months may be granted for continued treatment of cataplexy with narcolepsy when the member has demonstrated beneficial response to treatment as defined by a decrease in cataplexy episodes from baseline.

B. Excessive Daytime Sleepiness with Narcolepsy
Authorization of 12 months may be granted for continued treatment of excessive daytime sleepiness (EDS) with narcolepsy when the member has demonstrated beneficial response to treatment as defined by a decrease in daytime sleepiness with narcolepsy from baseline.

VI. REFERENCES

1. Xyrem [package insert]. Palo Alto, CA: Jazz Pharmaceuticals, Inc; December 2020.
2. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. http://www.micromedexsolutions.com/. Accessed February 2022.
3. Morgenthaler TI, Vishesh KK, Brown T, et al. Practice Parameters for the Treatment of Narcolepsy and Other Hypersomnias of Central Origin. *Sleep* 2007; 30(12):1705-11.
4. American Academy of Sleep Medicine. *International Classification of Sleep Disorders: Diagnostic and Coding Manual*. 3rd edition. Westchester, IL: American Academy of Sleep Medicine; 2014.
5. Krahn, L, Hershner S, et al. Quality Measures for the Care of Patients with Narcolepsy; *Journal of Clinical Sleep Medicine*; 2015; 11(3): 335-55.
6. Nuvigil [package insert]. North Wales, PA: Teva Pharmaceuticals USA, Inc.; July 2019.
7. Provigil [package insert]. North Wales, PA: Teva Pharmaceuticals USA, Inc.; July 2019.

Reference number(s)
4045-A

SPECIALTY GUIDELINE MANAGEMENT

XYWAV (calcium, magnesium, potassium, and sodium oxybates)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

A. Xywav is indicated for the treatment of cataplexy or excessive daytime sleepiness (EDS) in patients 7 years of age and older with narcolepsy.
B. Xywav is indicated for the treatment of idiopathic hypersomnia (IH) in adults.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

A. For initial requests, all of the following (if applicable):
    1. Documentation of a sleep lab evaluation.
    2. Chart notes, medical record documentation, or claims history supporting previous medications tried (if applicable), including response to therapy. If therapy is not advisable, documentation of clinical reason to avoid therapy.
    3. Documentation of the multiple sleep latency test (MSLT) showing fewer than two sleep onset rapid eye movement periods (SOREMPs) or no SOREMPs if the REM latency of the preceding polysomnogram was less than or equal to 15 minutes.
    4. Mean sleep latency on MSLT of less than or equal to 8 minutes.
    5. Total 24-hour sleep time of greater than or equal to 660 minutes on 24-hour polysomnographic monitoring or by wrist actigraphy in association with a sleep log.
B. For continuation of therapy requests, chart notes or medical record documentation supporting a beneficial response to therapy (e.g., decrease in daytime sleepiness, decrease in cataplexy episodes from baseline).

III. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with a sleep specialist (e.g., neurologist experienced with sleep disorders, physician certified in sleep medicine).

IV. CRITERIA FOR INITIAL APPROVAL

A. Cataplexy with Narcolepsy
Authorization of 12 months may be granted for treatment of cataplexy with narcolepsy when all of the following criteria are met:

1. The member is 7 years of age or older.
2. The diagnosis of narcolepsy has been confirmed by a sleep lab evaluation.
3. The member has a baseline history of at least 14 cataplexy attacks in a typical 2-week period.

B. Excessive Daytime Sleepiness with Narcolepsy

Authorization of 12 months may be granted for treatment of excessive daytime sleepiness (EDS) with narcolepsy when all of the following criteria are met:

1. The diagnosis of narcolepsy has been confirmed by a sleep lab evaluation.
2. If the member is 7 years of age or older and less than 18 years of age:
   i. The member has experienced an inadequate treatment response or intolerance to at least one central nervous system (CNS) stimulant drug (e.g., amphetamine, dextroamphetamine, methylphenidate) OR
   ii. The member has a contraindication to at least one central nervous system (CNS) stimulant drug (e.g., amphetamine, dextroamphetamine, methylphenidate).
3. If the member is 18 years of age or older:
   i. The member has experienced an inadequate treatment response or intolerance to armodafinil or modafinil OR
   ii. The member has a contraindication to both armodafinil and modafinil.

C. Idiopathic hypersomnia

Authorization of 12 months may be granted for treatment of idiopathic hypersomnia when the diagnosis of idiopathic hypersomnia has been confirmed by all of the following:

1. Presence of daytime lapses into sleep or daily irrepressible periods of need to sleep for at least 3 months.
2. Insufficient sleep syndrome has been ruled out such as by lack of improvement of sleepiness after an adequate trial of increased nocturnal time in bed, preferably confirmed by at least a week of sleep log with wrist actigraphy.
3. A multiple sleep latency test (MSLT) documents fewer than two sleep onset rapid eye movement periods (SOREMPs) or no SOREMPs if the REM latency on the preceding polysomnogram was less than or equal to 15 minutes.
4. Presence of at least one of the following:
   i. Mean sleep latency on MSLT of less than or equal to 8 minutes.
   ii. Total 24-hour sleep time of greater than or equal to 660 minutes on 24-hour polysomnographic monitoring after correcting any chronic sleep deprivation or by wrist actigraphy in association with a sleep log and averaged over at least 7 days of unrestricted sleep.
5. The member does not have cataplexy.
6. Hypersomnolence or multiple sleep latency test results are not better explained by another sleep disorder, other medical or psychiatric disorder, or use of drugs or medications.

V. CONTINUATION OF THERAPY

A. Cataplexy with Narcolepsy

Authorization of 12 months may be granted for continued treatment of cataplexy with narcolepsy when the member has demonstrated beneficial response to treatment as defined by a decrease in cataplexy episodes from baseline.

B. Excessive Daytime Sleepiness with Narcolepsy

Authorization of 12 months may be granted for continued treatment of excessive daytime sleepiness (EDS) with narcolepsy when the member has demonstrated beneficial response to treatment as defined by a decrease in daytime sleepiness with narcolepsy from baseline.

C. Idiopathic hypersomnia
Authorization of 12 months may be granted for continued treatment of idiopathic hypersomnia when the member has demonstrated beneficial response to treatment as defined by a decrease in daytime sleepiness from baseline.

VI. REFERENCES

1. Xywav [package insert]. Palo Alto, CA: Jazz Pharmaceuticals, Inc.; March 2022.
2. Morgenthaler TI, Vishesh KK, Brown T, et al. Practice Parameters for the Treatment of Narcolepsy and other Hypersomnias of Central Origin. *Sleep* 2007; 30(12):1705-11.
3. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. http://online.lexi.com/. Accessed March 1, 2023.
4. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. http://www.micromedexsolutions.com/. Accessed March 1, 2023.
5. Satela, M. International Classification of Sleep Disorders- third edition: highlights and modifications. *Chest.* Nov 2014; 146(5)L 1387-1394.
6. Maski K, Trotti LM, Kotagal S, Auger RR, et al. Treatment of central disorders of hypersomnolence: an American Academy of Sleep Medicine clinical practice guideline. *J Clin Sleep Med.* Published online September 1, 2021.

Reference number(s)
2596-A

SPECIALTY GUIDELINE MANAGEMENT

YONSA (fine-particle abiraterone acetate)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication
Yonsa is indicated in combination with methylprednisolone for the treatment of patients with metastatic castration-resistant prostate cancer (CRPC).

B. Compendial Use
Prostate Cancer

All other indications are considered experimental/investigational and not medically necessary.

II. EXCLUSIONS

Coverage will not be provided if the requested medication is used in combination with a second-generation oral anti-androgen (e.g., apalutamide [Erleada]) or an oral androgen metabolism inhibitor (e.g., abiraterone acetate [Zytiga]).

III. CRITERIA FOR INITIAL APPROVAL

Metastatic castration-resistant prostate cancer
Authorization of 12 months may be granted for treatment of metastatic castration-resistant prostate cancer when the member has had a bilateral orchiectomy or will be using the requested medication in combination with a GnRH agonist or degarelix.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

V. REFERENCES

1. Yonsa [package insert]. Cranbury, NJ: Sun Pharmaceutical Industries, Inc.; July 2022.
2. The NCCN Drugs & Biologics Compendium™ © 2023 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed August 6, 2023.

Reference number(s)
2145-A, 2684-A

SPECIALTY GUIDELINE MANAGEMENT

ZEPATIER (elbasvir and grazoprevir)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Zepatier is indicated for the treatment of chronic hepatitis C virus (HCV) genotype 1 or 4 infection in adult and pediatric patients 12 years of age and older or weighing at least 30 kg.

