Reference number(s)
4642-A

SPECIALTY GUIDELINE MANAGEMENT

ABECMA (idecabtagene vicleucel)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Abecma is indicated for the treatment of adult patients with relapsed or refractory multiple myeloma after four or more prior lines of therapy including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 monoclonal antibody.

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 notes, medical record documentation or claims history supporting previous lines of therapy.

III. CRITERIA FOR INITIAL APPROVAL

Multiple Myeloma
Authorization of 3 months may be granted for treatment of relapsed or refractory multiple myeloma in members 18 years of age and older when all of the following are met:

A. The member has received prior treatment with at least four prior lines of therapy, including at least one drug from each of the following categories:
   1. Immunomodulatory agent
   2. Proteasome inhibitor
   3. Anti-CD 38 monoclonal antibody
B. The member has not received a previous treatment course of the requested medication, another chimeric antigen receptor (CAR) T-cell therapy directed at any target, or any therapy that is targeted to B-cell maturation antigen (BCMA).
C. The member has an ECOG performance status of 0 to 2.
D. The member has adequate and stable kidney, liver, pulmonary and cardiac function.
E. The member has no history or presence of clinically relevant central nervous system (CNS) pathology
F. The member does not have clinically significant active infection.
G. The member does not have active graft versus host disease.
H. The member does not have an active inflammatory disorder.

IV. REFERENCES

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POLICY Document for ACTEMRA (tocilizumab)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, lower cost site of care and overall, clinically appropriate use. This document provides specific information to each of the three sections of the overall policy.

Section 1: Preferred Product
- Policy information specific to preferred medications

Section 2: Site of Care
- Policy information specific to site of care (outpatient, hospital outpatient, home infusion)

Section 3: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 1: Preferred Product

EXCEPTIONS CRITERIA
AUTOIMMUNE CONDITIONS

PREFERRED PRODUCTS: ENTYVIO, ILUMYA, SIMPONI ARIA AND STELARA IV

POLICY
This policy informs prescribers of preferred products and provides an exception process for targeted products through prior authorization.

I. PLAN DESIGN SUMMARY

This program applies to the autoimmune drug products specified in this policy. Coverage for targeted products is provided based on clinical circumstances that would exclude the use of the preferred product and may be based on previous use of a product. The coverage review process will ascertain situations where a clinical exception can be made. This program applies to all members requesting treatment with Cimzia vial. For plaque psoriasis, this program applies to all members requesting treatment with a targeted product. For all other indications, this program applies to all members who are new to treatment with a targeted product for the first time.

Each referral is reviewed based on all utilization management (UM) programs implemented for the client.

Table. Drugs for autoimmune conditions

	Product(s)
Preferred*	• **Entyvio** (vedolizumab) • **Ilumya** (tildrakizumab-asmn) • **Simponi Aria** (golimumab, intravenous) • **Stelara IV** (ustekinumab)**
Targeted	• **Actemra** (tocilizumab) • **Cimzia** (certolizumab pegol) • **Orencia** (abatacept)

Abbreviation: IV = intravenous
*: Medications considered formulary or preferred on your plan may still require a clinical prior authorization review

**Stelara IV is indicated for a one time induction dose for Crohn's disease and ulcerative colitis.

II. EXCEPTION CRITERIA

This program applies to members requesting treatment for an indication that is FDA-approved for the preferred products.

Coverage for a targeted product is provided when any of the following criteria is met:

A. For Cimzia, when any of the following criteria is met:
   1. For prefilled syringe request, member is currently receiving treatment with Cimzia prefilled syringes excluding when the requested targeted product is obtained as samples or via manufacturer's patient assistance programs, unless the request is for plaque psoriasis.
   2. Member has a documented inadequate response or intolerable adverse event with all of the preferred products (Entyvio, Ilumya, Simponi Aria, and Stelara IV) where the product's indications overlap.
   3. Member is currently pregnant or breastfeeding.

B. For all other targeted products, when any of the following criteria is met:
   1. Member is currently receiving treatment with the requested targeted product, excluding when the requested targeted product is obtained as samples or via manufacturer's patient assistance programs.
   2. Member has a documented inadequate response or intolerable adverse event with all of the preferred products (Entyvio, Ilumya, Simponi Aria, and Stelara IV) where the product's indications overlap, unless there is a documented clinical reason to avoid TNF inhibitors (see Appendix).

III. Appendix: Clinical reasons to avoid TNF inhibitors

- History of demyelinating disorder
- History of congestive heart failure
- History of hepatitis B virus infection
- Autoantibody formation/lupus-like syndrome
- History or risk of lymphoma or other malignancy
- History of being a primary non-responder to a TNF inhibitor

Section 2: Site of Care

CareFirst Site of Care Criteria
Administration of Intravenous Actemra

POLICY

I. CRITERIA FOR APPROVAL FOR ADMINISTRATION IN OUTPATIENT HOSPITAL SETTING

This policy provides coverage for administration of Actemra in an outpatient hospital setting for 3 months when a member is new to therapy or is reinitiating therapy after not being on therapy for at least 6 months.

This policy provides coverage for administration of Actemra in an outpatient hospital setting for a longer course of treatment when ANY of the following criteria are met:

A. The member has experienced an adverse reaction that did not respond to conventional interventions (eg, acetaminophen, steroids, diphenhydramine, fluids or other pre-medications) or a severe adverse event (anaphylaxis, anaphylactoid reactions, myocardial infarction, thromboembolism, or seizures) during or immediately after an infusion.

B. The member is medically unstable (eg respiratory, cardiovascular, or renal conditions).
C. The member has severe venous access issues that require the use of special interventions only available in the outpatient hospital setting.
D. The member has significant behavioral issues and/or physical or cognitive impairment that would impact the safety of the infusion therapy AND the patient does not have access to a caregiver.
E. The member is less than 14 years of age.

For situations where administration of Actemra does not meet the criteria for outpatient hospital infusion, coverage for Actemra is provided when administered in alternative sites such as; physician office, home infusion or ambulatory care.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the site of care prior authorization review (where applicable):

A. Medical records supporting the member has experienced an adverse reaction that did not respond to conventional interventions or a severe adverse event during or immediately after an infusion
B. Medical records supporting the member is medically unstable
C. Medical records supporting the member has severe venous access issues that requires specialized interventions only available in the outpatient hospital setting
D. Medical records supporting the member has behavioral issues and/or physical or cognitive impairment and no access to a caregiver

Section 3: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

ACTEMRA (tocilizumab)

POLICY

III. INDICATIONS

The indications below including FDA-approved indications and compendial 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.

IV. 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.

V. 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

VI. 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.

VII. 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.

VIII. 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.

IX. DOSAGE AND ADMINISTRATION

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

X. 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

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Reference number(s)
1848-A

LIMITED INDICATION SPECIALTY GUIDELINE MANAGEMENT

ACTHAR GEL (repository corticotropin injection)
PURIFIED CORTROPHIN GEL (repository corticotropin injection)

POLICY

I. INDICATIONS

The Limited Indication Specialty Guideline Management (LI SGM) program provides coverage for specific, but not all FDA labeled or compendial supported drug uses based on plan design and the scope of the pharmacy benefit. This program provides coverage for Acthar Gel for the treatment of infantile spasms and exacerbations of multiple sclerosis and coverage for Purified Cortrophin Gel for the treatment of exacerbations of multiple sclerosis if all of the approval criteria are met.

A. **Infantile Spasms (Acthar Gel only):** as monotherapy for the treatment of infantile spasms in infants and children under 2 years of age
B. **Multiple Sclerosis:** treatment of acute exacerbations of multiple sclerosis in adults

The use of Acthar and Purified Cortrophin Gel for the treatment of all other indications listed in the FDA product labeling has not been proven to be superior to conventional therapies (e.g., corticosteroids, immunosuppressive agents) and has a significantly higher cost than the standard of care agents. Use of Acthar and Purified Cortrophin Gel for these conditions is considered not medically necessary and is not a covered benefit.

A. Acthar Gel:
   1. **Rheumatic Disorders:** as adjunctive therapy for short-term administration (to tide the patient over an acute episode or exacerbation) in: psoriatic arthritis; rheumatoid arthritis, including juvenile rheumatoid arthritis; ankylosing spondylitis
   2. **Collagen Diseases:** during an exacerbation or as maintenance therapy in selected cases of: systemic lupus erythematosus, systemic dermatomyositis (polymyositis)
   3. **Dermatologic Diseases:** severe erythema multiforme, Stevens-Johnson syndrome
   4. **Allergic States:** serum sickness
   5. **Ophthalmic Diseases:** severe acute and chronic allergic and inflammatory processes involving the eye and its adnexa such as: keratitis, iritis, iridocyclitis, diffuse posterior uveitis and choroiditis, optic neuritis, chorioretinitis, anterior segment inflammation
   6. **Respiratory Diseases:** symptomatic sarcoidosis
   7. **Edematous State:** to induce a diuresis or a remission of proteinuria in nephrotic syndrome without uremia of the idiopathic type or that due to lupus erythematosus

B. Purified Cortrophin Gel:
   1. **Rheumatic Disorders**: as adjunctive therapy for short-term administration (to tide the patient over an acute episode or exacerbation) in: psoriatic arthritis; rheumatoid arthritis, including juvenile rheumatoid arthritis; ankylosing spondylitis; acute gouty arthritis.
   2. **Collagen Diseases**: during an exacerbation or as maintenance therapy in selected cases of: systemic lupus erythematosus, systemic dermatomyositis (polymyositis).
   3. **Dermatologic Diseases:** severe erythema multiforme (Stevens-Johnson syndrome), severe psoriasis
   4. **Allergic States**: atopic dermatitis, serum sickness

5. **Ophthalmic Diseases**: severe acute and chronic allergic and inflammatory processes involving the eye and its adnexa such as: allergic conjunctivitis, keratitis, iritis and iridocyclitis, diffuse posterior uveitis and choroiditis, optic neuritis, chorioretinitis, anterior segment inflammation
6. **Respiratory Diseases**: symptomatic sarcoidosis
7. **Edematous States**: to induce a diuresis or a remission of proteinuria in the nephrotic syndrome without uremia of the idiopathic type or that due to lupus erythematosus

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 requests for treatment of multiple sclerosis exacerbations: chart notes detailing the outcome of the most recent trial with IV methylprednisolone, including dosage and duration of treatment.

III. EXCLUSIONS

A. Coverage of Purified Cortrophin Gel for the treatment of infantile spasms will be excluded.
B. Use of Acthar Gel in combination with Purified Cortrophin Gel will be excluded.

IV. CRITERIA FOR INITIAL APPROVAL

A. Infantile Spasms (Acthar Gel only)
Authorization of 4 weeks may be granted for treatment of infantile spasms in members who are less than 2 years of age.

B. Multiple Sclerosis
Authorization of 3 weeks may be granted for treatment of acute exacerbations of multiple sclerosis when the member has had an inadequate response to a trial of IV methylprednisolone (for the current exacerbation).

V. CONTINUATION OF THERAPY

A. Infantile Spasms (Acthar Gel only)
Authorization of 4 weeks may be granted to members requesting Acthar Gel for continuation of therapy when the member has shown substantial clinical benefit from therapy.

B. Multiple Sclerosis
Authorization of 3 weeks may be granted for members requesting re-authorization of repository corticotropin therapy when all initial authorization criteria are met.

VI. REFERENCES

1. Acthar Gel [package insert]. Bedminster, NJ: Mallinckrodt ARD LLC.; October 2021.
2. Pellock JM, Hrachovy R, Shinnar S, et al. Infantile spasms: A U.S. consensus report. *Epilepsia*. 2010:51:2175-2189.

3. 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.
4. Hancock EC, Osborne JP, Edwards SW. Treatment of infantile spasms. *Cochrane Database Syst Rev*. 2013;6:CD001770.
5. Riikonen R. Recent advances in pharmacotherapy of infantile spasms. *CNS Drugs* 2014; 28:279-290.
6. Pavone P, et al. Infantile spasms syndrome, West Syndrome and related phenotypes: what we know in 2013. *Brain & Development* 2014; 739-751.
7. Citterio A, La Mantia L, Ciucci G, et al. Corticosteroids or ACTH for acute exacerbations in multiple sclerosis. *Cochrane Database Syst Rev 4*:CD001331.
8. Thompson AJ, Kennard C, Swash M, et al. Relative efficacy of intravenous methylprednisolone and ACTH in the treatment of acute relapse in MS. *Neurology* 1989; 39:969-971.
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11. Sellebjerg F, Barnes D, Filippini G, at al. EFNS guidelines on treatment of multiple sclerosis relapses: report of an EFNS task force on treatment of multiple sclerosis. *European Journal of Neurology* 2005; 12:939-946.
12. Purified Cortrophin Gel [package insert]. Baudette, MN: ANI Pharmaceuticals, Inc.; November 2021.