Zepatier is indicated for use with ribavirin in certain patient populations.

All other indications are considered experimental/investigational and not medically necessary.

II. EXCLUSIONS

Coverage will not be provided for members with decompensated cirrhosis/moderate or severe hepatic impairment (Child Turcotte Pugh Class B or C).

Note: When the requested drug is being used in a combination therapy regimen, exclusions to the other antiviral drugs also apply.

III. CRITERIA FOR INITIAL APPROVAL

A. Hepatitis C virus infection, in combination with ribavirin (RBV)

1. Genotype 1a infection

i. Authorization of up to 16 weeks total may be granted for members with baseline NS5A resistance-associated substitutions (RASs)/polymorphisms (see Section V) who are either of the following:
   a. Treatment-naïve
   b. Failed prior treatment with peginterferon alfa (PEG-IFN) and RBV with or without an HCV protease inhibitor (boceprevir, simeprevir or telaprevir)

ii. Authorization of up to 12 weeks total may be granted for members without baseline NS5A resistance-associated substitutions (RASs)/polymorphisms (see Section V) who have failed prior treatment with PEG-IFN and RBV with an HCV protease inhibitor (boceprevir, simeprevir or telaprevir).

2. Genotype 1b infection

Authorization of up to 12 weeks total may be granted for members who failed prior treatment with PEG-IFN and RBV with an HCV protease inhibitor (boceprevir, simeprevir or telaprevir).

3. Genotype 4 infection

Authorization of up to 16 weeks total may be granted for members who failed prior treatment with PEG-IFN and RBV.

B. Hepatitis C virus infection, without RBV

1. Genotype 1a infection

Authorization of up to 12 weeks total may be granted for members without baseline NS5A resistance-associated substitutions (RASs)/polymorphisms who are either of the following:

i. Treatment-naïve
ii. Failed prior treatment with PEG-IFN and RBV without an HCV protease inhibitor (boceprevir, simeprevir or telaprevir)

2. Genotype 1b infection

Authorization of up to 12 weeks total may be granted for members who are either of the following:

i. Treatment-naïve
ii. Failed prior treatment with PEG-IFN and RBV without an HCV protease inhibitor (boceprevir, simeprevir or telaprevir)

3. Genotype 4 infection

Authorization of up to 12 weeks total may be granted for members who are treatment-naïve.

4. Kidney transplant recipients

Authorization of up to 12 weeks total may be granted for members without baseline NS5A resistance-associated substitutions (RASs)/polymorphisms (see Section V) who have HCV genotype 1 or 4 infection and are treatment-naïve or who have not failed prior treatment with a direct-acting antiviral.

C. HCV and HIV coinfection

Authorization may be granted for members with HCV and HIV coinfection when the criteria for approval of the requested regimen in Section A or B above are met.

IV. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

V. APPENDIX: NS5A RESISTANCE-ASSOCIATED SUBSTITUTIONS (POLYMORPHISMS)

NS5A resistance-associated substitutions (polymorphisms) at amino acid positions M28, Q30, L31 or Y93. Examples include M28A/T, Q30H/R, L31M/V, and Y93C/H/N.

VI. REFERENCES

1. Zepatier [package insert]. Whitehouse Station, NJ: Merck & Co., Inc.; December 2021.
2. AASLD/IDSA/IAS–USA. Recommendations for testing, managing, and treating hepatitis C. https://www.hcvguidelines.org. Last changes made September 29, 2021. Accessed October 15, 2021.

Reference number(s)
1685-A

SPECIALTY GUIDELINE MANAGEMENT

ZELBORAF (vemurafenib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met, and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
1. Zelboraf is indicated for the treatment of patients with unresectable or metastatic melanoma with BRAF V600E mutation as detected by an FDA-approved test.

   Limitation of use: Zelboraf is not indicated for treatment of patients with wild-type BRAF melanoma.

2. Zelboraf is indicated for the treatment of patients with Erdheim-Chester Disease with BRAF V600 mutation.

B. Compendial Uses
1. Non-small cell lung cancer, BRAF V600E mutation-positive
2. Hairy cell leukemia
3. Thyroid carcinoma
   a. Papillary carcinoma
   b. Follicular carcinoma
   c. Hürthle cell carcinoma
4. Glioma, BRAF V600 activating mutation-positive
5. Meningioma, BRAF V600 activating mutation-positive
6. Astrocytoma, BRAF V600 activating mutation-positive
7. Cutaneous melanoma
8. Histiocytic Neoplasms
   a. Erdheim-Chester Disease
   b. Langerhans Cell Histiocytosis

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of BRAF mutation documentation is necessary to initiate the prior authorization review for applicable indications as outlined in Section III.

III. CRITERIA FOR INITIAL APPROVAL

A. Cutaneous Melanoma

Authorization of 12 months may be granted for treatment of cutaneous melanoma with a BRAF V600 activating mutation (e.g., V600E or V600K) in any of the following settings:

1. Unresectable or metastatic disease when used as a single agent or in combination with cobimetinib (Cotellic) with or without atezolizumab (Tecentriq).
2. Adjuvant treatment of resected stage III disease in combination with cobimetinib (Cotellic) when the member has had an unacceptable toxicity to dabrafenib (Tafinlar) in combination with trametinib (Mekinist) or dabrafenib/trametinib are less desirable based on side-effect profiles.
3. Limited resectable local satellite/in-transit recurrent disease in combination with cobimetinib (Cotellic) when the member has had an unacceptable toxicity to dabrafenib (Tafinlar) in combination with trametinib (Mekinist) or dabrafenib/trametinib are less desirable based on side-effect profiles.

B. Central Nervous System Cancer

Authorization of 12 months may be granted for treatment of BRAF V600 mutation-positive (e.g., BRAF V600E or V600K mutation) gliomas, meningiomas, or astrocytomas.

C. Histiocytic Neoplasms

Authorization of 12 months may be granted for treatment of BRAF V600 mutation-positive (e.g., BRAF V600E or V600K mutation) Erdheim-Chester disease or Langerhans cell histiocytosis as a single agent.

D. Non-small Cell Lung Cancer (NSCLC)

Authorization of 12 months may be granted for treatment of BRAF V600E mutation-positive advanced or metastatic NSCLC, as a single agent, if the combination of dabrafenib (Tafinlar) plus trametinib (Mekinist) is not tolerated.

E. Hairy Cell Leukemia

Authorization of 12 months may be granted for treatment of hairy cell leukemia for either of the following:

1. Subsequent therapy as a single agent or in combination with rituximab, or
2. Initial therapy in combination with obinutuzumab for members who are unable to tolerate purine analogs

F. Thyroid Carcinoma

Authorization of 12 months may be granted when all of the following criteria are met:

1. Member has follicular, Hürthle cell, or papillary thyroid carcinoma that is not amenable to radioactive iodine (RAI) therapy.
2. Tumor is positive for BRAF mutation (e.g., BRAF V600E or V600K).

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

V. REFERENCES

1. Zelboraf [package insert]. South San Francisco, CA: Genentech USA, Inc.; May 2020.
2. The NCCN Drugs & Biologics Compendium 2021 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed November 5, 2021.
3. Usubalieva A, Pierson CR, Kavran CA, et al. Primary Meningeal Pleomorphic Xanthoastrocytoma With Anaplastic Features: A Report of 2 Cases, One With BRAFV600E Mutation and Clinical Response to

the BRAF Inhibitor Dabrafenib. Journal of neuropathology and experimental neurology. 2015;74(10):960-969. doi:10.1097/NEN.0000000000000240.

4. Mordechai O, Postovsky S, Vlodavsky E, et al. Metastatic Rhabdoid Meningioma with BRAF V600E Mutation and Good Response to Personalized Therapy: Case Report and Review of the Literature. Pediatric Hematology and Oncology. 2015; 32:3, 207-211, DOI: 10.3109/08880018.2014.936058
5. Lassaletta, A, Guerreiro Stucklin, A, Ramaswamy, V, et al. Profound clinical and radiological response to BRAF inhibition in a 2-month-old diencephalic child with hypothalamic/chiasmatic glioma. Pediatric Blood and Cancer. 2016; 63: 2038-2041. doi:10.1002/pbc.26086.
6. Meletah SK, Pavlick D, Brennan T, et al. Personalized Treatment for a Patient with a BRAF V600E Mutation using Dabrafenib and a Tumor Treatment Fields Device in a High-Grade Glioma Arising from Ganglioglioma. Journal of the National Comprehensive Cancer Network. 2016; 14(11): 1345-1350.
7. National Comprehensive Cancer Network. Thyroid Carcinoma (Version 3.2022). Available at: https://www.nccn.org/professionals/physician_gls/pdf/thyroid.pdf. Accessed November 14, 2022.