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

1. Actimmune [package insert]. Deerfield, IL: Horizon Therapeutics USA, Inc.; May 2021.

2. The NCCN Drugs & Biologics Compendium 2020 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed July 27, 2021.

Reference number(s)
2118-A

SPECIALTY GUIDELINE MANAGEMENT

ADAGEN (pegademase bovine) 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
Adagen is indicated for enzyme replacement therapy for adenosine deaminase (ADA) deficiency in patients with severe combined immunodeficiency disease (SCID) who are not suitable candidates for—or who have failed—bone marrow transplantation. Adagen is recommended for use in infants from birth or in children of any age at the time of diagnosis.

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: enzyme assay or genetic testing results supporting diagnosis of ADA deficiency.

III. CRITERIA FOR INITIAL APPROVAL

Authorization of 12 months may be granted for treatment of severe combined immunodeficiency disease (SCID) associated with adenosine deaminase (ADA) deficiency when the condition has failed to respond to a bone marrow transplant (BMT) or the member is not currently a suitable candidate for BMT.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for SCID associated with ADA deficiency who are experiencing benefit from therapy as evidenced by disease stability or disease improvement.

V. REFERENCE

1. Adagen [package insert]. Gaithersburg, MD: Leadiant Biosciences, Inc.; November 2017.

POLICY Document for ADAKVEO (crizanlizumab-tmca)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, lower cost site of care and overall, clinically appropriate use. This document provides specific information to each of the three sections of the overall policy.

Section 1: Site of Care

- Policy information specific to site of care (outpatient, hospital outpatient, home infusion)

Section 2: Clinical Criteria

- Policy information specific to the clinical appropriateness for the medication

Section 1: Site of Care

CareFirst Site of Care Criteria
Administration of Intravenous Adakveo

POLICY

I. CRITERIA FOR APPROVAL FOR ADMINISTRATION IN OUTPATIENT HOSPITAL SETTING

This policy provides coverage for administration of Adakveo in an outpatient hospital setting for up to 45 days when a member is new to therapy or is reinitiating therapy after not being on therapy for at least 6 months.

This policy provides coverage for administration of Adakveo in an outpatient hospital setting for a longer course of treatment when ANY of the following criteria are met:

A. The member has experienced an adverse reaction that did not respond to conventional interventions (eg, acetaminophen, steroids, diphenhydramine, fluids, other pre-medications or slowing of infusion rate) or a severe adverse event (anaphylaxis, anaphylactoid reactions, myocardial infarction, thromboembolism, or seizures) during or immediately after an infusion.
B. The member is medically unstable (eg respiratory, cardiovascular, or renal conditions).
C. The member has severe venous access issues that require the use of a special interventions only available in the outpatient hospital setting.
D. The member has significant behavioral issues and/or physical or cognitive impairment that would impact the safety of the infusion therapy AND the patient does not have access to a caregiver.
E. The member is less than 14 years of age.

For situations where administration of Adakveo does not meet the criteria for outpatient hospital infusion, coverage for Adakveo is provided when administered in alternative sites such as; physician office, home infusion or ambulatory care.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the site of care prior authorization review (where applicable):

A. Medical records supporting the member has experienced an adverse reaction that did not respond to conventional interventions or a severe adverse event during or immediately after an infusion
B. Medical records supporting the member is medically unstable

C. Medical records supporting the member has severe venous access issues that require specialized interventions only available in the outpatient hospital setting
D. Medical records supporting the member has behavioral issues and/or physical or cognitive impairment and no access to a caregiver

Section 2: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

ADAKVEO (crizanlizumab-tmca)

POLICY

III. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Adakveo is indicated to reduce the frequency of vasoocclusive crises (VOCs) in adults and pediatric patients aged 16 years and older with sickle cell disease.

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

IV. PRESCRIBER SPECIALTIES

Adakveo must be prescribed by or in consultation with a hematologist or specialist in sickle cell disease.

V. CRITERIA FOR INITIAL APPROVAL

Sickle cell disease, to reduce the frequency of vasoocclusive crises
Authorization of 12 months may be granted for use in reducing the frequency of vasoocclusive crises (VOCs) in members 16 years of age or older with sickle cell disease, when both of the following criteria are met:
1. The member has experienced at least one vasoocclusive crisis within the previous 12 months
2. The member meets either of the following (1 or 2):
   i. Member has sickle hemoglobin C (HbSC) or sickle β^+-thalassemia (HbSβ^+) genotype
   ii. Member has homozygous hemoglobin S (HbSS) or sickle β^0-thalassemia (HbSβ^0) genotype AND meets any of the following:
      a. Has experienced, at any time in the past, an inadequate response or intolerance to a trial of hydroxyurea.
      b. Has a contraindication to hydroxyurea.
      c. Will be using Adakveo with concurrent hydroxyurea therapy.

VI. CONTINUATION OF THERAPY

Sickle cell disease, to reduce the frequency of vasoocclusive crises
Authorization of 12 months may be granted for continued treatment when the member has experienced a reduction in the frequency of vasoocclusive crises, or has maintained such reduction, since initiating therapy with Adakveo.

REFERENCES

SECTION 1

1. Adakveo [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation.; September 2022.

SECTION 2

1. Adakveo [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; July 2021.
2. Ataga KI, Kutlar A, Kanter J, et al. Crizanlizumab for the prevention of pain crises in sickle cell disease. *N Engl J Med*. 2017;376(5):429-439.

Reference number(s)
1700-A

SPECIALTY GUIDELINE MANAGEMENT

ADCETRIS (brentuximab vedotin)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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. Classical Hodgkin Lymphoma (cHL)
   i. Treatment of cHL after failure of autologous hematopoietic stem cell transplantation (auto-HSCT) or after failure of at least two prior multi-agent chemotherapy regimens in patients who are not auto-HSCT candidates
   ii. Treatment of cHL at high risk of relapse or progression as post-auto-HSCT consolidation
   iii. Previously untreated Stage III or IV classical Hodgkin lymphoma (cHL), in combination with doxorubicin, vinblastine, and dacarbazine
   iv. Treatment of pediatric patients 2 years and older with previously untreated high risk classical Hodgkin lymphoma (cHL) in combination with doxorubicin, vincristine, etoposide, prednisone and cyclophosphamide
2. Systemic anaplastic large cell lymphoma (sALCL)
   i. Treatment of systemic anaplastic large cell lymphoma (sALCL) after failure of at least one prior multi-agent chemotherapy regimen
   ii. Previously untreated systemic anaplastic large cell lymphoma (sALCL) or other CD30-expressing peripheral T-cell lymphomas (PTCL), including angioimmunoblastic T-cell lymphoma and PTCL not otherwise specified, in combination with cyclophosphamide, doxorubicin, and prednisone
3. Treatment of primary cutaneous anaplastic large cell lymphoma (pcALCL) or CD30-expressing mycosis fungoides (MF) in patients who have received prior systemic therapy

B. Compendial Uses
1. cHL stage I-II unfavorable
2. CD30+ B-Cell Lymphomas
   i. Monomorphic post-transplant lymphoproliferative disorders (B-cell type)
   ii. Monomorphic post-transplant lymphoproliferative disorders (T-cell type)
   iii. Diffuse large B-cell lymphoma
   iv. HIV-Related B-cell lymphomas (CD30+ HIV-related diffuse large B-cell lymphoma, primary effusion lymphoma, and human herpesvirus-8 (HHV8)-positive diffuse large B-cell lymphoma)
   v. High-grade B-Cell lymphomas
   vi. Pediatric primary mediastinal large B-cell lymphoma
3. CD30+ Primary Cutaneous Lymphomas
   i. Mycosis Fungoides (MF)/Sezary Syndrome (SS)
   ii. Lymphomatoid papulosis (LyP)
   iii. Cutaneous anaplastic large cell lymphoma
4. CD30+ T-Cell Lymphomas
   i. Hepatosplenic T-cell lymphoma
   ii. Adult T-cell leukemia/lymphoma

iii. Breast implant-associated anaplastic large cell lymphoma (ALCL)
iv. Peripheral T-cell lymphoma (PTCL)
v. Extranodal NK/T-cell Lymphoma
vi. Angioimmunoblastic T-cell lymphoma

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 CD30 expression on the surface of the cell (initial requests).

III. CRITERIA FOR INITIAL APPROVAL

A. Classical Hodgkin lymphoma (cHL)

Authorization of 12 months may be granted for treatment of CD30+ cHL when any of the following are met:

1. The requested drug will be used as a single agent, or
2. The requested drug will be used in combination with doxorubicin, vinblastine, and dacarbazine, or
3. The requested drug will be used in combination with bendamustine for subsequent therapy, or
4. The requested drug will be used in combination with dacarbazine, or
5. The requested drug will be used in combination with nivolumab for subsequent therapy, or
6. The requested drug will be used in combination with gemcitabine for subsequent therapy, or
7. The requested drug will be used in combination with ifosfamide, carboplatin and etoposide for subsequent therapy, or
8. The requested drug will be used in combination with etoposide, prednisone and doxorubicin, or
9. The requested drug will be used in combination with cyclophosphamide, prednisone, and dacarbazine for subsequent therapy, or
10. The requested drug will be used in combination with doxorubicin, vincristine, etoposide, prednisone and cyclophosphamide

B. B-Cell Lymphomas

Authorization of 12 months may be granted for treatment of CD30+ B-cell lymphomas with any of the following subtypes:

1. Monomorphic post-transplant lymphoproliferative disorders (B-cell type) when both of the following are met:
   i. The requested drug will be used for subsequent therapy, and
   ii. The member is not a candidate for transplant.
2. Monomorphic post-transplant lymphoproliferative disorders (T-cell type) when the requested drug will be used in combination with cyclophosphamide, doxorubicin, and prednisone.
3. Diffuse large B-cell lymphoma when all of the following are met:
   i. The requested drug will be used as subsequent therapy, and
   ii. The member is not a candidate for transplant.
4. HIV-Related B-cell lymphomas (HIV-related diffuse large B-cell lymphoma, primary effusion lymphoma, and human herpesvirus-8 (HHV8)-positive diffuse large B-cell lymphoma) when both of the following are met:
   i. The requested drug will be used for subsequent therapy, and
   ii. The member is not a candidate for transplant.
5. Pediatric primary mediastinal large B-cell lymphoma when both of the following are met:
   i. The requested drug will be used for relapsed or refractory disease, and

ii. The requested drug will be used in combination with nivolumab or pembrolizumab

6. High-grade B-cell lymphomas when both of the following are met:
   i. The requested drug will be used for subsequent therapy, and
   ii. The member is not a candidate for transplant.

C. Primary Cutaneous Lymphomas

Authorization of 12 months may be granted for treatment of CD30+ primary cutaneous lymphomas with any of the following subtypes:

1. Mycosis fungoides (MF)/Sezary syndrome (SS)
2. Lymphomatoid papulosis (LyP) when both of the following are met:
   i. The requested drug will be used as a single agent, and
   ii. The disease is relapsed or refractory.
3. Cutaneous anaplastic large cell lymphoma when either of the following are met:
   i. The requested drug will be used as a single agent, or
   ii. The requested drug will be used in combination with cyclophosphamide, doxorubicin, and prednisone (CHP).

D. T-Cell Lymphomas

Authorization of 12 months may be granted for treatment of CD30+ T-cell lymphomas with any of the following subtypes:

1. Hepatosplenic T-cell lymphoma when either of the following are met:
   i. The requested drug will be used as a single agent after two or more primary treatment regimens, or
   ii. The requested drug will be used in combination with cyclophosphamide, doxorubicin, and prednisone.
2. Adult T-cell leukemia/lymphoma when either of the following are met:
   i. The requested drug will be used as a single agent for subsequent therapy, or
   ii. The requested drug will be used in combination with cyclophosphamide, doxorubicin, and prednisone.
3. Breast implant associated anaplastic large cell lymphoma (ALCL) when either of the following are met:
   i. The requested drug will be used as a single agent, or
   ii. The requested drug will be used in combination with cyclophosphamide, doxorubicin, and prednisone.
4. Peripheral T-cell lymphoma (PTCL) [including the following subtypes: anaplastic large cell lymphoma, peripheral T-cell lymphoma not otherwise specified, angioimmunoblastic T-cell lymphoma, enteropathy associated T-cell lymphoma, monomorphic epitheliotropic intestinal T-cell lymphoma, nodal peripheral T-cell lymphoma with TFH phenotype, or follicular T-cell lymphoma] when either of the following are met:
   i. The requested drug will be used a single agent for subsequent or palliative therapy, or
   ii. The requested drug will be used in combination with cyclophosphamide, doxorubicin, and prednisone.
5. Extranodal NK/T-cell lymphoma when all of the following are met:
   i. The requested drug will be used as a single agent, and
   ii. The member has relapsed or refractory disease, and
   iii. The member has had an inadequate response or contraindication to asparaginase-based therapy (e.g., pegaspargase).
6. Systemic anaplastic large cell lymphoma when either of the following are met:
   i. The requested drug will be used as a single agent, or
   ii. The requested drug will be used in combination with cyclophosphamide, doxorubicin, and prednisone (CHP).

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. Adcetris [package insert]. Bothell, WA: Seagen Inc; November 2022.
2. The NCCN Drugs & Biologics Compendium® © 2023 National Comprehensive Cancer Network, Inc. Available at: https://www.nccn.org. Accessed April 5, 2023.

Reference number(s)
5711-A

SPECIALTY GUIDELINE MANAGEMENT

ADSTILADRIN (nadofaragene firadenovec-vncg)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Adstiladrin is indicated for the treatment of adult patients with high-risk Bacillus Calmette-Guerin (BCG)-unresponsive non-muscle invasive bladder cancer (NMIBC) with carcinoma in situ (CIS) with or without papillary tumors.

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

II. CRITERIA FOR INITIAL APPROVAL

Bladder Cancer
Authorization of 12 months may be granted for treatment of bladder cancer when all of the following criteria are met:
1. The member has non-muscle invasive bladder cancer
2. The disease is high-risk
3. The disease is Bacillus Calmette-Guerin (BCG)-unresponsive

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 recurrence while on the current regimen.

IV. REFERENCES

1. Adstiladrin [package insert]. Kastrup, Denmark: Ferring Pharmaceuticals; December 2022.

POLICY Document for ALDURAZYME (laronidase)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, lower cost site of care and overall, clinically appropriate use. This document provides specific information to each of the three sections of the overall policy.

Section 1: Site of Care
- Policy information specific to site of care (outpatient, hospital outpatient, home infusion)

Section 2: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 1: Site of Care

Care First Site of Care Criteria
Administration of Intravenous Aldurazyme

POLICY

I. CRITERIA FOR APPROVAL FOR ADMINISTRATION IN OUTPATIENT HOSPITAL SETTING

This policy provides coverage for administration of Aldurazyme in an outpatient hospital setting for up to 54 days when a member is new to therapy or is reinitiating therapy after not being on therapy for at least 6 months.

This policy provides coverage for administration of Aldurazyme in an outpatient hospital setting for a longer course of treatment when ANY of the following criteria are met:

A. The member has experienced an adverse reaction to the drug that did not respond to conventional interventions (eg, acetaminophen, steroids, diphenhydramine, fluids, other pre-medications or slowing of infusion rate) or a severe adverse event (anaphylaxis, anaphylactoid reactions, myocardial infarction, thromboembolism, or seizures) during or immediately after infusion (up to 3 hours post infusion).
B. The member has developed laboratory confirmed laronidase IgE antibodies which increases the risk for infusion related reactions.
C. The member is medically unstable (eg respiratory, cardiovascular, or renal conditions).
D. The member has severe venous access issues that require the use of special interventions only available in the outpatient setting.
E. The member has significant behavioral issues and/or physical or cognitive impairment that would impact the safety of the infusion therapy AND the patient does not have access to a caregiver.
F. The member is less than 14 years of age.

For situations where administration of Aldurazyme does not meet the criteria for outpatient hospital infusion, coverage for Aldurazyme is provided when administered in alternative sites such as; physician office, home infusion or ambulatory care.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the site of care prior authorization review (where applicable):

A. Medical records supporting the member has experienced an adverse reaction that did not respond to conventional interventions or a severe adverse event during or immediately after an infusion

B. Medical records supporting the member has developed laronidase IgE antibodies
C. Medical records supporting the member is medically unstable
D. Medical records supporting the member has severe venous access issues that requires specialized interventions only available in the outpatient hospital setting
E. Medical records supporting the member has behavioral issues and/or physical or cognitive impairment and no access to a caregiver

Section 2: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

ALDURAZYME (laronidase)

POLICY

III. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Aldurazyme is indicated for adult and pediatric patients with Hurler and Hurler-Scheie forms of Mucopolysaccharidosis I (MPS I) and for patients with the Scheie form who have moderate to severe symptoms.

Limitations of use:
- *The risks and benefits of treating mildly affected patients with the Scheie form have not been established.*
- *Aldurazyme has not been evaluated for effects on the central nervous system manifestations of the disorder.*

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

IV. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
A. Initial requests: alpha-L-iduronidase enzyme assay and/or genetic testing results supporting diagnosis.
B. Continuation requests: chart notes documenting a clinically positive response to therapy, which shall include improvement, stabilization, or slowing of disease progression.

V. CRITERIA FOR INITIAL APPROVAL

Mucopolysaccharidosis I (MPS I)
Authorization of 12 months may be granted for treatment of MPS I when both of the following criteria are met:
1. Diagnosis of MPS I was confirmed by enzyme assay demonstrating a deficiency of alpha-L-iduronidase enzyme activity and/or by genetic testing.

2. Member has the Hurler (i.e severe MPS I) or Hurler-Scheie (i.e.attenuated MPS I) OR the member has the Scheie form (Scheie syndrome/i.e. attenuated MPS I) with moderate to severe symptoms (e.g., normal intelligence, less progressive physical problems, corneal clouding, joint stiffness, valvular heart disease).

VI. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for mucopolysaccharidosis I (MPS I) who have a clinically positive response to therapy, which shall include improvement, stabilization, or slowing of disease progression.

REFERENCES

SECTION 1

1. Aldurazyme [package insert]. Novato, CA: BioMarin Pharmaceutical Inc.; December 2019.
2. Giugliani R, Rojas VM, Martins AM, et al. A dose-optimization trial of laronidase (Aldurazyme) in patients with mucopolysaccharidosis I. *Mol Genet Metab.* 2009;96(1):13-19.
3. Clarke LA, Wraith JE, Beck M, et al. Long-term efficacy and safety of laronidase in the treatment of mucopolysaccharidosis I. *Pediatrics.* 2009;123(1):229-240.

SECTION 2

1. Aldurazyme [package insert]. Cambridge, MA: Genzyme Corporation; December 2019.
2. Wraith JE, Clarke LA, Beck M, et al. Enzyme replacement therapy for mucopolysaccharidosis I: a randomized, double-blinded, placebo-controlled, multinational study of recombinant human alpha-L-iduronidase (laronidase). *J Pediatr*. 2004;144:581-588.
3. Muenzer J, Wraith JE, Clarke LA; International Consensus Panel on Management and Treatment of Mucopolysaccharidosis I. Mucopolysaccharidosis I: management and treatment guidelines. Pediatrics. 2009 Jan;123(1):19-29.

Reference number
2329-A

SPECIALTY GUIDELINE MANAGEMENT

ALIQOPA (copanlisib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Aliqopa is indicated for the treatment of adult patients with relapsed follicular lymphoma (FL) who have received at least two prior systemic therapies.

B. Compendial Uses
1. Gastric MALT lymphoma, subsequent therapy for relapsed or refractory disease after 2 prior therapies
2. Non-gastric MALT lymphoma, subsequent therapy for relapsed or refractory disease after 2 prior therapies
3. Nodal marginal zone lymphoma, subsequent therapy as a single agent for relapsed or refractory disease after 2 prior therapies
4. Splenic marginal zone lymphoma, subsequent therapy as a single agent for relapsed or refractory disease after 2 prior therapies

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

II. CRITERIA FOR INITIAL APPROVAL

A. Follicular Lymphoma (FL)
Authorization of 12 months may be granted to members with follicular lymphoma (FL) when the requested medication will be used as subsequent therapy after at least two prior therapies.

B. Gastric MALT Lymphoma and Non-gastric MALT Lymphoma
Authorization of 12 months may be granted to members with gastric or non-gastric mucosa-associated lymphoid tissue (MALT) lymphoma when the requested medication will be used as subsequent therapy after at least two prior therapies.

C. Nodal Marginal Zone Lymphoma
Authorization of 12 months may be granted to members with nodal marginal zone lymphoma when the requested medication will be used as subsequent therapy after at least two prior therapies as a single agent.

D. Splenic Marginal Zone Lymphoma
Authorization of 12 months may be granted to members with splenic marginal zone lymphoma when the requested medication will be used as subsequent therapy after at least two prior therapies 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. Aliqopa [package insert]. Whippany, NJ: Bayer HealthCare Pharmaceuticals, Inc.; February 2022.
2. National Comprehensive Cancer Network. The NCCN Drugs & Biologics Compendium. http://www.nccn.org. Accessed June 2, 2022.

POLICY Document for Alpha1-Proteinase Inhibitors

ARALAST NP (alpha$_1$-proteinase inhibitor [human])
GLASSIA (alpha$_1$-proteinase inhibitor [human])
PROLASTIN-C (alpha$_1$-proteinase inhibitor [human])
ZEMAIRA (alpha$_1$-proteinase inhibitor [human])

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, and overall, clinically appropriate use. This document provides specific information to both sections of the overall policy.

Section 1: Preferred Product
- Policy information specific to preferred medications

Section 2: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 1: Preferred Product

EXCEPTIONS CRITERIA
ALPHA1-PROTEINASE INHIBITORS

PREFERRED PRODUCT: PROLASTIN-C

POLICY
This policy informs prescribers of preferred products and provides an exception process for targeted products through prior authorization.

I. PLAN DESIGN SUMMARY

This program applies to the alpha$_1$-proteinase inhibitor products specified in this policy. Coverage for targeted products is provided based on clinical circumstances that would exclude the use of the preferred product and may be based on previous use of a product. The coverage review process will ascertain situations where a clinical exception can be made. This program applies to all members requesting treatment with a targeted product.

Each referral is reviewed based on all utilization management (UM) programs implemented for the client.

Table. Alpha1-Proteinase Inhibitor Products

	Product(s)
Preferred*	• **Prolastin-C** (alpha$_1$-proteinase inhibitor [human])
Targeted	• **Aralast NP** (alpha$_1$-proteinase inhibitor [human]) • **Glassia** (alpha$_1$-proteinase inhibitor [human]) • **Zemaira** (alpha$_1$-proteinase inhibitor [human])

*: Medications considered formulary or preferred on your plan may still require a clinical prior authorization review.

II. EXCEPTION CRITERIA

This program applies to members requesting treatment for an indication that is FDA-approved for the preferred product.

Coverage for a targeted product is provided when the member has had a documented intolerable adverse event to the preferred product, and the adverse event was not an expected adverse event attributed to the active ingredient as described in the prescribing information.

Section 2: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT
Alpha$_1$-Proteinase Inhibitors

ARALAST NP (alpha$_1$-proteinase inhibitor [human])
GLASSIA (alpha$_1$-proteinase inhibitor [human])
PROLASTIN-C (alpha$_1$-proteinase inhibitor [human])
ZEMAIRA (alpha$_1$-proteinase 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 Indications

1. Aralast NP
   Chronic augmentation therapy in adults with clinically evident emphysema due to severe congenital deficiency of alpha$_1$-proteinase inhibitor (alpha$_1$-antitrypsin deficiency)

2. Glassia
   Chronic augmentation and maintenance therapy in adults with clinically evident emphysema due to severe hereditary deficiency of alpha$_1$-proteinase inhibitor (alpha$_1$-antitrypsin deficiency)

3. Prolastin-C
   Chronic augmentation and maintenance therapy in adults with clinical evidence of emphysema due to severe hereditary deficiency of alpha$_1$-proteinase inhibitor (alpha$_1$-antitrypsin deficiency)

4. Zemaira
   Chronic augmentation and maintenance therapy in adults with alpha$_1$-proteinase inhibitor deficiency and clinical evidence of emphysema

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:

1. Pretreatment serum alpha$_1$-antitrypsin (AAT) level
2. Pretreatment post-bronchodilation forced expiratory volume in 1 second (FEV$_1$)
3. AAT protein phenotype or genotype

CVS/caremark

III. CRITERIA FOR INITIAL APPROVAL

Authorization of 12 months may be granted for treatment of emphysema due to alpha$_1$-antitrypsin (AAT) deficiency when all of the following criteria are met:

1. The member's pretreatment serum AAT level is less than 11 micromol/L (80 mg/dL by radial immunodiffusion or 50 mg/dL by nephelometry).[5,6]
2. The member's pretreatment post-bronchodilation forced expiratory volume in 1 second (FEV_1) is greater than or equal to 25% and less than or equal to 80% of the predicted value.[6]
3. The member has a documented PiZZ, PiZ (null), or Pi (null, null) (homozygous) AAT deficiency or other phenotype or genotype associated with serum AAT concentrations of less than 11 micromol/L (80 mg/dL by radial immunodiffusion or 50 mg/dL by nephelometry).[6]
4. The member does not have the PiMZ or PiMS AAT deficiency.[7]

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment of emphysema due to alpha$_1$-antitrypsin (AAT) deficiency when the member is experiencing beneficial clinical response from therapy.

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.

REFERENCES:

SECTION 1

1. Aralast NP [package insert]. Lexington, MA: Baxalta US Inc.; January 2019.
2. Glassia [package insert]. Lexington, MA: Takeda Pharmaceuticals USA Inc; March 2022.
3. Prolastin-C [package insert]. Research Triangle Park, NC: Grifols Therapeutics Inc.; May 2020.
4. Zemaira [package insert]. Kankakee, IL: CSL Behring LLC; April 2019.