Reference number(s)
3747-A

SPECIALTY GUIDELINE MANAGEMENT

ZEPOSIA (ozanimod)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

A. Treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.
B. Treatment of moderately to severely active ulcerative colitis (UC) in adults.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

A. Ulcerative colitis (UC)
Continuation requests: Chart notes or medical record documentation supporting positive clinical response to therapy or remission.

III. PRESCRIBER SPECIALTIES

The medication must be prescribed by or in consultation with one of the following:
A. Ulcerative colitis: gastroenterologist
B. Multiple sclerosis: neurologist

IV. CRITERIA FOR INITIAL APPROVAL

A. Relapsing Forms of Multiple Sclerosis
Authorization of 12 months may be granted to members who have been diagnosed with a relapsing form of multiple sclerosis (including relapsing-remitting and secondary progressive disease for those who continue to experience relapse).

B. Clinically Isolated Syndrome
Authorization of 12 months may be granted to members for the treatment of clinically isolated syndrome of multiple sclerosis.

C. Ulcerative Colitis

Authorization of 12 months may be granted for adult members for treatment of moderately to severely active ulcerative colitis.

V. CONTINUATION OF THERAPY

A. Relapsing Forms of Multiple Sclerosis and Clinically Isolated Syndrome

Authorization of 12 months may be granted when the member is experiencing disease stability or improvement while receiving Zeposia.

B. Ulcerative Colitis

1. Authorization of 12 months may be granted for all adult members (including new members) who are using the requested medication for moderately to severely active ulcerative colitis and who achieve or maintain remission.

2. Authorization of 12 months may be granted for all adult members (including new members) who are using the requested medication for moderately to severely active ulcerative colitis who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition when there is improvement in any of the following from baseline:
   i. Stool frequency
   ii. Rectal bleeding
   iii. Urgency of defecation
   iv. C-reactive protein (CRP)
   v. Fecal calprotectin (FC)
   vi. Appearance of the mucosa on endoscopy, computed tomography enterography (CTE), magnetic resonance enterography (MRE), or intestinal ultrasound
   vii. Improvement on a disease activity scoring tool (e.g., Ulcerative Colitis Endoscopic Index of Severity [UCEIS], Mayo score)

VI. OTHER

A. For all indications: Zeposia will not be used concomitantly with immunomodulators, biologic drugs, targeted synthetic drugs, or disease modifying multiple sclerosis agents (Note: Ampyra and Nuedexta are not disease modifying).
B. For multiple sclerosis: authorization may be granted for pediatric members less than 18 years of age when benefits outweigh risks.

VII. DOSAGE AND ADMINISTRATION

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

VIII. REFERENCES

1. Zeposia [package insert]. Summit, NJ: Celgene Corporation; April 2022.
2. Talley NJ, Abreu MT, Achkar J, et al. An evidence-based systematic review on medical therapies for inflammatory bowel disease. *Am J Gastroenterol*. 2011;106(Suppl 1):S2-S25.
3. Rubin DT, Ananthakrishnan AN, et al. 2019 ACG Clinical Guideline: Ulcerative Colitis in Adults. *Am J Gastroenterol.* 2019;114:384-413.

4. Feuerstein JD, Isaacs KL, Schneider Y, et al. AGA Clinical Practice Guidelines on the Management of Moderate to Severe Ulcerative Colitis. *Gastroenterology*. 2020; 158:1450-1461.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME
(generic)

(zileuton extended-release)

ZYFLO
(zileuton)

Status: CVS Caremark® Criteria
Type: Initial Prior Authorization

POLICY

FDA-APPROVED INDICATIONS

Zileuton extended-release
Zileuton extended-release tablet is indicated for the prophylaxis and chronic treatment of asthma in adults and children 12 years of age and older.
Zileuton extended-release tablet is not indicated for use in the reversal of bronchospasm in acute asthma attacks.
Therapy with zileuton extended-release tablet can be continued during acute exacerbations of asthma.

Zyflo
Zyflo is indicated for the prophylaxis and chronic treatment of asthma in adults and children 12 years of age and older.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for the prophylaxis or chronic treatment of asthma

AND

- The patient is 12 years of age and older

AND

- The patient has experienced an inadequate treatment response to any of the following: A) An orally inhaled corticosteroid (ICS), B) A combination product containing an orally inhaled corticosteroid and long-acting beta agonist (ICS/LABA)
  [Note: The patient may continue to use an ICS containing product.]

OR

- The patient has experienced an intolerance to any of the following: A) An orally inhaled corticosteroid (ICS), B) A combination product containing an orally inhaled corticosteroid and long-acting beta agonist (ICS/LABA)

OR

- The patient has a contraindication that would prohibit a trial of any of the following: A) An orally inhaled corticosteroid (ICS), B) A combination product containing an orally inhaled corticosteroid and long-acting beta agonist (ICS/LABA)

REFERENCES

1. Zileuton Extended-Release [package insert]. East Brunswick, NJ: Rising Pharmaceuticals, Inc.; March 2023.
2. Zyflo [package insert]. Cary, NC: Chiesi USA, Inc.; January 2017.
3. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Waltham, MA: UpToDate, Inc.; 2023. https://online.lexi.com. Accessed March 15, 2023.
4. Micromedex (electronic version). Merative, Ann Arbor, Michigan, USA. Available at: https://www.micromedexsolutions.com/ (cited: 03/15/2023).

5. Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention. Updated 2022. Available at: http://www.ginasthma.org. Accessed March 15, 2023.
6. 2020 Focused Updates to the Asthma Management Guidelines. A Report from the National Asthma Education and Prevention Program Coordinating Committee Expert Panel Working Group. Available at: https://www.nhlbi.nih.gov/health-topics/asthma-management-guidelines-2020-updates. Accessed March 15, 2023.

QUANTITY LIMIT CRITERIA

DRUG CLASS	**ANTIEMETICS**
BRAND NAME* **(generic)**	**ZOFRAN (ALL DOSAGE FORMS) (ondansetron and ondansetron hydrochloride)** **ZUPLENZ (ondansetron oral soluble film)**
Status: CVS Caremark Criteria	
Type: Quantity Limit	***Ref # 259-H***

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Ondansetron Injection

Prevention of Nausea and Vomiting Associated with Initial and Repeat Courses of Emetogenic Cancer Chemotherapy

Ondansetron Injection is indicated for the prevention of nausea and vomiting associated with initial and repeat courses of emetogenic cancer chemotherapy, including high-dose cisplatin. Ondansetron is approved for patients aged 6 months and older.

Prevention of Postoperative Nausea and/or Vomiting

Ondansetron Injection is indicated for the prevention of postoperative nausea and/or vomiting. As with other antiemetics, routine prophylaxis is not recommended for patients in whom there is little expectation that nausea and/or vomiting will occur postoperatively. In patients in whom nausea and/or vomiting must be avoided postoperatively, ondansetron injection is recommended even when the incidence of postoperative nausea and/or vomiting is low. For patients who do not receive prophylactic ondansetron injection and experience nausea and/or vomiting postoperatively, ondansetron injection may be given to prevent further episodes. Ondansetron is approved for patients aged 1 month and older.

Zofran Tablets, Zofran ODT, and Zofran Oral Solution

Zofran is indicated for the prevention of nausea and vomiting associated with:

- highly emetogenic cancer chemotherapy, including cisplatin greater than or equal to 50 mg/m^2
- initial and repeat courses of moderately emetogenic cancer chemotherapy
- radiotherapy in patients receiving either total body irradiation, single high-dose fraction to the abdomen, or daily fractions to the abdomen

Zofran is also indicated for the prevention of postoperative nausea and/or vomiting.

Zuplenz

Zuplenz (ondansetron) oral soluble film is indicated for the prevention of nausea and vomiting associated with:

- Highly emetogenic cancer chemotherapy, including cisplatin ≥ 50 mg/m^2
- Initial and repeat courses of moderately emetogenic cancer chemotherapy
- Radiotherapy in patients receiving either total body irradiation, single high-dose fraction to the abdomen, or daily fractions to the abdomen

Zuplenz is also indicated for the prevention of postoperative nausea and/or vomiting. As with other antiemetics, routine prophylaxis is not recommended for patients in whom there is little expectation that nausea and/or vomiting will occur postoperatively. In patients where nausea and/or vomiting must be avoided postoperatively, Zuplenz is recommended even where the incidence of postoperative nausea and/or vomiting is low.