SECTION 2

1. Aralast NP [package insert]. Westlake Village, CA: Baxalta US Inc.; December 2018.
2. Glassia [package insert]. Westlake Village, CA: Baxalta US Inc.; June 2017.
3. Prolastin-C [package insert]. Research Triangle Park, NC: Grifols Therapeutics Inc.; May 2020.
4. Zemaira [package insert]. Kankakee, IL: CSL Behring LLC; April 2019.
5. American Thoracic Society/European Respiratory Society statement: standards for the diagnosis and management of individuals with alpha-1 antitrypsin deficiency. *Am J Respir Crit Care Med*. 2003;168:818-900.
6. Marciniuk DD, Hernandez P, Balter M, et al. Alpha-1 antitrypsin deficiency targeted testing and augmentation therapy: a Canadian Thoracic Society clinical practice guideline. *Can Respir J*. 2012;19:109-116.
7. Sandhaus RA, Turino G, Brantly ML, et al. The diagnosis and management of alpha-1 antitrypsin deficiency in the adult. *Chronic Obstr Pulm Dis*. 2016;3(3):668-82.

POLICY Document for AMONDYS 45 (casimersen)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, lower cost site of care and overall, clinically appropriate use. This document provides specific information to each of the three sections of the overall policy.

Section 1: Site of Care
- Policy information specific to site of care (outpatient, hospital outpatient, home infusion)

Section 2: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 1: Site of Care

CareFirst Site of Care Criteria
Administration of Intravenous Amondys 45

POLICY

I. CRITERIA FOR APPROVAL FOR ADMINISTRATION IN OUTPATIENT HOSPITAL SETTING

This policy provides coverage for administration of Amondys 45 in an outpatient hospital setting for up to 45 days when a member is new to therapy or reinitiating therapy after not being on therapy for at least 6 months.

This policy provides coverage for administration of Amondys 45 in an outpatient hospital setting for a longer course of treatment when ANY of the following criteria are met:

A. The member has experienced an adverse reaction to the drug that did not respond to conventional interventions (eg, acetaminophen, steroids, diphenhydramine, fluids or other pre-medications) or a severe adverse event (anaphylaxis, anaphylactoid reactions, myocardial infarction, thromboembolism, or seizures) during or immediately after an infusion.
B. The member is medically unstable (eg respiratory, cardiovascular, or renal conditions).
C. The member has severe venous access issues that require the use of special interventions only available in the outpatient hospital setting.
D. The member has significant behavioral issues and/or physical or cognitive impairment that would impact the safety of the infusion therapy AND the patient does not have access to a caregiver.
E. The member is less than 14 years of age.

For situations where administration of Amondys 45 does not meet the criteria for outpatient hospital infusion, coverage for Amondys 45 is provided when administered in alternative sites such as; physician office, home infusion or ambulatory care.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the site of care prior authorization review (where applicable):

A. Medical records supporting the member has experienced an adverse reaction that did not respond to conventional interventions or a severe adverse event during or immediately after an infusion
B. Medical records supporting the member is medically unstable

C. Medical records supporting the member has severe venous access issues that requires specialized interventions only available in the outpatient hospital setting
D. Medical records supporting the member has behavioral issues and/or physical or cognitive impairment and no access to a caregiver

Section 2: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

AMONDYS 45 (casimersen)

POLICY

III. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Amondys 45 is indicated for the treatment of Duchenne muscular dystrophy (DMD) in patients who have a confirmed mutation of the DMD gene that is amenable to exon 45 skipping.

This indication is approved under accelerated approval based on an increase in dystrophin production in skeletal muscle observed in patients treated with Amondys 45. Continued approval for this indication may be contingent upon verification of a clinical benefit in confirmatory trials.

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

IV. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
A. Initial requests: laboratory confirmation of Duchenne muscular dystrophy (DMD) diagnosis with a *DMD* gene mutation that is amenable to exon 45 skipping (refer to examples in Appendix).
B. Continuation of therapy requests: documentation (e.g., chart notes) of response to therapy.

V. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with a physician who specializes in the treatment of Duchenne muscular dystrophy (DMD).

VI. 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. Genetic testing was conducted to confirm the diagnosis of DMD and to identify the specific type of *DMD* gene mutation.
B. The *DMD* gene mutation is amenable to exon 45 skipping (refer to examples in Appendix).
C. Treatment with Amondys 45 is initiated before the age of 14.

D. Member is able to achieve an average distance of at least 300 meters while walking independently over 6 minutes.
E. Member will not exceed a dose of 30 mg/kg once weekly.

VII. 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 has demonstrated a response to therapy as evidenced by remaining ambulatory (e.g., able to walk with or without assistance, not wheelchair dependent).
B. The member will not exceed a dose of 30 mg/kg once weekly.

VIII. APPENDIX

Examples of DMD gene mutations (exon deletions) amenable to exon 45 skipping (not an all-inclusive list):

1. Deletion of exon 44
2. Deletion of exon 46-47
3. Deletion of exon 46-48
4. Deletion of exon 46-49
5. Deletion of exon 46-51
6. Deletion of exon 46-53
7. Deletion of exon 46-55

REFERENCES

SECTION 1
1. Amondys 45 [package insert]. Cambridge, MA: Sarepta Therapeutics Inc; February 2021.

SECTION 2
2. Amondys 45 [package insert]. Cambridge, MA: Sarepta Therapeutics; February 2021.
3. ClinicalTrials.gov. Study of SRP-4045 and SRP-4053 in DMD patients (ESSENCE). Available at: https://clinicaltrials.gov/ct2/show/NCT02500381. Accessed March 1, 2021.
4. Fletcher, S., et. al. Dystrophin Isoform Induction In Vivo by Antisense-mediated Alternative Splicing. The American Society of Gene & Cell Therapy. 2010;18(6):1218-1223.
5. Polavarapu K, Preethish-Kumar V, Sekar D, et al. Mutation pattern in 606 Duchenne muscular dystrophy children with a comparison between familial and non-familial forms: a study in an Indian large single-center cohort. J Neurol. 2019;266(9):2177-2185.

POLICY Document for AMVUTTRA (vutrisiran)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, lower cost site of care and overall, clinically appropriate use. This document provides specific information to each of the three sections of the overall policy.

Section 1: Preferred Product
- Policy information specific to preferred medications

Section 2: Site of Care
- Policy information specific to site of care (outpatient, hospital outpatient, home infusion)

Section 3: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 1: Preferred Product

EXCEPTIONS CRITERIA

hATTR DISORDERS

PREFERRED PRODUCT: ONPATTRO

POLICY
This policy informs prescribers of preferred products and provides an exception process for targeted products through prior authorization.

I. PLAN DESIGN SUMMARY

This program applies to the products for the treatment of polyneuropathy of hereditary transthyretin-mediated amyloidosis specified in this policy. Coverage for the targeted product is provided based on clinical circumstances that would exclude the use of the preferred product and may be based on previous use of a product. The coverage review process will ascertain situations where a clinical exception can be made. This program applies to members who are new to treatment with a targeted product for the first time.

Each referral is reviewed based on all utilization management (UM) programs implemented for the client.

Table. Polyneuropathy of hereditary transthyretin-mediated (hATTR) amyloidosis Products

	Product(s)
Preferred*	• **Onpattro** (patisiran) injection
Targeted	• **Amvuttra** (vutrisiran) injection • **Tegsedi** (inotersen) injection

*: Medications considered formulary or preferred on your plan may still require a clinical prior authorization review.

II. EXCEPTION CRITERIA

This program applies to members requesting treatment for an indication that is FDA-approved for the preferred product.

Coverage for the targeted product is provided when either of the following criteria is met:
A. Member is currently receiving treatment with the targeted product, excluding when the requested targeted product is obtained as samples or via manufacturer's patient assistance programs.
B. Member has a documented inadequate response or intolerable adverse event with the preferred product.

Section 2: Site of Care

CareFirst Site of Care Criteria
Administration of Subcutaneous Amvuttra

POLICY

I. CRITERIA FOR APPROVAL FOR ADMINISTRATION IN OUTPATIENT HOSPITAL SETTING

This policy provides coverage for provider administered Amvuttra in an outpatient hospital setting for up to 45 days when a member is new to therapy or is reinitiating therapy after not being on therapy for at least 6 months.

This policy provides coverage for administration of Amvuttra in an outpatient hospital setting for a longer course of treatment when ANY of the following criteria are met:
A. The member has experienced an adverse reaction to the drug that did not respond to conventional interventions (eg, acetaminophen, steroids, diphenhydramine, fluids or other pre-medications) or a severe adverse event (anaphylaxis, anaphylactoid reactions, myocardial infarction, thromboembolism, or seizures) during or immediately after administration.
B. The member is medically unstable (eg respiratory, cardiovascular, or renal conditions).
C. The member has significant behavioral issues and/or physical or cognitive impairment that would impact the safety of drug administration AND the patient does not have access to a caregiver.
D. The member is less than 14 years of age.

For situations where administration of Amvuttra does not meet the criteria for outpatient hospital administration, coverage for Amvuttra is provided when administered in alternative sites such as; physician office, home infusion or ambulatory care.

II. REQUIRED DOCUMENTATION
The following information is necessary to initiate the site of care prior authorization review (where applicable):
A. Medical records supporting the member has experienced an adverse reaction that did not respond to conventional interventions or a severe adverse event during or immediately after administration
B. Medical records supporting the member is medically unstable
C. Medical records supporting the member has behavioral issues and/or physical or cognitive impairment and no access to a caregiver

Section 3: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

AMVUTTRA (vutrisiran)

CVS/caremark™

POLICY

III. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Amvuttra 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.

IV. 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

V. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with a neurologist, geneticist, or physician specializing in the treatment of amyloidosis.

VI. 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 inotersen (Tegsedi), patisiran (Onpattro) or tafamidis (Vyndaqel, Vyndamax).

VII. 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 Amvuttra 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.

REFERENCES:

SECTION 1

1. Onpattro [package insert]. Cambridge, MA: Alnylam Pharmaceuticals, Inc.; January 2023.
2. Tegsedi [package insert]. Waltham, MA: Sobi Inc; June 2022.
3. Amvuttra [package insert]. Cambridge, MA: Alnylam Pharmaceuticals, Inc.; June 2022.

SECTION 2

1. Amvuttra [package insert]. Cambridge, MA: Alnylam Pharmaceuticals, Inc; June 2022.

SECTION 3

1. Amvuttra [package insert]. Cambridge, MA: Alnylam Pharmaceuticals, Inc.; June 2022.
2. 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.
3. 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 June 14, 2022.

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.
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POLICY Document for ARANESP (darbepoetin alfa)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, and overall, clinically appropriate use. This document provides specific information to both sections of the overall policy.

Section 1: Preferred Product
- Policy information specific to preferred medications

Section 2: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 1: Preferred Product

EXCEPTIONS CRITERIA
ERYTHROPOIESIS STIMULATING AGENTS
PREFERRED PRODUCTS: ARANESP AND RETACRIT

POLICY
This policy informs prescribers of preferred products and provides an exception process for targeted products through prior authorization.

I. PLAN DESIGN SUMMARY

This program applies to the erythropoiesis stimulating agents specified in this policy. Coverage for targeted products is provided based on clinical circumstances that would exclude the use of the preferred products and may be based on previous use of a product. The coverage review process will ascertain situations where a clinical exception can be made. This program applies to all members who are requesting treatment with the targeted products, Epogen or Procrit. This program also applies to members who are new to treatment with the targeted product, Mircera, for the first time.

Each referral is reviewed based on all utilization management (UM) programs implemented for the client.

Table. Erythropoiesis stimulating agents

	Product(s)
Preferred*	• **Aranesp** (darbepoetin alfa) • **Retacrit** (epoetin alfa-epbx)
Targeted	• **Epogen** (epoetin alfa) • **Mircera** (methoxy polyethylene glycol-epoetin beta) • **Procrit** (epoetin alfa)

*: Medications considered formulary or preferred on your plan may still require a clinical prior authorization review.

II. EXCEPTION CRITERIA

This program applies to members requesting treatment for an indication that is FDA-approved for the preferred products.

A. Mircera

Coverage for the targeted product is provided when the member meets either of the following criteria:

1. Member is currently receiving treatment with a targeted product, excluding when the requested targeted product is obtained as samples or via manufacturer's patient assistance programs.
2. Member has a documented inadequate response or intolerable adverse event with both of the preferred products, Retacrit and Aranesp.

B. Epogen or Procrit

Coverage for the targeted products are provided when both of the following criteria are met:

1. Member has had a documented intolerable adverse event with the preferred product, Retacrit, and the adverse event was not an expected adverse event attributed to the active ingredient as described in the prescribing information.
2. Member has experienced a documented inadequate response or intolerable adverse event with the preferred product, Aranesp, when prescribed for the treatment of anemia due to chronic kidney disease or the treatment of anemia due to myelosuppressive chemotherapy in cancer.

Section 2: Clinical Criteria

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

a. Anemia Due to Chronic Kidney Disease
Treatment of anemia due to chronic kidney disease (CKD), including patients on dialysis and patients not on dialysis.

b. 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.

REFERENCES:

SECTION 1

1. Aranesp [package insert]. Thousand Oaks, CA: Amgen Inc.; January 2019.
2. Epogen [package insert]. Thousand Oaks, CA: Amgen Inc.; July 2018.
3. Procrit [package insert]. Horsham, PA: Janssen Products, LP; July 2018.
4. Mircera [package insert]. St. Gallen, Switzerland: Vifor (International) Inc.; June 2018.
5. Retacrit [package insert]. Lake Forest, IL: Hospira Inc.; August 2020.

SECTION 2

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.
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Reference number
2073-A

SPECIALTY GUIDELINE MANAGEMENT

ARZERRA (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.

A. FDA-Approved Indications
Chronic lymphocytic leukemia (CLL):
1. Arzerra is indicated in combination with chlorambucil, for the treatment of previously untreated patients with CLL for whom fludarabine-based therapy is considered inappropriate.
2. Arzerra is indicated in combination with fludarabine and cyclophosphamide for the treatment of patients with relapsed CLL.
3. Arzerra is indicated for extended treatment of patients who are in complete or partial response after at least two lines of therapy for recurrent or progressive CLL.
4. Arzerra is indicated for the treatment of patients with CLL refractory to fludarabine and alemtuzumab.

B. Compendial Uses
1. CLL
2. Small lymphocytic lymphoma (SLL) (managed in the same manner as CLL)
3. Waldenström's macroglobulinemia/lymphoplasmacytic lymphoma

Note: Arzerra is only available through the manufacturer's oncology patient access program.

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

II. CRITERIA FOR INITIAL APPROVAL

A. Chronic Lymphocytic Leukemia (CLL) and Small Lymphocytic Lymphoma (SLL)
Authorization of 6 months may be granted for the treatment of CLL or SLL.

B. Waldenström's Macroglobulinemia/Lymphoplasmacytic Lymphoma (WM/LPL)
Authorization of 6 months may be granted for the treatment of Waldenström's macroglobulinemia/lymphoplasmacytic lymphoma when all of the following criteria are met:
1. The disease is relapsed, refractory, or progressive, and
2. The member is intolerant to 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

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Reference number
2833-A

SPECIALTY GUIDELINE MANAGEMENT

ASPARLAS (calaspargase pegol - mknl)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Asparlas is indicated as a component of a multi-agent chemotherapeutic regimen for the treatment of acute lymphoblastic leukemia in pediatric and young adult patients age 1 month to 21 years.

B. Compendial Uses
1. Lymphoblastic lymphoma (managed in the same manner as ALL)
2. Acute lymphoblastic leukemia (ALL) as a substitute for pegaspargase in patients 21 years and younger for more sustained asparaginase activity
3. Pediatric acute lymphoblastic leukemia (ALL) as a substitute for pegaspargase in patients age 1 month to 21 years for more sustained asparaginase activity

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

II. CRITERIA FOR INITIAL APPROVAL

Authorization of 12 months may be granted for the treatment of acute lymphoblastic leukemia or lymphoblastic lymphoma when all of the following criteria are met:
A. The requested medication will be used in conjunction with multi-agent chemotherapy.
B. The member is 21 years of age or younger.

III. CONTINUATION OF THERAPY

Authorization of 12 months total 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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POLICY Document for
AVASTIN (bevacizumab)
ALYMSYS (bevacizumab-maly)
MVASI (bevacizumab-awwb)
VEGZELMA (bevacizumab-adcd)
ZIRABEV (bevacizumab-bvzr)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, and overall, clinically appropriate use. This document provides specific information to both sections of the overall policy.

Section 1: Preferred Product
- Policy information specific to preferred medications

Section 2: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 3: Oncology Clinical Policy
- Policy information specific to regimen review per NCCN Guidelines.

Section 1: Preferred Product

EXCEPTIONS CRITERIA
BEVACIZUMAB-ONCOLOGY PRODUCTS

PREFERRED PRODUCTS: ALYMSYS, MVASI AND ZIRABEV

POLICY
This policy informs prescribers of preferred products and provides an exception process for targeted products through prior authorization.

I. PLAN DESIGN SUMMARY

This program applies to the bevacizumab products specified in this policy. Coverage for targeted products is provided based on clinical circumstances that would exclude the use of the preferred product and may be based on previous use of a product. The coverage review process will ascertain situations where a clinical exception can be made. This program applies to all members requesting treatment with a targeted product.

Each referral is reviewed based on all utilization management (UM) programs implemented for the client.

Table. Bevacizumab-Oncology Products

	Product(s)
Preferred*	• **Alymsys** (bevacizumab-maly) • **Mvasi** (bevacizumab-awwb) • **Zirabev** (bevacizumab-bvzr)

Targeted	• **Avastin** (bevacizumab)

*: Medications considered formulary or preferred on your plan may still require a clinical prior authorization review.

II. EXCEPTION CRITERIA

Coverage for the targeted product is provided when the member has had a documented intolerable adverse event to all of the preferred products and the adverse event was not an expected adverse event attributed to the active ingredient as described in the prescribing information (i.e., known adverse reaction for both the reference product and biosimilar products).

Section 2: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

AVASTIN (bevacizumab)
ALYMSYS (bevacizumab-maly)
MVASI (bevacizumab-awwb)
VEGZELMA (bevacizumab-adcd)
ZIRABEV (bevacizumab-bvzr)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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. Metastatic Colorectal Cancer (mCRC)
   a. Avastin, Alymsys, Mvasi, Vegzelma or Zirabev, in combination with intravenous fluorouracil-based chemotherapy, is indicated for the first- or second-line treatment of patients with metastatic colorectal cancer.
   b. Avastin, Alymsys, Mvasi, Vegzelma or Zirabev, in combination with fluoropyrimidine-irinotecan- or fluoropyrimidine-oxaliplatin-based chemotherapy, is indicated for the second-line treatment of patients with metastatic colorectal cancer who have progressed on a first-line bevacizumab product-containing regimen.
2. First-Line Non-Squamous Non-Small Cell Lung Cancer (NSCLC)
   Avastin, Alymsys, Mvasi, Vegzelma or Zirabev, in combination with carboplatin and paclitaxel, is indicated for the first-line treatment of patients with unresectable, locally advanced, recurrent or metastatic non–squamous non–small cell lung cancer.
3. Recurrent Glioblastoma (RGM)
   Avastin, Alymsys, Mvasi, Vegzelma or Zirabev, is indicated for the treatment of recurrent glioblastoma in adults.
4. Metastatic Renal Cell Carcinoma (mRCC)
   Avastin, Alymsys, Mvasi, Vegzelma or Zirabev, in combination with interferon alfa, is indicated for the treatment of metastatic renal cell carcinoma.
5. Persistent, Recurrent, or Metastatic Cervical Cancer
   Avastin, Alymsys, Mvasi, Vegzelma or Zirabev, in combination with paclitaxel and cisplatin or paclitaxel and topotecan, is indicated for the treatment of patients with persistent, recurrent, or metastatic cervical cancer.
6. Epithelial Ovarian, Fallopian Tube, or Primary Peritoneal Cancer

a. Avastin, Mvasi, Vegzelma or Zirabev, in combination with carboplatin and paclitaxel, followed by Avastin, Mvasi, Vegzelma or Zirabev as a single agent, is indicated for the treatment of patients with stage III or IV epithelial ovarian, fallopian tube, or primary peritoneal cancer following initial surgical resection.
b. Avastin, Alymsys, Mvasi, Vegzelma or Zirabev, in combination with paclitaxel, pegylated liposomal doxorubicin, or topotecan, is indicated for the treatment of patients with platinum-resistant recurrent epithelial ovarian, fallopian tube or primary peritoneal cancer who received no more than 2 prior chemotherapy regimens.
c. Avastin, Mvasi, Vegzelma or Zirabev, in combination with carboplatin and paclitaxel, or with carboplatin and gemcitabine, followed by Avastin, Mvasi, Vegzelma or Zirabev as a single agent, is indicated for the treatment of patients with platinum-sensitive recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer.

7. Hepatocellular Carcinoma
Avastin, in combination with atezolizumab, is indicated for the treatment of patients with unresectable or metastatic hepatocellular carcinoma (HCC) who have not received prior systemic therapy.

B. Compendial Uses
1. Breast Cancer
2. Central Nervous System (CNS) Cancers
   a. Glioma (WHO Grade 1)
   b. Diffuse high grade gliomas
   c. Glioblastoma
   d. IDH mutant astrocytoma (WHO Grade 2, 3, or 4)
   e. Oligodendroglioma (WHO Grade 2 or 3)
   f. Intracranial and Spinal Ependymoma (excluding subependymoma)
   g. Medulloblastoma
   h. Primary Central Nervous System Lymphoma
   i. Meningiomas
   j. Limited and Extensive Brain Metastases
   k. Metastatic Spine Tumors
3. Malignant Pleural Mesothelioma, Malignant Peritoneal Mesothelioma, Pericardial Mesothelioma, Tunica Vaginalis Testis Mesothelioma
4. Ovarian Cancer, Fallopian Tube Cancer, Primary Peritoneal Cancer
5. Soft Tissue Sarcoma
   a. Angiosarcoma
   b. Solitary Fibrous Tumor/Hemangiopericytoma
6. Uterine Neoplasms/Endometrial Carcinoma
7. Vulvar Carcinoma
8. Small Bowel Adenocarcinoma
9. Ampullary Adenocarcinoma
10. Appendiceal Adenocarcinoma
11. Anal Adenocarcinoma
12. Renal Cell Carcinoma
13. Ophthalmic Disorders
   a. Diabetic Macular Edema
   b. Neovascular (wet) Age-Related Macular Degeneration (AMD)
   c. Macular Edema following Retinal Vein Occlusion (RVO)
   d. Proliferative Diabetic Retinopathy
   e. Choroidal Neovascularization (CNV)
   f. Neovascular Glaucoma; adjunct
   g. Retinopathy of Prematurity
   h. Polypoidal Choroidal Vasculopathy

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

II. CRITERIA FOR INITIAL APPROVAL

A. Ophthalmic Disorders

Authorization of 6 months may be granted for treatment of the following retinal disorders:

1. Diabetic Macular Edema
2. Neovascular (wet) Age-Related Macular Degeneration
3. Macular Edema following Retinal Vein Occlusion
4. Proliferative Diabetic Retinopathy
5. Choroidal Neovascularization (including myopic choroidal neovascularization, angioid streaks, choroiditis [including choroiditis secondary to ocular histoplasmosis], idiopathic degenerative myopia, retinal dystrophies, rubeosis iridis, pseudoxanthoma elasticum, and trauma)
6. Neovascular Glaucoma
7. Retinopathy of Prematurity
8. Polypoidal Choroidal Vasculopathy

B. Colorectal Cancer (CRC)

Authorization of 12 months may be granted for treatment of colorectal cancer, including appendiceal adenocarcinoma and anal adenocarcinoma.

C. Small Bowel Adenocarcinoma

Authorization of 12 months may be granted for treatment of small bowel adenocarcinoma.

D. Ampullary Adenocarcinoma

Authorization of 12 months may be granted for treatment of intestinal-type ampullary adenocarcinoma that is progressive, unresectable, or metastatic.

E. Non-Small Cell Lung Cancer (NSCLC)

Authorization of 12 months may be granted for treatment of recurrent, unresectable, advanced, or metastatic non-squamous NSCLC.

F. CNS Cancer

Authorization of 12 months may be granted for treatment of the following types of CNS cancer:

1. Glioma (WHO Grade 1)
2. Diffuse high grade gliomas
3. Glioblastoma
4. IDH mutant astrocytoma (WHO Grade 2, 3 or 4)
5. Oligodendroglioma (WHO Grade 2 or 3)
6. Intracranial and Spinal Ependymoma (excludes subependymoma)
7. Medulloblastoma
8. Primary Central Nervous System Lymphoma
9. Meningiomas
10. Limited and Extensive Brain Metastases
11. Metastatic Spine Tumors

G. Ovarian Cancer/Fallopian Tube Cancer/Primary Peritoneal Cancer

Authorization of 12 months may be granted for treatment of epithelial ovarian cancer, fallopian tube cancer, primary peritoneal cancer, and malignant sex cord stromal tumors.

H. Uterine Neoplasms/Endometrial Carcinoma

Authorization of 12 months may be granted for treatment of progressive, advanced, recurrent, or metastatic uterine neoplasms or endometrial carcinoma.

I. Cervical/Vaginal Cancer

Authorization of 12 months may be granted for treatment of persistent, recurrent, or metastatic cervical or

vaginal cancer.

J. Breast Cancer
Authorization of 12 months may be granted for treatment of recurrent or metastatic breast cancer.

K. Renal Cell Carcinoma
Authorization of 12 months may be granted for treatment of relapsed or stage IV renal cell carcinoma.