RATIONALE

Ondansetron Injection

Prevention of Nausea and Vomiting Associated with Initial and Repeat Courses of Emetogenic Chemotherapy

Adults

The prescribing information for adult intravenous (IV) dosage of ondansetron recommends three 0.15-mg/kg doses up to a maximum of 16 mg per dose. The first dose is infused over 15 minutes beginning 30 minutes before the start of emetogenic chemotherapy. Subsequent doses (0.15 mg/kg up to a maximum of 16 mg per dose) are administered 4 and 8 hours after the first dose of ondansetron.[1,7,8] According to the National Comprehensive Cancer Network (NCCN) Antiemesis Guidelines, the FDA recommends a maximum of 16 mg for a single dose of intravenous ondansetron to prevent prolongation of the QT interval. The guidelines recommend a single 8–16 mg IV dose prior to chemotherapy and then 8-16 mg IV daily on days 2 and 3.[9]

Pediatrics

For pediatric patients 6 months of age and older, the intravenous dosage of ondansetron is three 0.15-mg/kg doses up to a maximum of 16 mg per dose. The first dose is to be administered 30 minutes before the start of emetogenic chemotherapy. Subsequent doses (0.15 mg/kg up to a maximum of 16 mg per dose) are administered 4 and 8 hours after the first dose. The drug should be infused intravenously over 15 minutes.[1,7,8]

Prevention of Postoperative Nausea and Vomiting

Adults

The recommended adult intravenous dosage of ondansetron is 4 mg undiluted administered intravenously in not less than 30 seconds, preferably over 2 to 5 minutes, immediately before induction of anesthesia, or postoperatively if the patient did not receive prophylactic antiemetics and experiences nausea and/or vomiting occurring within 2 hours after surgery. Alternatively, 4 mg undiluted may be administered intramuscularly as a single injection for adults. While recommended as a fixed dose for patients weighing more than 40 kg, few patients above 80 kg have been studied. In patients who do not achieve adequate control of postoperative nausea and vomiting following a single, prophylactic, preinduction, intravenous dose of ondansetron 4 mg, administration of a second intravenous dose of 4 mg ondansetron postoperatively does not provide additional control of nausea and vomiting.[1,7,8]

Pediatrics

For pediatric patients 1 month through 12 years of age, the dosage is a single 0.1-mg/kg dose for patients weighing 40 kg or less, or a single 4-mg dose for patients weighing more than 40 kg. The rate of administration should not be less than 30 seconds, preferably over 2 to 5 minutes. Prevention of nausea and vomiting was only studied in pediatric patients 12 years of age and younger who had not received prophylactic ondansetron.[1,7,8]

For pediatric patients older than 12 years of age, recommended intravenous and intramuscular dosing of ondansetron is the same as in adults.[1,7,8]

For Ondansetron injection, the limits are designed to allow for treatment at the recommended doses on day 1 of chemotherapy. Ten mL of Ondansetron 2 mg/mL will be allowed per chemotherapy cycle. The limit allows a quantity sufficient for two chemotherapy cycles per 28 days (i.e., one chemotherapy cycle every 2 weeks) with consideration of available packaging. These limits also accommodate the dosing recommendations for prevention of post-operative nausea and vomiting. If the patient is requesting more than the initial quantity limit the claim will reject with a message indicating that a prior authorization is required.

Oral agents (Zofran and Zuplenz)

Prevention of Nausea and Vomiting Associated with Highly Emetogenic Cancer Chemotherapy
The recommended adult oral dosage of Zofran or Zuplenz in preventing nausea and vomiting with highly emetogenic cancer chemotherapy is 24 mg given as one 24 mg tablet or three 8 mg tablets or three 8 mg ODTs or three 8 mg oral soluble films or 30 mL (six teaspoonfuls equivalent to 24 mg of ondansetron) of 4 mg/5 mL oral solution administered 30 minutes before the start of single-day highly emetogenic chemotherapy.[2-6,8] Multiday, single-dose administration of a 24 mg dosage has not been studied.[6]

Safety and effectiveness of orally administered ondansetron have not been established for the prevention of nausea and vomiting associated with highly emetogenic cancer chemotherapy in pediatric patients.[2-6]

Prevention of Nausea and Vomiting Associated with Moderately Emetogenic Cancer Chemotherapy
The recommended adult oral dosage is one 8 mg tablet or one 8 mg ODT or one 8 mg oral soluble film or 10 mL (two teaspoonfuls equivalent to 8 mg of ondansetron) of the oral solution given 30 minutes before the start of chemotherapy with a subsequent 8 mg dose 8 hours after the first dose. One 8 mg tablet or one 8 mg ODT or one 8 mg oral soluble film or 10 mL (two teaspoonfuls equivalent to 8 mg of ondansetron) of the oral solution should be administered twice a day (every 12 hours) for one to two days after completion of chemotherapy.[2-8]

For pediatric patients aged 12 to 17 years of age, the recommended dosage is one 8 mg tablet or one 8 mg ODT or one 8 mg oral soluble film or 10 mL (two teaspoonfuls equivalent to 8 mg of ondansetron) of the oral solution administered 30 minutes before the start of chemotherapy, with a subsequent 8-mg dose (one 8 mg tablet or one 8 mg ODT or one 8 mg oral soluble film or 10 mL [two teaspoonfuls equivalent to 8 mg of ondansetron]) 8 hours after the first dose. One 8 mg tablet or one 8 mg ODT or 10 mL (two teaspoonfuls equivalent to 8 mg of ondansetron) of the oral solution should be administered twice a day (every 12 hours) for one to two days after completion of chemotherapy.[2-8]

For pediatric patients aged 4 through 11 years, the oral dosage is one 4 mg tablet or one 4 mg ODT or one 4 mg oral soluble film or 5 mL (one teaspoonful equivalent to 4 mg of ondansetron) of the oral solution administered 30 minutes before the start of emetogenic chemotherapy with subsequent doses four and eight hours after the first dose. One 4 mg tablet or one 4 mg ODT or one 4 mg oral soluble film or 5 mL (one teaspoonful equivalent to 4 mg of ondansetron) of the oral solution should be administered three times a day (every eight hours) for one to two days after completion of chemotherapy.[2-8]

Prevention of Nausea and Vomiting Associated with Radiotherapy, Either Total Body Irradiation or Single High-dose Fraction or Daily Fractions to the Abdomen:
The recommended adult oral dosage for nausea and vomiting associated with radiotherapy is one 8 mg tablet or one 8 mg ODT or one 8 mg oral soluble film or 10 mL (two teaspoonfuls equivalent to 8 mg of ondansetron) of oral solution given up to three times daily.

- For total body irradiation, one 8 mg tablet or one 8 mg ODT or one 8 mg oral soluble film or 10 mL (two teaspoonfuls equivalent to 8 mg of ondansetron) of the oral solution should be administered one to two hours before each fraction of radiotherapy administered each day.
- For single high-dose fraction radiotherapy to the abdomen, one 8 mg tablet or one 8 mg ODT or one 8 mg oral soluble film or 10 mL (two teaspoonfuls equivalent to 8 mg of ondansetron) of the oral solution should be administered one to two hours before radiotherapy, with subsequent 8-mg doses every eight hours after the first dose for one to two days after completion of radiotherapy.
- For daily fractionated radiotherapy to the abdomen, one 8 mg tablet or one 8 mg ODT or one 8 mg oral soluble film or 10 mL (two teaspoonfuls equivalent to 8 mg of ondansetron) of the oral solution should be administered one to two hours before radiotherapy, with subsequent 8-mg doses every eight hours after the first dose for each day radiotherapy is given.[2-8]

Safety and effectiveness of orally administered ondansetron have not been established for the prevention of radiation-induced nausea and vomiting in pediatric patients.[2-6]

The NCCN Antiemesis Guidelines state that the risk of nausea and vomiting for persons receiving chemotherapy of high and moderate emetic risk lasts for at least 3 days for high and 2 days for moderate after the last dose of anticancer agents. Patients need to be protected throughout the full period of risk. For moderately emetogenic chemotherapy, repeated doses may be given on days 2 and 3 for dolasetron, granisetron and ondansetron.[9]

Prevention of Postoperative Nausea and/or Vomiting

The recommended dosage for postoperative nausea and/or vomiting is 16 mg given as two 8 mg tablets or two 8 mg ODT or two 8 mg oral soluble films or 20 mL (four teaspoonfuls equivalent to 16 mg of ondansetron) of the oral solution one hour before induction of anesthesia.[2-8]