L. Soft Tissue Sarcoma
1. Authorization of 12 months may be granted for treatment of angiosarcoma, as single agent therapy.
2. Authorization of 12 months may be granted for treatment of solitary fibrous tumor or hemangiopericytoma, in combination with temozolomide.

M. Mesothelioma
1. Authorization of 12 months may be granted for treatment of malignant pleural mesothelioma, malignant peritoneal mesothelioma, pericardial mesothelioma, or tunica vaginalis testis mesothelioma when any of the following criteria are met:
   a. As first-line therapy for unresectable disease in combination with pemetrexed and either cisplatin or carboplatin, followed by single-agent maintenance bevacizumab
   b. As subsequent therapy in combination with pemetrexed and either cisplatin or carboplatin if immunotherapy was administered as first-line treatment
2. Authorization of 12 months may be granted for treatment of malignant peritoneal mesothelioma, pericardial mesothelioma, or tunica vaginalis testis mesothelioma when used in combination with atezolizumab as subsequent therapy.

N. Vulvar Carcinoma
Authorization of 12 months may be granted for treatment of unresectable locally advanced, recurrent, or metastatic vulvar carcinoma, including squamous cell carcinoma and adenocarcinoma.

O. Hepatocellular Carcinoma
Authorization of 12 months may be granted for treatment of unresectable or metastatic hepatocellular carcinoma, when the requested medication will be used as initial treatment in combination with atezolizumab.

III. CONTINUATION OF THERAPY

A. Ophthalmic Disorders
For ophthalmic disorders, authorization of 12 months may be granted for continued treatment of an indication outlined in Section II for members who have demonstrated a positive clinical response to therapy (e.g., improvement or maintenance in best corrected visual acuity [BCVA] or visual field, or a reduction in the rate of vision decline or the risk of more severe vision loss).

B. All Other Indications
For all other indications, 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.

Section 3: Oncology Clinical Policy

PROGRAM DESCRIPTION

The National Comprehensive Care Network® (NCCN®) is an alliance of leading cancer centers devoted to patient care, research and education dedicated to improving the quality, effectiveness, and efficiency of cancer care so patients can

live better lives.[1] It is comprised of oncology experts who convene regularly to establish the best treatments for patients. NCCN develops various resources for use by stakeholders in the health care delivery system. These resources include, but are not limited to, the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®), the NCCN Drugs & Biologics Compendium (NCCN Compendium®) and the NCCN Chemotherapy Order Templates (NCCN Templates®).

NCCN Templates® are based on NCCN Guidelines® and NCCN Compendium®. The NCCN Compendium lists the appropriate drugs and biologics as treatment options for specific cancers using U.S. Food and Drug Administration (FDA)-approved disease indications and specific NCCN panel recommendations. Each recommendation is supported by a level of evidence category.

NCCN Categories of Evidence and Consensus[2]

- Category 1: Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
- Category 2A: Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
- Category 2B: Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.
- Category 3: Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

POLICY

Policy for Regimen Prior Authorization

A regimen prior authorization allows submission of a single prior authorization request for all oncology drugs or biologics within an NCCN template that require prior authorization.

PROCEDURE

This policy provides coverage of a regimen review when all of the following criteria are met:

1. Regimen prior authorization reviews, based on NCCN templates, are initiated through the provider portal.
   - If the prior authorization request is submitted via phone or fax, each drug or biologic will need to be submitted and reviewed as a separate prior authorization request for review with drug-specific criteria.
2. The prior authorization review is requested for an oncology drug or biologic.
3. The member is eligible for regimen review.
4. The indication is for a cancer that is eligible for regimen review. Currently, the cancer types in scope for regimen review include the following:
   - Ampullary Adenocarcinoma
   - Anal Carcinoma
   - B-Cell Lymphomas
   - Basal Cell Skin Cancer
   - Biliary Tract Cancers
   - Bone Cancer
   - Breast Cancer
   - Bladder Cancer
   - Central Nervous System Cancers
   - Cervical Cancer
   - Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma
   - Chronic Myeloid leukemia
   - Colon Cancer
   - Dermatofibrosarcoma Protuberans
   - Esophageal Cancer
   - Gastric Cancer

- Gastrointestinal Stromal Tumors
- Gestational Trophoblastic Neoplasms
- Hairy Cell Leukemia
- Head and Neck Cancers
- Hodgkin Lymphoma
- Hepatocellular Carcinoma
- Kaposi Sarcoma
- Kidney Cancer
- Melanoma: Cutaneous
- Melanoma: Uveal
- Merkel Cell Carcinoma
- Mesothelioma: Peritoneal
- Mesothelioma: Pleural
- Myelodysplastic Syndromes
- Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Gene Fusions
- Myeloproliferative Neoplasms
- Neuroendocrine and Adrenal Tumors
- Non-Small Cell Lung Cancer
- Occult Primary
- Ovarian Cancer
- Pancreatic Cancer
- Penile Cancer
- Prostate Cancer
- Rectal Cancer
- Small Bowl Adenocarcinoma
- Small Cell Lung Cancer
- Soft Tissue Sarcoma
- Squamous Cell Skin Cancer
- Systemic Mastocytosis
- Systemic Light Chain Amyloidosis
- Testicular Cancer
- Thymomas and Thymic Carcinomas
- Thyroid Carcinoma
- Uterine Neoplasms
- Vulvar Cancer
- Waldenström Macroglobulinemia / Lymphoplasmacytic Lymphoma

In addition, the following criteria must be met for approval:

1. The requested regimen for the drug(s) or biologic(s) and indication is consistent with an NCCN recommendation with a level of evidence category of 1 or 2A.
2. The NCCN template must be accepted by the provider without modification.

Further review may be indicated when the above criteria are not met.

Authorizations may be granted for 12 months or as medically required, based on the member's condition and provider's assessment.

Supportive Care: Myeloid Growth Factor Therapy

Granulocyte colony stimulating factors are recommended for primary prophylaxis based on the febrile neutropenia risk of the chemotherapy regimen. Febrile neutropenia risk levels vary by NCCN Chemotherapy Order template and are listed at the top of the template. Regimens associated with a high or intermediate risk of febrile neutropenia may include a granulocyte colony stimulating factor as part of the prior authorization.

Continuation of Therapy

To submit a request for continuation of therapy, a new regimen prior authorization review must be requested. Upon template selection, the template must be modified to include the appropriate therapies being used for maintenance

treatment. The regimen request will be submitted for further review.

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

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Reference number(s)
3918-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 gender non-conforming or transgender 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 patients 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

Authorization of 12 months may be granted for gender dysphoria when all of the following criteria are met:

1. The member is able to make an informed decision to engage in hormone therapy.
2. The member has a diagnosis of gender dysphoria.
3. The member's comorbid conditions are reasonably controlled.
4. The member has been educated on any contraindications and side effects to therapy.
5. The member has been informed of fertility preservation options.

VI. CONTINUATION OF THERAPY

A. Primary hypogonadism or hypogonadotropic hypogonadism

For members requesting authorization for continuation of therapy with primary hypogonadism or hypogonadotropic hypogonadism who are not currently receiving Aveed therapy through samples or a manufacturer's patient assistance program, authorization of 12 months may be granted if the member meets criteria V.A.1 and V.A.2 above. All other members (including new members) must meet all initial authorization criteria.

B. Gender dysphoria

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for gender dysphoria when all of the following criteria are met:

1. The member is able to make an informed decision to engage in hormone therapy.
2. The member has a diagnosis of gender dysphoria.
3. The member's comorbid conditions are reasonably controlled.
4. The member has been educated on any contraindications and side effects to therapy.
5. Before the start of therapy, the member has been informed of fertility preservation options.

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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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POLICY Document for BAVENCIO (avelumab)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, and overall, clinically appropriate use. This document provides specific information to both sections of the overall policy.

Section 1: Site of Care
- Policy information specific to site of care (outpatient, hospital outpatient, home infusion)

Section 2: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 3: Oncology Clinical Policy
- Policy information specific to regimen review per NCCN Guidelines.

Section 1: Site of Care

CareFirst Site of Care Criteria
Administration of Intravenous Checkpoint Inhibitors
Bavencio, Imfinzi, Jemperli, Keytruda, Libtayo, Opdivo, Opdualag, Tecentriq, Yervoy and Zynyz

POLICY

I. CRITERIA FOR APPROVAL FOR ADMINISTRATION IN OUTPATIENT HOSPITAL SETTING

This policy provides coverage for administration of a checkpoint inhibitor in an outpatient hospital setting for the initial 6 months approval and up to 45 days for renewal of therapy.

This policy provides coverage for administration of a checkpoint inhibitor in an outpatient hospital setting for a longer course of treatment when ANY of the following criteria are met:

A. The member has experienced an adverse reaction that did not respond to conventional interventions (eg, acetaminophen, steroids, diphenhydramine, fluids, other pre-medications or slowing of infusion rate) or a severe adverse event (anaphylaxis, anaphylactoid reactions, myocardial infarction, thromboembolism, or seizures) during or immediately after an infusion or has experienced severe toxicity requiring continuous monitoring (e.g. Grade 2-4 bullous dermatitis, transaminitis, pneumonitis, Stevens-Johnson syndrome, acute pancreatitis, primary adrenal insufficiency aseptic meningitis, encephalitis, transverse myelitis, myocarditis, pericarditis, arrhythmias, impaired ventricular function, conduction abnormalities).
B. The member is medically unstable (eg respiratory, cardiovascular, or renal conditions).
C. The member has severe venous access issues that require the use of a special interventions only available in the outpatient hospital setting.
D. The member has significant behavioral issues and/or physical or cognitive impairment that would impact the safety of the infusion therapy AND the patient does not have access to a caregiver.
E. The member is receiving provider administered combination chemotherapy.
F. The member is less than 14 years of age.

For situations where administration of a checkpoint inhibitor does not meet the criteria for outpatient hospital infusion, coverage for a checkpoint inhibitor is provided when administered in alternative sites such as physician office, home infusion or ambulatory care.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the site of care prior authorization review (where applicable):

A. Medical records supporting the member has experienced an adverse reaction that did not respond to conventional interventions or a severe adverse event during or immediately after an infusion or a severe toxicity requiring continuous monitoring
B. Medical records supporting the member is medically unstable
C. Medical records supporting the member has severe venous access issues that require specialized interventions only available in the outpatient hospital setting
D. Medical records supporting the member has behavioral issues and/or physical or cognitive impairment and no access to a caregiver
E. Medical records supporting the member is receiving provider administered combination therapy.

Section 2: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

BAVENCIO (avelumab)

POLICY

III. INDICATIONS

The indications below including FDA-approved indications and compendial 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. Metastatic Merkel Cell Carcinoma (MCC)
      Treatment of adults and pediatric patients 12 years and older with metastatic Merkel cell carcinoma.

   2. Locally Advanced or Metastatic Urothelial Carcinoma (UC): *First-line maintenance treatment of urothelial carcinoma*
      Maintenance treatment of patients with locally advanced or metastatic urothelial carcinoma that has not progressed with first-line platinum-containing chemotherapy.

   3. Locally Advanced or Metastatic Urothelial Carcinoma (UC): *Previously-treated urothelial carcinoma*
      Treatment of patients with locally advanced or metastatic urothelial carcinoma who have disease progression during or following platinum-containing chemotherapy or have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy.

   4. Advanced Renal Cell Carcinoma (RCC)
      First-line treatment of patients with advanced renal cell carcinoma in combination with axitinib.

B. Compendial Indications
   1. Urothelial carcinoma
      a. Bladder cancer
      b. Primary carcinoma of the urethra
      c. Upper genitourinary (GU) tract tumors
      d. Urothelial carcinoma of the prostate
   2. Merkel cell carcinoma
   3. Renal cell carcinoma

4. Gestational trophoblastic neoplasia
5. Endometrial carcinoma

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

IV. EXCLUSIONS

Coverage will not be provided for members who have experienced disease progression while on PD-1 or PD-L1 inhibitor therapy.

V. CRITERIA FOR INITIAL APPROVAL

A. Merkel Cell Carcinoma

Authorization of 6 months may be granted as a single agent for the treatment of Merkel cell carcinoma in members with metastatic disease.

B. Urothelial Carcinoma – Bladder Cancer

Authorization of 6 months may be granted for treatment of bladder cancer as a single agent when either of the following criteria is met:

1. Used as subsequent therapy:
2. Used as maintenance therapy if there is no progression on first-line platinum-containing chemotherapy.

C. Urothelial Carcinoma – Primary Carcinoma of the Urethra

Authorization of 6 months may be granted for treatment of primary carcinoma of the urethra as a single agent when either of the following criteria is met:

1. Used as subsequent systemic therapy for recurrent, locally advanced, or metastatic disease
2. Used as maintenance therapy if there is no progression on first-line platinum-containing chemotherapy.