Safety and effectiveness of orally administered ondansetron have not been established for the prevention of postoperative nausea and vomiting in pediatric patients.[2-6]

For patients with severe hepatic impairment (Child-Pugh score of 10 or greater), clearance is reduced and apparent volume of distribution is increased with a resultant increase in plasma half-life. In such patients, a total daily dose of 8 mg should not be exceeded.[1-8]

Corresponding doses of Zofran Tablets, Zofran ODT, and Zofran Oral Solution may be used interchangeably.[2-5]

For oral Zofran, the limits are designed to allow for treatment at the recommended doses on the day of chemotherapy or radiation plus an additional one to two days post-treatment. Based on dosing recommendations, one 24 mg tablet, nine 4 mg or 8 mg tablets or 8 mg soluble films or orally disintegrating tablets, or eighteen 4 mg soluble films (to account for 2 films per 8 mg dose) or 100 mL (based on available packaging) of oral solution are sufficient for treatment through one chemotherapy cycle or radiation treatment. The initial limits for oral dosage forms of Zofran are sufficient for two chemotherapy cycles per 28 days (i.e., one chemotherapy cycle every 2 weeks). These limits also accommodate the dosing recommendations for post-operative nausea and vomiting. If the patient is requesting more than the initial quantity limit the claim will reject with a message that a prior authorization is required.

REFERENCES

1. Ondansetron Injection [package insert]. Weston, Florida: Apotex Corp; July 2021.
2. Ondansetron Tablets [package insert]. Saddle Brook, New Jersey: Rising Health, LLC; December 2021.
3. Ondansetron Orally Disintegrating Tablets [package insert]. East Windsor, New Jersey: Aurobindo Pharma USA, Inc.; November 2021.
4. Ondansetron Oral Solution [package insert]. East Windsor, New Jersey: Aurobindo Pharma USA, Inc.; November 2021.
5. Zofran Tablets [package insert]. East Hanover, New Jersey: Novartis Pharmaceuticals Corporation; October 2021.
6. Zuplenz [package insert]. Raleigh, North Carolina: Fortovia Therapeutics Inc.; June 2019.
7. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: UpToDate, Inc.; 2021; Accessed December 23, 2021.
8. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. https://www.micromedexsolutions.com/. Accessed December 22, 2021.
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Written by:	UM Development (LS)
Date Written:	01/2000
Revised:	(JG) 08/ 2002; (MG) 07/2003, 10/2004, 09/2005; (AK) 04/2006; (AM) 03/2007 (added 0.1 mg/mL injectable strength); (CT) 04/2007, 04/2008, 10/2008(2) (Sancuso added); (SE) 03/2009; (KD) 03/2010; (CY) 04/2011(Brand Kytril removed), 02/2012 (PONV removed for granisetron injectable, Sancuso limit reduced); (PL) 01/2013, (PL) 01/2014; (CF) 01/2015, 01/2016; (KM) 01/2017 (no clinical changes), (ME) 01/2018 (no clinical changes); (KC) 01/2019 (no clinical changes), (ME) 01/2020 (no clinical changes), 01/2021 (no clinical changes), (MRS) 01/2022 (no clinical changes)

Reviewed:	Medical Affairs 01/2000, 08/2002, 08/2003, 10/2004, 09/2005; (MM) 04/2006; (WLF) 03/2007, 04/2007, 04/2008, 10/2008, 03/2009, 03/2010; (KP) 04/2011, 02/2012; (LMS) 01/2013, (KP) 01/2014; (SES) 01/2015; (GAD) 01/2016; (CHART) 01/30/20, 01/28/21, 02/03/22
External Review:	10/2002, 08/2003, 11/2004, 08/2006, 08/2007, 08/2008, 10/2008, 08/2009, 08/2010, 08/2011, 04/2012, 06/2013, 04/2014, 04/2015, 04/2016, 04/2017, 04/2018, 04/2019, 04/2020, 04/2021, 04/2022

LIMIT CRITERIA

Limits do not accumulate together, patient is allowed the maximum limit for each drug and strength

Drug	4 Week Limit*	12 Week Limit*
Ondansetron injection	20 mL / 21 days (available in boxes of 5 or 10 vials of 2 mL each)	Does Not Apply*
Ondansetron 24 mg tablets	2 tablets / 21 days	Does Not Apply*
Ondansetron (Zofran) 4 mg and 8 mg tablets/ODT	18 tablets / 21 days	Does Not Apply*
Ondansetron (Zofran) oral solution	200 mL / 21 days	Does Not Apply*
Zuplenz 4 mg oral soluble film	36 films / 21 days	Does Not Apply*
Zuplenz 8 mg oral soluble film	18 films / 21 days	Does Not Apply*

** The duration of 21 days is used for a 28-day fill period to allow time for refill processing.*

**** These drugs are for short-term acute use; therefore, the mail limit will be the same as the retail limit. The intent is for prescriptions of the requested drug to be filled one month at a time, even if filled at mail order; there should be no 3 month supplies filled.***

PRIOR AUTHORIZATION CRITERIA

BRAND NAME
(generic)

ZYFLO
(zileuton)

(zileuton extended-release)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

POLICY

FDA-APPROVED INDICATIONS

Zyflo
Zyflo is indicated for the prophylaxis and chronic treatment of asthma in adults and children 12 years of age and older.

Zileuton extended-release
Zileuton extended-release tablet is indicated for the prophylaxis and chronic treatment of asthma in adults and children 12 years of age and older.
Zileuton extended-release tablet is not indicated for use in the reversal of bronchospasm in acute asthma attacks.
Therapy with zileuton extended-release tablet can be continued during acute exacerbations of asthma.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for the prophylaxis or chronic treatment of asthma in a patient 12 years of age and older

AND

- The patient has experienced an inadequate treatment response to any of the following: A) An orally inhaled corticosteroid (ICS), B) A combination product containing an orally inhaled corticosteroid and long-acting beta agonist (ICS/LABA)
  [Note: The patient may continue to use an ICS containing product.]
  OR
- The patient has experienced an intolerance to any of the following: A) An orally inhaled corticosteroid (ICS), B) A combination product containing an orally inhaled corticosteroid and long-acting beta agonist (ICS/LABA)
  OR
- The patient has a contraindication that would prohibit a trial of any of the following: A) An orally inhaled corticosteroid (ICS), B) A combination product containing an orally inhaled corticosteroid and long-acting beta agonist (ICS/LABA)

REFERENCES

1. Zyflo [package insert]. Cary, NC: Chiesi USA, Inc.; January 2017.
2. Zileuton Extended-Release [package insert]. Upper Saddle River, NJ: DASH Pharmaceuticals LLC; November 2020.
3. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: UpToDate, Inc.; 2021; Accessed February 18, 2022.
4. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed February 18, 2022.
5. Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention. 2021. Available at: http://www.ginasthma.org. Accessed February 2022.

6. 2020 Focused Updates to the Asthma Management Guidelines. A Report from the National Asthma Education and Prevention Program Coordinating Committee Expert Panel Working Group. Available at: https://www.nhlbi.nih.gov/health-topics/asthma-management-guidelines-2020-updates. Accessed February 2022.
7. National Heart, Lung, and Blood Institute National Asthma Education and Prevention Program Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma Full Report 2007. Available at http://www.nhlbi.nih.gov/health-pro/guidelines/current/asthma-guidelines. Accessed February 2022.

QUANTITY LIMIT CRITERIA

DRUG CLASS	**ANTIEMETICS**
BRAND NAME (generic)	**ZOFRAN (ALL DOSAGE FORMS) (ondansetron and ondansetron hydrochloride)** **ZUPLENZ (ondansetron oral soluble film)**
Status: CVS Caremark Criteria	
Type: Quantity Limit	

POLICY

FDA-APPROVED INDICATIONS

Ondansetron Injection

Prevention of Nausea and Vomiting Associated with Initial and Repeat Courses of Emetogenic Cancer Chemotherapy

Ondansetron Injection is indicated for the prevention of nausea and vomiting associated with initial and repeat courses of emetogenic cancer chemotherapy, including high-dose cisplatin. Ondansetron is approved for patients aged 6 months and older.

Prevention of Postoperative Nausea and/or Vomiting

Ondansetron Injection is indicated for the prevention of postoperative nausea and/or vomiting. As with other antiemetics, routine prophylaxis is not recommended for patients in whom there is little expectation that nausea and/or vomiting will occur postoperatively. In patients in whom nausea and/or vomiting must be avoided postoperatively, ondansetron injection is recommended even when the incidence of postoperative nausea and/or vomiting is low. For patients who do not receive prophylactic ondansetron injection and experience nausea and/or vomiting postoperatively, ondansetron injection may be given to prevent further episodes. Ondansetron is approved for patients aged 1 month and older.

Zofran Tablets, Zofran ODT, and Zofran Oral Solution

Zofran is indicated for the prevention of nausea and vomiting associated with:

- highly emetogenic cancer chemotherapy, including cisplatin greater than or equal to 50 mg/m^2
- initial and repeat courses of moderately emetogenic cancer chemotherapy
- radiotherapy in patients receiving either total body irradiation, single high-dose fraction to the abdomen, or daily fractions to the abdomen

Zofran is also indicated for the prevention of postoperative nausea and/or vomiting.

Zuplenz

Zuplenz is indicated for the prevention of nausea and vomiting associated with:

- highly emetogenic cancer chemotherapy, including cisplatin greater than or equal to 50 mg/m^2 , in adults
- initial and repeat courses of moderately emetogenic cancer chemotherapy in adults and pediatric patients 4 years of age and older
- radiotherapy in patients receiving either total body irradiation, single high-dose fraction to the abdomen, or daily fractions to the abdomen

Zuplenz is also indicated for the prevention of postoperative nausea and/or vomiting in adults.

INITIAL LIMIT QUANTITY
Limits do not accumulate together; patient is allowed the maximum limit for each drug and strength

Drug	4 Week Limit*	12 Week Limit*
Ondansetron 2mg/mL injection	20 mL / 21 days	Does Not Apply*
Ondansetron 24 mg tablets	2 tablets / 21 days	Does Not Apply*
Ondansetron (Zofran) 4 mg and 8 mg tablets/ODT	18 tablets / 21 days	Does Not Apply*
Ondansetron 4mg/5mL oral solution	200 mL / 21 days	Does Not Apply*
Zuplenz (ondansetron) 4 mg oral soluble film	36 films / 21 days	Does Not Apply*
Zuplenz (ondansetron) 8 mg oral soluble film	18 films / 21 days	Does Not Apply*

** The duration of 21 days is used for a 28-day fill period to allow time for refill processing.*

** These drugs are for short-term acute use; therefore, the mail limit will be the same as the retail limit. The intent is for prescriptions of the requested drug to be filled one month at a time, even if filled at mail order; there should be no 3 month supplies filled.*

REFERENCES

1. Ondansetron Injection [package insert]. Rockford, IL: Mylan Institutional LLC; October 2022.
2. Ondansetron Tablets [package insert]. Saddle Brook, NJ: Rising Health, LLC; July 2022.
3. Ondansetron Orally Disintegrating Tablets [package insert]. East Windsor, NJ: Aurobindo Pharma USA, Inc.; November 2021.
4. Ondansetron Oral Solution [package insert]. Memphis, TN: Northstar Rx LLC; December 2021.
5. Zofran Tablets [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; October 2021.
6. Zuplenz [package insert]. Warren, NJ: Aquestive Therapeutics; August 2021.
7. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2022; Accessed November 14, 2022.
8. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed November 11, 2022.
9. National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology. Antiemesis. Version 2.2022. Available at: https://www.nccn.org/professionals/physician_gls/pdf/antiemesis.pdf. Accessed November 16, 2022.

Reference number(s)
4384-A

SPECIALTY GUIDELINE MANAGEMENT

ZOKINVY (lonafarnib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
Zokinvy is a farnesyltransferase inhibitor indicated in patients 12 months of age and older with a body surface area of 0.39 m^2 and above:
1. To reduce risk of mortality in Hutchinson-Gilford Progeria Syndrome
2. For treatment of processing deficient Progeroid Laminopathies with heterozygous *LMNA* mutation with progerin-like protein accumulation
3. For treatment of processing deficient Progeroid Laminopathies with homozygous or compound heterozygous *ZMPSTE24* mutations

Limitations of Use
Not indicated for other Progeroid Syndromes or processing-proficient Progeroid Laminopathies. Based upon its mechanism of action, Zokinvy would not be expected to be effective in these populations.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

A. Hutchinson-Gilford Progeria Syndrome
Submission of the following information is necessary to initiate the prior authorization review for Hutchinson-Gilford Progeria Syndrome: Genetic testing results confirming the member has a *LMNA* mutation.

B. Processing Deficient Progeroid Laminopathy with Progerin-Like Protein Accumulation
Submission of the following information is necessary to initiate the prior authorization review for Processing Deficient Progeroid Laminopathy with Progerin-Like Protein Accumulation: Genetic testing results confirming the member has a heterozygous *LMNA* mutation

C. Processing Deficient Progeroid Laminopathy without Progerin-Like Protein Accumulation
Submission of the following information is necessary to initiate the prior authorization review for Processing Deficient Progeroid Laminopathy without Progerin-Like Protein Accumulation: Genetic testing results confirming the member has either homozygous or compound heterozygous *ZMPSTE24* mutations

III. CRITERIA FOR INITIAL APPROVAL

A. Hutchinson-Gilford Progeria Syndrome

Authorization of 12 months may be granted for treatment of Hutchinson-Gilford Progeria Syndrome when all of the following criteria are met:

1. The member is 12 months of age or older
2. The member has a body surface area of 0.39 m^2 or above
3. The diagnosis of Hutchinson-Gilford Progeria Syndrome has been confirmed with genetic testing indicating the patient has a *LMNA* mutation.

B. Processing Deficient Progeroid Laminopathy with Progerin-Like Protein Accumulation

Authorization of 12 months may be granted for treatment of Processing Deficient Progeroid Laminopathy with Progerin-Like Protein Accumulation when all of the following criteria are met:

1. The member is 12 months of age or older
2. The member has a body surface area of 0.39 m^2 or above
3. The diagnosis of Processing Deficient Progeroid Laminopathy has been confirmed with genetic testing indicating the patient has a heterozygous *LMNA* mutation.

C. Processing Deficient Progeroid Laminopathy without Progerin-Like Protein Accumulation

Authorization of 12 months may be granted for treatment of Processing Deficient Progeroid Laminopathy without Progerin-Like Protein Accumulation when all of the following criteria are met:

1. The member is 12 months of age or older
2. The member has a body surface area of 0.39 m^2 or above
3. The diagnosis of Processing Deficient Progeroid Laminopathy has been confirmed with genetic testing indicating the patient has homozygous or compound heterozygous *ZMPSTE24* mutations.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment of an indication listed in Section III when all of the following criteria are met:

1. Member meets all initial authorization criteria
2. Member is experiencing benefit from therapy

V. REFERENCES

1. Zokinvy [package insert]. Palo Alto, CA: Eiger BioPharmaceuticals, Inc.; November 2020.
2. Progeria Research Foundation (PRF). The Progeria Handbook: A Guide for Families & Health Care Providers of Children with Progeria. Second Edition. PRF. https://www.progeriaresearch.org/wp-content/uploads/2019/03/PRF_Handbook_2019_eFile.pdf. Accessed November 27, 2020.
3. Gordon LB, Brown WT, Collins FS. Hutchinson-Gilford Progeria Syndrome. *GeneReviews.* University of Washington, Seattle; 2019.
4. AHFS DI (Adult and Pediatric) [database online]. Hudson, OH: Lexi-Comp, Inc.; http://online.lexi.com/lco/action/index/dataset/complete_ashp [available with subscription]. Accessed March 15, 2021.
5. Micromedex Solutions [database online]. Ann Arbor, MI: Truven Health Analytics Inc. Updated periodically. www.micromedexsolutions.com [available with subscription]. Accessed March 15, 2021.

Reference number
1863-A

SPECIALTY GUIDELINE MANAGEMENT

ZOLINZA (vorinostat)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication
Zolinza is indicated for the treatment of cutaneous manifestations in patients with cutaneous T-cell lymphoma (CTCL) who have progressive, persistent, or recurrent disease on or following two systemic therapies

B. Compendial Uses
Mycosis fungoides (MF)/Sézary syndrome (SS)

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Cutaneous T-cell Lymphoma (CTCL)
Authorization of 12 months may be granted for the treatment of CTCL (e.g., MF, SS).

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

IV. REFERENCES

1. Zolinza [package insert]. Whitehouse Station, NJ: Merck & Co., Inc.; January 2020.
2. The NCCN Drugs & Biologics Compendium® © 2022 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed January 4, 2022.