D. Urothelial Carcinoma – Upper Genitourinary (GU) Tract Tumors or Urothelial Carcinoma of the Prostate

Authorization of 6 months may be granted for the treatment of upper genitourinary (GU) tract tumors or urothelial carcinoma of the prostate as a single agent when either of the following criteria is met:

1. Used as subsequent therapy for locally advanced or metastatic disease.
2. Used as maintenance therapy if there is no progression on first-line platinum-containing chemotherapy.

E. Renal Cell Carcinoma

Authorization of 6 months may be granted for treatment of advanced, relapsed, or stage IV renal cell carcinoma with clear cell histology when given in combination with axitinib as first-line treatment for the disease.

F. Gestational Trophoblastic Neoplasia

Authorization of 6 months may be granted as a single agent for treatment of gestational trophoblastic neoplasia for multiagent chemotherapy-resistant disease when either of the following criteria is met:

1. Member has recurrent or progressive intermediate trophoblastic tumor (placental site trophoblastic tumor or epithelioid trophoblastic tumor) following treatment with a platinum-based regimen.
2. Member has high-risk disease.

G. Endometrial Carcinoma

Authorization of 6 months may be granted as a single agent for subsequent treatment of recurrent or metastatic microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) tumors.

VI. CONTINUATION OF THERAPY

Authorization of 6 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.

Section 3: Oncology Clinical Policy

PROGRAM DESCRIPTION

The National Comprehensive Care Network® (NCCN®) is an alliance of leading cancer centers devoted to patient care, research and education dedicated to improving the quality, effectiveness, and efficiency of cancer care so patients can live better lives.[1] It is comprised of oncology experts who convene regularly to establish the best treatments for patients. NCCN develops various resources for use by stakeholders in the health care delivery system. These resources include, but are not limited to, the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®), the NCCN Drugs & Biologics Compendium (NCCN Compendium®) and the NCCN Chemotherapy Order Templates (NCCN Templates®).

NCCN Templates® are based on NCCN Guidelines® and NCCN Compendium®. The NCCN Compendium lists the appropriate drugs and biologics as treatment options for specific cancers using U.S. Food and Drug Administration (FDA)-approved disease indications and specific NCCN panel recommendations. Each recommendation is supported by a level of evidence category.

NCCN Categories of Evidence and Consensus[2]

- Category 1: Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
- Category 2A: Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
- Category 2B: Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.
- Category 3: Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

POLICY

Policy for Regimen Prior Authorization
A regimen prior authorization allows submission of a single prior authorization request for all oncology drugs or biologics within an NCCN template that require prior authorization.

PROCEDURE

This policy provides coverage of a regimen review when all of the following criteria are met:
1. Regimen prior authorization reviews, based on NCCN templates, are initiated through the provider portal.
   - If the prior authorization request is submitted via phone or fax, each drug or biologic will need to be submitted and reviewed as a separate prior authorization request for review with drug-specific criteria.
2. The prior authorization review is requested for an oncology drug or biologic.
3. The member is eligible for regimen review.
4. The indication is for a cancer that is eligible for regimen review. Currently, the cancer types in scope for regimen review include the following:
   - Ampullary Adenocarcinoma
   - Anal Carcinoma
   - B-Cell Lymphomas

- Basal Cell Skin Cancer
- Biliary Tract Cancers
- Bone Cancer
- Breast Cancer
- Bladder Cancer
- Central Nervous System Cancers
- Cervical Cancer
- Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma
- Chronic Myeloid leukemia
- Colon Cancer
- Dermatofibrosarcoma Protuberans
- Esophageal Cancer
- Gastric Cancer
- Gastrointestinal Stromal Tumors
- Gestational Trophoblastic Neoplasms
- Hairy Cell Leukemia
- Head and Neck Cancers
- Hodgkin Lymphoma
- Hepatocellular Carcinoma
- Kaposi Sarcoma
- Kidney Cancer
- Melanoma: Cutaneous
- Melanoma: Uveal
- Merkel Cell Carcinoma
- Mesothelioma: Peritoneal
- Mesothelioma: Pleural
- Myelodysplastic Syndromes
- Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Gene Fusions
- Myeloproliferative Neoplasms
- Neuroendocrine and Adrenal Tumors
- Non-Small Cell Lung Cancer
- Occult Primary
- Ovarian Cancer
- Pancreatic Cancer
- Penile Cancer
- Prostate Cancer
- Rectal Cancer
- Small Bowl Adenocarcinoma
- Small Cell Lung Cancer
- Soft Tissue Sarcoma
- Squamous Cell Skin Cancer
- Systemic Mastocytosis
- Systemic Light Chain Amyloidosis
- Testicular Cancer
- Thymomas and Thymic Carcinomas
- Thyroid Carcinoma
- Uterine Neoplasms
- Vulvar Cancer
- Waldenström Macroglobulinemia / Lymphoplasmacytic Lymphoma

In addition, the following criteria must be met for approval:

1. The requested regimen for the drug(s) or biologic(s) and indication is consistent with an NCCN recommendation with a level of evidence category of 1 or 2A.
2. The NCCN template must be accepted by the provider without modification.

Further review may be indicated when the above criteria are not met.

Authorizations may be granted for 12 months or as medically required, based on the member's condition and provider's assessment.

Supportive Care: Myeloid Growth Factor Therapy
Granulocyte colony stimulating factors are recommended for primary prophylaxis based on the febrile neutropenia risk of the chemotherapy regimen. Febrile neutropenia risk levels vary by NCCN Chemotherapy Order template and are listed at the top of the template. Regimens associated with a high or intermediate risk of febrile neutropenia may include a granulocyte colony stimulating factor as part of the prior authorization.

Continuation of Therapy
To submit a request for continuation of therapy, a new regimen prior authorization review must be requested. Upon template selection, the template must be modified to include the appropriate therapies being used for maintenance treatment. The regimen request will be submitted for further review.

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

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Reference number(s)
1705-A

SPECIALTY GUIDELINE MANAGEMENT

TREANDA (bendamustine)
BENDEKA (bendamustine)
BELRAPZO (bendamustine)
VIVIMUSTA (bendamustine)
bendamustine

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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 lymphocytic leukemia (CLL)
2. Indolent B-cell non-Hodgkin lymphoma (NHL) that has progressed during or within six months of treatment with rituximab or a rituximab-containing regimen

B. Compendial Uses
1. Classical Hodgkin lymphoma (CHL)
2. Nodular lymphocyte predominant Hodgkin lymphoma (NLPHL)
3. Multiple myeloma (MM)
4. CLL/small lymphocytic lymphoma (SLL)
5. B-cell lymphomas:
    a. Human immunodeficiency virus (HIV)-related B-cell lymphoma
    b. Diffuse large B-cell lymphoma (DLBCL)
    c. Follicular lymphoma
    d. High grade B-cell lymphoma
    e. Histologic transformation of indolent lymphomas to diffuse large B-cell lymphoma
    f. Marginal zone lymphoma
        i. Nodal marginal zone lymphoma
        ii. Gastric mucosa associated lymphoid tissue (MALT) lymphoma (extranodal marginal zone lymphoma of the stomach)
        iii. Nongastric MALT lymphoma (nongastric extranodal marginal zone lymphoma)
        iv. Splenic marginal zone lymphoma
    g. Mantle cell lymphoma (MCL)
    h. Post-transplant lymphoproliferative disorders
6. T-cell lymphomas:
    a. Adult T-cell leukemia/lymphoma (ATLL)
    b. Hepatosplenic T-Cell lymphoma
    c. Peripheral T-cell lymphoma (PTCL)
    d. Breast implant associated anaplastic large cell lymphoma (ALCL)
7. Waldenström's macroglobulinemia/lymphoplasmacytic lymphoma/Bing-Neel syndrome
8. Systemic light chain amyloidosis

9. Hematopoietic cell transplantation
10. Cold agglutinin disease

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

II. CRITERIA FOR INITIAL APPROVAL

A. B-cell lymphoma

Authorization of 12 months may be granted for treatment of B-cell lymphomas with any of the following subtypes:

1. HIV-related B-cell lymphoma (HIV-related diffuse large B-cell lymphoma, primary effusion lymphoma, and human herpesvirus-8 (HHV8)-positive diffuse large B-cell lymphoma, plasmablastic lymphoma) when all of the following criteria are met:
   i. The requested drug is used as subsequent therapy
   ii. The requested drug is used in combination with polatuzumab vedotin-piiq with or without rituximab
   iii. The member is not a candidate for transplant or the requested drug will be used as a bridging option until CAR T-cell product is available
2. Diffuse large B-cell lymphoma (DLBCL) when all of the following criteria are met:
   i. The requested drug is used as subsequent therapy
   ii. The requested drug is used in combination with polatuzumab vedotin-piiq with or without rituximab
   iii. The member is not a candidate for transplant or the requested drug will be used as a bridging option until CAR T-cell product is available
3. Follicular lymphoma
4. High-grade B-cell lymphoma when all of the following criteria are met:
   i. The requested drug is used as subsequent therapy
   ii. The requested drug will be used in combination with polatuzumab vedotin-piiq with or without rituximab
   iii. The member is not a candidate for transplant or the requested drug will be used as a bridging option until CAR T-cell product is available.
5. Histologic transformation of indolent lymphomas to diffuse large B-cell lymphoma when all of the following criteria are met:
   i. The requested drug is used in combination with polatuzumab vedotin-piiq with or without rituximab.
   ii. The requested drug is used as subsequent therapy.
   iii. The member is not a candidate for transplant.
6. Mantle cell lymphoma (MCL) when either of the following criteria are met:
   i. The requested drug is used in combination with rituximab, or
   ii. The requested drug as a component of RBAC500 (rituximab, bendamustine, and cytarabine).
7. Marginal zone lymphoma
   i. Nodal marginal zone lymphoma when used in combination with rituximab or obinutuzumab.
   ii. Gastric MALT lymphoma (extranodal marginal zone lymphoma of the stomach) when used in combination with rituximab or obinutuzumab.
   iii. Nongastric MALT lymphoma (nongastric extranodal marginal zone lymphoma) when used in combination with rituximab or obinutuzumab.
   iv. Splenic marginal zone lymphoma when used in combination with rituximab or obinutuzumab.
8. Post-transplant lymphoproliferative disorders when all of the following criteria are met:
   i. The requested drug is used as subsequent therapy
   ii. The member is not a candidate for transplant or the requested drug will be used as a bridging option until CAR T-cell product is available

iii. The requested drug will be used in combination with polatuzumab vedotin-piiq with or without rituximab

B. T-cell lymphoma

Authorization of 12 months may be granted for treatment of T-cell lymphomas with any of the following subtypes:

1. Adult T-cell leukemia/lymphoma (ATLL) when all of the following criteria are met:
   i. The requested drug is used as a single agent
   ii. The requested drug is used as subsequent therapy
2. Hepatosplenic T-Cell lymphoma when all of the following criteria are met:
   i. The requested drug is used as a single agent
   ii. The requested drug is used for refractory disease after 2 first-line therapy regimens
3. Peripheral T-cell lymphoma (PTCL) [including the following subtypes: anaplastic large cell lymphoma, peripheral T-cell lymphoma not otherwise specified, angioimmunoblastic T-cell lymphoma, enteropathy associated T-cell lymphoma, monomorphic epitheliotropic intestinal T-cell lymphoma, nodal peripheral T-cell lymphoma with TFH phenotype, or follicular T-cell lymphoma] when all of the following criteria are met:
   i. The requested drug is used as a single agent
   ii. The requested drug is used as palliative or subsequent therapy
4. Breast implant associated anaplastic large cell lymphoma (ALCL) when all of the following are met:
   i. The requested drug is used as a single agent
   ii. The requested drug is used as subsequent therapy

C. Chronic lymphocytic leukemia/small lymphocytic leukemia (CLL/SLL)

Authorization of 12 months may be granted for treatment of CLL/SLL without chromosome 17p deletion or TP53 mutation

D. Waldenström's macroglobulinemia/lymphoplasmacytic lymphoma/Bing-Neel syndrome

Authorization of 12 months may be granted for treatment of Waldenström's macroglobulinemia/lymphoplasmacytic lymphoma or Bing-Neel syndrome when either of the following criteria are met:

1. The requested drug will be used in combination with rituximab, or
2. The requested drug will be used as a single agent.

E. Multiple myeloma (MM)

Authorization of 12 months may be granted for treatment of MM when all of the following criteria are met:

1. The disease is relapsed or progressive and the member has tried more than 3 prior therapies, and
2. The requested drug will be used in any of the following regimens:
   i. In combination with lenalidomide and dexamethasone, or
   ii. In combination with bortezomib and dexamethasone, or
   iii. In combination with carfilzomib and dexamethasone, or
   iv. As a single agent.

F. Classical Hodgkin lymphoma (cHL)

Authorization of 12 months may be granted for treatment of cHL when all of the following criteria are met:

1. The requested drug will be used as subsequent therapy or palliative therapy, and
2. The requested drug will be used in any of the following regimens:
   i. In combination with brentuximab vedotin, or
   ii. In combination with gemcitabine and vinorelbine, or

iii. In combination with carboplatin and etoposide
iv. As a single agent.