Reference number(s)
2244-A

SPECIALTY GUIDELINE MANAGEMENT

ZORBTIVE (somatropin)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Zorbtive is indicated for the treatment of short bowel syndrome in adult patients receiving specialized nutritional support. Zorbtive should be used in conjunction with optimal management of short bowel syndrome.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Short bowel syndrome (SBS)
Authorization of a total duration of 4 weeks may be granted to members who depend on parenteral nutrition support who are prescribed Zorbtive for the treatment of SBS.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

1. Zorbtive [package insert]. Rockland, MA: EMD Serono, Inc.; September 2019.

Reference number(s)
1706-A

SPECIALTY GUIDELINE MANAGEMENT

ZYDELIG (idelalisib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
Relapsed chronic lymphocytic leukemia (CLL), in combination with rituximab, in patients for whom rituximab alone would be considered appropriate therapy due to other co-morbidities

Limitations of use:
Zydelig is not indicated and is not recommended for first-line treatment of any patient, including patients with chronic lymphocytic leukemia (CLL), small lymphocytic lymphoma (SLL), follicular lymphoma (FL), and other indolent non-Hodgkin lymphomas.
Zydelig is not indicated and is not recommended in combination with bendamustine and rituximab, or in combination with rituximab for the treatment of patients with FL, SLL, and other indolent non-Hodgkin lymphomas.

B. Compendial Uses
Relapsed or refractory CLL/SLL

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL)
Authorization of 12 months may be granted for treatment of relapsed or refractory CLL/SLL when either of the following criteria are met:
1. The requested drug will be used as a single agent, or
2. The requested drug will be used in combination with rituximab.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

IV. REFERENCES

1. Zydelig [package insert]. Foster City, CA: Gilead Sciences, Inc.; February 2022.

2. The NCCN Drugs & Biologics Compendium® © 2023 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed June 2, 2023.

Reference number(s)
5348-A

SPECIALTY GUIDELINE MANAGEMENT

ZTALMY (ganaxolone)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Ztalmy is indicated for the treatment of seizures associated with cyclin-dependent kinase-like 5 (CDKL5) deficiency disorder (CDD) in patients 2 years of age and older.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
A. Initial requests: Chart notes or medical record documentation of enzyme assay or genetic testing demonstrating pathogenic or likely pathogenic mutation in the CDKL5 gene
B. Continuation requests: Documentation (e.g., chart notes) that the member has experienced a positive clinical response to therapy (e.g., decrease in seizures)

III. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with a neurologist.

IV. CRITERIA FOR INITIAL APPROVAL

Cyclin-Dependent Kinase-Like 5 (CDKL5) deficiency disorder (CDD)
Authorization of 6 months may be granted for treatment of cyclin-dependent kinase-like 5 (CDKL5) deficiency disorder (CDD) when the member has a confirmed pathogenic or likely pathogenic mutation in the CDKL5 gene.

V. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for CDKL5 deficiency disorder when the member achieves or maintains a positive clinical response to therapy (e.g., decrease in seizures).

VI. REFERENCE

1. Ztalmy [package insert]. Radnor, PA: Marinus Pharmaceuticals, Inc.; November 2022.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME
(generic)

ZYFLO
(zileuton)

ZYFLO CR
(zileuton)

Status: Client Requested Criteria
Type: Initial Prior Authorization ***Ref # C20106-A***

FDA-APPROVED INDICATIONS

Zyflo (zileuton) is indicated for prophylaxis and chronic treatment of asthma in adults and children > 12 years of age. It is not indicated for the relief of acute bronchospasm. Current guidelines do not describe a role for zileuton in the management of asthma (GINA 2018) and it is not routinely used.

COVERAGE CRITERIA

- The patient is 12 years of age or older
  AND
- The drug is being used for the prophylaxis and chronic treatment of persistent asthma
  AND
- The patient does not have active liver disease
  AND
- The patient has experienced a failure, contraindication, or intolerance to an oral inhaled corticosteroid
  AND
- The patient has experienced a failure, contraindication, or intolerance to Singular (montelukast) and Accolate (zafirlukast)

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines.

Zyflo (zileuton) is considered a leukotriene modifier; specifically, a 5-lipoxygenase inhibitor which inhibits leukotriene formation. Leukotrienes augment neutrophil and eosinophil migration, neutrophil and monocyte aggregation, leukocyte adhesion, increased capillary permeability, and smooth muscle contraction (which contribute to inflammation, edema, mucous secretion, and bronchoconstriction in the airway).

Current guidelines note that leukotriene receptor antagonists (LTRA), such as Singulair (montelukast) and Accolate (zafirlukast) are less effective than inhaled corticosteroids (ICS), particularly for exacerbations (Evidence A). They may be appropriate for initial controller treatment for some patients who are unable to use ICS; for patients who experience intolerable side effects from ICS; or for patients with concomitant allergic rhinitis (Evidence B).

Singular (montelukast) is indicated for prophylaxis and chronic treatment of asthma in adults and children > 12 months of age and for allergic rhinitis (perennial or seasonal), in adults and children > 6 months of age. Before prescribing

montelukast, health professionals should consider its benefits and risks, and patients should be counseled about the risk of neuropsychiatric events.

Accolate (zafirlukast) is indicated for prophylaxis and chronic treatment of asthma in adults and children > 5 years of age.

REFERENCES

1. CareFirst Prior Authorization Policy.

Written by:	UM Development (ME)
Date Written:	10/2020
Revised:	
Reviewed:	Medical Affairs: (SAM) 10/2020

Reference number(s)
C24373-A

CAREFIRST: ZYNTEGLO

Client Requested: The intent of the criteria is to ensure that patients follow selection elements as established by CareFirst.

COVERAGE CRITERIA

Betibeglogene autotemcel is considered **medically necessary** for individuals with transfusion-dependent β-thalassemia if they meet criteria 1 through 6:

1. Documented diagnosis of β-thalassemia by globin gene testing.
2. Require regular peripheral blood transfusions to maintain target hemoglobin levels.
3. Documented history of receiving transfusions of ≥100 ml per kilogram of body weight of packed red cells per year or who had disease that had been managed under standard thalassemia guidelines with ≥8 transfusions per year in the previous 2 years at the time of treatment decision.
4. Karnofsky performance status of ≥80 for adults (≥16 years of age) or a Lansky performance status of ≥80 for adolescents (<16 years of age).
5. Negative serologic test for HIV infection (as per US FDA prescribing label, apheresis material from individuals with a positive test for HIV will not be accepted for betibeglogene autotemcel manufacturing).
6. Individual does not have
    i. Availability of human leukocyte antigen-identical or human leukocyte antigen-matched donor.
    ii. T2*-weighted magnetic resonance imaging measurement of myocardial iron of less than 10 msec or other evidence of severe iron overload in the opinion of treating physician.
    iii. Advanced liver disease (meets any one of the following):
        a. Persistent aspartate transaminase, alanine transaminase, or direct bilirubin value greater than 3 times the upper limit of normal.
        b. Baseline prothrombin time or partial thromboplastin time greater than 1.5 times the upper limit of normal.
        c. Magnetic resonance imaging of the liver demonstrating clear evidence of cirrhosis.
        d. Liver biopsy demonstrating cirrhosis, any evidence of bridging fibrosis, or active hepatitis.
    iv. Baseline estimated glomerular filtration rate less than 70 mL/min/1.73 m^2.
    v. History of receiving prior gene therapy or allogenic hematopoietic stem cell transplant.
    vi. Any prior or current malignancy (with the exception of adequately treated cone biopsied in situ carcinoma of the cervix uteri and basal or squamous cell carcinoma of the skin) or myeloproliferative or significant immunodeficiency disorder.
    vii. Any immediate family member (i.e. parent or siblings) with a known Familial Cancer Syndrome (including but not limited to hereditary breast and ovarian cancer syndrome, hereditary nonpolyposis colorectal cancer syndrome and familial adenomatous polyposis).
    viii. Active, uncontrolled HCV or HBV infection.
    ix. Contraindication to the use of granulocyte colony stimulating factor (G-CSF), plerixafor, busulfan, or any other medicinal products required during myeloablative conditioning, including hypersensitivity to the active substances or to any of the excipients.
    x. A white blood cell count less than 3 X 10^9/L, and/or platelet count less than 100 X 10^9/L not related to hypersplenism.

Betibeglogene autotemcel is considered **investigational** when the above criteria are not met. Betibeglogene autotemcel is considered **investigational** for all other indications. Repeat treatment of betibeglogene autotemcel is considered **investigational**.

Reference number(s)
C24373-A

DOCUMENT HISTORY
Created: Specialty Clinical Development (KS) 11/2022
Revised:
Reviewed: CDPR/

Reference number(s)
1668-A

SPECIALTY GUIDELINE MANAGEMENT

ZYKADIA (ceritinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication
Zykadia is indicated for the treatment of adult patients with metastatic non-small cell lung cancer (NSCLC) whose tumors are anaplastic lymphoma kinase (ALK)-positive as detected by an FDA-approved test.

B. Compendial Uses
1. NSCLC, recurrent, advanced or metastatic ALK rearrangement-positive or ROS1 rearrangement-positive tumors
2. Inflammatory myofibroblastic tumor (IMT) with ALK translocation
3. Brain metastases from ALK rearrangement-positive NSCLC
4. Erdheim-Chester Disease (ECD) with ALK-fusion

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: ALK mutation or translocation status or ROS-1 mutation status (where applicable).

III. CRITERIA FOR INITIAL APPROVAL

A. Non-Small Cell Lung Cancer (NSCLC)
Authorization of 12 months may be granted for treatment of NSCLC as a single agent when the member meets either of the following criteria:
1. Member has recurrent, advanced, or metastatic ALK-positive NSCLC (including brain metastases from NSCLC).
2. Member has recurrent, advanced, or metastatic ROS1-positive NSCLC.

B. Inflammatory Myofibroblastic Tumor (IMT)
Authorization of 12 months may be granted for treatment of ALK-positive IMT as a single agent when either of the following criteria are met:
1. The member has uterine sarcoma and the disease is advanced, recurrent, metastatic, or inoperable
2. The member has a soft tissue sarcoma (not including uterine sarcoma)

C. Erdheim-Chester Disease (ECD)

Authorization of 12 months may be granted for treatment of symptomatic or relapsed/refractory ALK-positive Erdheim-Chester Disease as a single agent.

IV. CONTINUATION OF THERAPY

A. Non-Small Cell Lung Cancer (NSCLC)

Authorization of 12 months may be granted for continued treatment of non-small cell lung cancer (NSCLC) in members requesting reauthorization when there is no evidence of unacceptable toxicity while on the current regimen.

B. All Other Indications

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for all other indications listed in Section III when there is no evidence of unacceptable toxicity or disease progression while on the current regimen

V. REFERENCES

1. Zykadia [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corp; October 2021.
2. The NCCN Drugs & Biologics Compendium 2023 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed March 1, 2023.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME
(generic)

ZYVOX
(linezolid)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

POLICY

FDA-APPROVED INDICATIONS

Nosocomial Pneumonia

Zyvox is indicated for the treatment of nosocomial pneumonia caused by Staphylococcus aureus (methicillin-susceptible and -resistant isolates) or Streptococcus pneumoniae.

Community-acquired Pneumonia

Zyvox is indicated for the treatment of community-acquired pneumonia caused by Streptococcus pneumoniae, including cases with concurrent bacteremia, or Staphylococcus aureus (methicillin-susceptible isolates only).

Complicated Skin and Skin Structure Infections

Zyvox is indicated for the treatment of complicated skin and skin structure infections, including diabetic foot infections, without concomitant osteomyelitis, caused by Staphylococcus aureus (methicillin-susceptible and -resistant isolates), Streptococcus pyogenes, or Streptococcus agalactiae. Zyvox has not been studied in the treatment of decubitus ulcers.

Uncomplicated Skin and Skin Structure Infections

Zyvox is indicated for the treatment of uncomplicated skin and skin structure infections caused by Staphylococcus aureus (methicillin susceptible isolates only) or Streptococcus pyogenes.

Vancomycin-resistant Enterococcus faecium Infections

Zyvox is indicated for the treatment of vancomycin-resistant Enterococcus faecium infections, including cases with concurrent bacteremia.

Limitations of Use

Zyvox is not indicated for the treatment of Gram-negative infections. It is critical that specific Gram-negative therapy be initiated immediately if a concomitant Gram-negative pathogen is documented or suspected.
The safety and efficacy of Zyvox formulations given for longer than 28 days have not been evaluated in controlled clinical trials.

Usage

To reduce the development of drug-resistant bacteria and maintain the effectiveness of Zyvox and other antibacterial drugs, Zyvox should be used only to treat infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

Off Label Uses

Combination regimen with Pretomanid and linezolid for the treatment of adults with pulmonary tuberculosis (TB) resistant to isoniazid, rifamycins, a fluoroquinolone and a second line injectable antibacterial drug OR adults with pulmonary TB resistant to isoniazid and rifampin, who are treatment-intolerant or nonresponsive to standard therapy. [2, 9,10]

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The patient is being converted from IV linezolid (Zyvox) as prescribed or directed by an Infectious Disease specialist for a NON-Tuberculosis (TB) bacterial infection

OR

- The patient has any of the following: A) an infection caused by vancomycin-resistant Enterococcus faecium including cases with concurrent bacteremia, B) a nosocomial (institution-acquired) pneumonia caused by Staphylococcus aureus (methicillin-susceptible and -resistant isolates) or Streptococcus pneumoniae, C) community-acquired pneumonia caused by Streptococcus pneumoniae, including cases with concurrent bacteremia, or Staphylococcus aureus (methicillin-susceptible isolates only), D) a complicated skin and skin structure infection including diabetic foot infections, without concomitant osteomyelitis, caused by Staphylococcus aureus (methicillin-susceptible and -resistant isolates), Streptococcus pyogenes, or Streptococcus agalactiae, E) an uncomplicated skin and skin structure infection caused by Staphylococcus aureus (methicillin-susceptible isolates only) or Streptococcus pyogenes

  AND

  - The infection is proven or strongly suspected to be caused by susceptible bacteria

OR

- The requested drug is being prescribed for pulmonary tuberculosis (TB) resistant to isoniazid, rifamycins, a fluoroquinolone and a second line injectable antibacterial drug OR TB resistant to isoniazid and rifampin, that is treatment-intolerant or nonresponsive to standard therapy

  AND

  - The requested drug is being prescribed as part of a combination regimen with Pretomanid and Sirturo (bedaquiline)

AND

- The patient will use the requested drug orally or intravenously

REFERENCES

1. Zyvox [package insert]. New York, NY: Pharmacia & Upjohn Co Division of Pfizer Inc; November 2021.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, Ohio: UpToDate, Inc.; 2022; Accessed December 5, 2022.
3. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com/. Accessed December 5, 2022.
4. Diagnosis and Treatment of Adults with Community-Acquired Pneumonia. An Official Clinical Practice Guideline of the American Thoracic Society and Infectious Diseases Society of America. American Journal of Respiratory and Critical Care Medicine, Volume 200, Issue 7, 1 October 2019, Pages e45-e67.
5. Lipsky B, Berendt A, Cornia P, et al. 2012 Infectious Diseases Society of America Clinical Practice Guideline for the Diagnosis and Treatment of Diabetic Foot Infections. *Clinical Infectious Diseases* 2012; 54(12):132-173.
6. Kalil A, Metersky M, Klompas M, et al. Management of Adults With Hospital-acquired and Ventilator-associated Pneumonia: 2016 Clinical Practice Guidelines by the Infectious Diseases Society of America and the American Thoracic Society. *Clinical Infectious Diseases* 2016;1-51.
7. Stevens D, Bisno A, Chambers H, et al. Practice Guidelines for the Diagnosis and Management of Skin and Soft-Tissue Infections: 2014 Update by the Infectious Diseases Society of America. *Clinical Infectious Diseases* 2014;1-43.
8. Gorwitz RJ, Jernigan DB, Powers JH, Jernigan JA, and Participants in the CDC Convened Experts' Meeting on Management of MRSA in the Community. Strategies for clinical management of MRSA in the community: Summary of an experts' meeting convened by the Centers for Disease Control and Prevention. 2006. Available at http://www.cdc.gov/mrsa/community/clinicians/index.html. Accessed December 2021.
9. Pretomanid [package insert]. Morgantown, West Virginia: Mylan Specialty L.P.; December 2022.
10. WHO Consolidated Guidelines on Tuberculosis. Module 4: Treatment - Drug-Resistant Tuberculosis Treatment. Geneva: World Health Organization; 2020. Licence: CC BY-NC-SA 3.0 IGO. Available at: https://www.who.int/publications/i/item/9789240007048. Accessed February 2023.
11. WHO Consolidated Guidelines on Tuberculosis. Module 5: Management of Tuberculosis in Children and Adolescents.

Geneva: World Health Organization; 2022. Licence: CC BY-NC-SA 3.0 IGO. Available at: https://www.who.int/publications/i/item/9789240007048. Accessed February 2023.