G. Nodular lymphocyte predominant Hodgkin lymphoma (NLPHL)
Authorization of 12 months may be granted for treatment of nodular lymphocyte predominant Hodgkin lymphoma when all of the following criteria are met:
1. The requested drug will be used as subsequent therapy
2. The requested drug will be used in combination with rituximab

H. Systemic light chain amyloidosis
Authorization of 12 months may be granted for treatment of systemic light chain amyloidosis when all of the following criteria are met:
1. The requested drug will be used in combination with dexamethasone
2. The requested drug will be used to treat relapsed or refractory disease

I. Hematopoietic Cell Transplantation
Authorization of 12 months may be granted for use in hematopoietic cell transplantation when all of the following criteria are met:
1. The requested drug will be used as conditioning for autologous transplant
2. The requested drug will be used in combination with etoposide, cytarabine and melphalan

J. Cold agglutinin disease
Authorization of 12 months may be granted for treatment of cold agglutinin disease when 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.

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CVS/caremark

POLICY Document for BENLYSTA (belimumab)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, lower cost site of care and overall, clinically appropriate use. This document provides specific information to each of the three sections of the overall policy.

Section 1: Site of Care
- Policy information specific to site of care (outpatient, hospital outpatient, home infusion)

Section 2: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 1: Site of Care

CareFirst Site of Care Criteria
Administration of Intravenous Benlysta

POLICY

I. CRITERIA FOR APPROVAL FOR ADMINISTRATION IN OUTPATIENT HOSPITAL SETTING

This policy provides coverage for administration of Benlysta in an outpatient hospital setting for up to 22 days when a member is new to therapy or is reinitiating therapy after not being on therapy for at least 6 months.

This policy provides coverage for administration of Benlysta in an outpatient hospital setting for a longer course of treatment when ANY of the following criteria are met:

A. The member has experienced an adverse reaction to the medication that did not respond to conventional interventions (eg, acetaminophen, steroids, diphenhydramine, fluids, other pre-medications or slowing of the infusion rate) or a severe adverse event (anaphylaxis, anaphylactoid reactions, myocardial infarction, thromboembolism, or seizures) during or immediately after an infusion.
B. The member is medically unstable (eg respiratory, cardiovascular, or renal conditions).
C. The member has severe venous access issues that require the use of special interventions only available in the outpatient hospital setting.
D. The member has significant behavioral issues and/or physical or cognitive impairment that would impact the safety of the infusion therapy AND the patient does not have access to a caregiver.
E. The member is less than 14 years of age.

For situations where administration of Benlysta does not meet the criteria for outpatient hospital infusion, coverage for Benlysta is provided when administered in alternative sites such as; physician office, home infusion or ambulatory care.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the site of care prior authorization review (where applicable):

A. Medical records supporting the member has experienced an adverse reaction that did not respond to conventional interventions or a severe adverse event during or immediately after an infusion
B. Medical records supporting the member is medically unstable

C. Medical records supporting the member has severe venous access issues that requires specialized interventions only available in the outpatient hospital setting
D. Medical records supporting the member has behavioral issues and/or physical or cognitive impairment and no access to a caregiver

Section 2: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

BENLYSTA (belimumab)

POLICY

III. INDICATIONS

The indications below including FDA-approved indications and compendial 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.

IV. 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.

V. 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.

VI. 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).

VII. 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.

REFERENCES

SECTION 1
1. Benlysta [package insert]. Rockville, MD: Human Genome Sciences, Inc.; March 2021.

SECTION 2
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.
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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.
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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.

Reference number(s)
3349-A

SPECIALTY GUIDELINE MANAGEMENT

BEOVU (brolucizumab-dbll)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Beovu is indicated for:
1. Neovascular (wet) age-related macular degeneration.
2. Diabetic macular edema

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

II. CRITERIA FOR INITIAL APPROVAL

A. Neovascular (Wet) Age-Related Macular Degeneration
Authorization of 6 months may be granted for treatment of neovascular (wet) age-related macular degeneration.

B. Diabetic Macular Edema
Authorization of 6 months may be granted for treatment of diabetic macular edema.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment of an indication listed in Section II for members who have demonstrated a positive clinical response to therapy (e.g., improvement or maintenance in best corrected visual acuity [BCVA] or visual field, or a reduction in the rate of vision decline or the risk of more severe vision loss).

IV. REFERENCES

1. Beovu [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; May 2022.
2. Dugel PU, Koh A, Ogura Y et al. HAWK and HARRIER: Phase 3, Multicenter, Randomized, Double-Masked Trials of Brolucizumab for Neovascular Age-Related Macular Degeneration. Ophthalmology. 2020; 127:72-84.

POLICY Document for BERINERT (C1 esterase inhibitor [human])

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, and overall, clinically appropriate use. This document provides specific information to both sections of the overall policy.

Section 1: Preferred Product
- Policy information specific to preferred medications

Section 2: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 1: Preferred Product

EXCEPTIONS CRITERIA
HEREDITARY ANGIOEDEMA

PREFERRED PRODUCT: RUCONEST

POLICY
This policy informs prescribers of preferred products and provides an exception process for targeted products through prior authorization.

I. PLAN DESIGN SUMMARY

This program applies to the hereditary angioedema products specified in this policy. Coverage for targeted products is provided based on clinical circumstances that would exclude the use of the preferred product and may be based on previous use of a product. The coverage review process will ascertain situations where a clinical exception can be made. This program applies to all members requesting treatment with a targeted product

Each referral is reviewed based on all utilization management (UM) programs implemented for the client.

Table. C1 esterase inhibitors for the treatment of acute attacks of hereditary angioedema

	Products
Preferred*	• **Ruconest** (C1 esterase inhibitor [recombinant])
Targeted	• **Berinert** (C1 esterase inhibitor [human])

*: Medications considered formulary or preferred on your plan may still require a clinical prior authorization review.

II. EXCEPTION CRITERIA

This program applies to members requesting treatment for an indication that is FDA-approved for the preferred product.

Coverage for the targeted product is provided when any of the following criteria is met:

A. Member is using the targeted product for short-term preprocedural prophylaxis (i.e., prior to surgical or major dental procedures).
B. Member has a documented inadequate response to the preferred product.
C. Member has a documented intolerable adverse event with the preferred product.
D. Member has a documented contraindication to the preferred product (i.e., known or suspected allergy to rabbits or rabbit-derived products).
E. Member is less than 13 years of age.
F. Targeted product is being requested for treatment of laryngeal attacks.

Section 2: Clinical Criteria

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.

Prophylaxis should be considered based on the attack frequency, attack severity, comorbid conditions, and member's quality of life.

CVS/caremark

REFERENCES:

SECTION 1

1. Ruconest [package insert]. Warren, NJ: Pharming Healthcare, Inc.; April 2020.
2. Berinert [package insert]. Kankakee, IL: CSL Behring LLC; September 2021.

SECTION 2

1. Berinert [package insert]. Kankakee, IL: CSL Behring LLC; September 2021.
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.
3. Cicardi M, Bork K, Caballero T, et al. Evidence-based recommendations for the therapeutic management of angioedema owing to hereditary C1 inhibitor deficiency: consensus report of an International Working Group. *Allergy.* 2012;67:147-157.
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Reference number(s)
2261-A

SPECIALTY GUIDELINE MANAGEMENT

BESPONSA (inotuzumab ozogamicin)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Besponsa is indicated for the treatment of adults with relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL).

B. Compendial Use
Pediatric acute lymphoblastic leukemia (ALL)

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 CD22 protein on the surface of the B-cell

III. CRITERIA FOR INITIAL APPROVAL

Acute lymphoblastic leukemia (ALL)
Authorization of 12 months may be granted for treatment of relapsed or refractory ALL when all of the following criteria are met:
1. Member has B-cell precursor ALL.
2. The tumor is CD22-positive as confirmed by testing or analysis to identify the CD22 protein on the surface of the B-cell.
3. Member meets one of the following:
   i. Member has Philadelphia chromosome-positive disease
   ii. Member has Philadelphia chromosome-negative disease.
4. The requested drug will be used in one of the following settings:
   i. As a single agent
   ii. In combination with a tyrosine kinase inhibitor for Philadelphia chromosome-positive disease (e.g., imatinib, dasatinib, nilotinib, bosutinib, ponatinib)
   iii. In combination with cyclophosphamide, dexamethasone, vincristine, methotrexate and cytarabine with or without blinatumomab
5. Member will not receive more than 6 treatment cycles of the requested drug.

IV. CONTINUATION OF THERAPY

Authorization of 12 months (up to 6 cycles total) 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. Besponsa [package insert]. Philadelphia, PA: Wyeth Pharmaceuticals LLC, Inc.; March 2018.
2. Kantarjian Hagop M, DeAngelo Daniel J., Stelljes Matthias, et al. Inotuzumab Ozogamicin versus Standard Therapy for Acute Lymphoblastic Leukemia. *N Engl J Med.* 2016; 375: 740-53.
3. The NCCN Drugs & Biologics Compendium® © 2022 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed April 5, 2022.

Reference number(s)
5060-A

SPECIALTY GUIDELINE MANAGEMENT

BESREMI (ropeginterferon alfa-2b-njft)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Besremi is indicated for the treatment of adults with polycythemia vera.

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

II. CRITERIA FOR INITIAL APPROVAL

Polycythemia Vera
Authorization of 12 months may be granted for treatment of polycythemia vera.

III. CONTINUATION OF THERAPY

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.)

IV. REFERENCES

1. Besremi [package insert]. Burlington, MA: PharmaEssentia USA Corporation; November 2021.

Reference number(s)
4070-A

SPECIALTY GUIDELINE MANAGEMENT

BLENREP (belantamab mafodotin-blmf)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Blenrep is indicated for the treatment of adult patients with relapsed or refractory multiple myeloma who have received at least 4 prior therapies, including an anti-CD38 monoclonal antibody, a proteasome inhibitor, 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 treatment of relapsed, refractory or progressive multiple myeloma as a single agent in members who have received at least 4 prior therapies, including at least one drug from each of the following categories:
1. Anti-CD38 monoclonal antibody (e.g., daratumumab)
2. Proteasome inhibitor (e.g., bortezomib, ixazomib, carfilzomib)
3. Immunomodulatory agent (e.g., lenalidomide, pomalidomide)

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. Blenrep [package insert]. Research Triangle Park, NC: GlaxoSmithKline; February 2022.
2. The NCCN Drugs & Biologics Compendium® © 2022 National Comprehensive Cancer Network, Inc. Available at: https://www.nccn.org. Accessed October 3, 2022.

Reference number(s)
2228-A

SPECIALTY GUIDELINE MANAGEMENT

BLINCYTO (blinatumomab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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. Blincyto is indicated for the treatment of CD19-positive B-cell precursor acute lymphoblastic leukemia (ALL) in first or second complete remission with minimal residual disease (MRD) greater than or equal to 0.1% in adults and children.
   2. Blincyto is indicated for the treatment of relapsed or refractory CD19-positive B-cell precursor acute lymphoblastic leukemia (ALL) in adults and children.

B. Compendial Uses
   1. Acute lymphoblastic leukemia (ALL)

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 CD19 protein on the surface of the B cell

III. CRITERIA FOR INITIAL APPROVAL

B-cell Precursor Acute Lymphoblastic Leukemia
Authorization of 9 months may be granted for treatment of CD19-positive B-cell precursor acute lymphoblastic leukemia (ALL) when one of the following criteria are met:
A. The requested medication will be used as consolidation or maintenance therapy.
B. The requested medication will be used for relapsed or refractory 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. Blincyto [package insert]. Thousand Oaks, CA: Amgen Inc.; February 2022.

2. The NCCN Drugs & Biologics Compendium 2022 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed May 31, 2022.

POLICY Document for VELCADE (bortezomib) bortezomib

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, and overall, clinically appropriate use. This document provides specific information to both sections of the overall policy.

Section 1: Preferred Product
- Policy information specific to preferred medications

Section 2: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 1: Preferred Product

EXCEPTIONS CRITERIA

MULTIPLE MYELOMA

PREFERRED PRODUCTS: NINLARO, VELCADE

POLICY
This policy informs prescribers of preferred products and provides an exception process for targeted products through prior authorization.

I. PLAN DESIGN SUMMARY

This program applies to the multiple myeloma products specified in this policy. Coverage for targeted products is provided based on clinical circumstances that would exclude the use of the preferred product and may be based on previous use of a product. The coverage review process will ascertain situations where a clinical exception can be made. This program applies to members who are new to treatment with a targeted product for the first time.

Each referral is reviewed based on all utilization management (UM) programs implemented for the client.

Table. Multiple Myeloma Therapies

	Product(s)
Preferred*	• **Ninlaro** (ixazomib) • **Velcade** (bortezomib)
Targeted	• **Kyprolis** (carfilzomib)

*: Medications considered formulary or preferred on your plan may still require a clinical prior authorization review.

II. EXCEPTION CRITERIA

This program applies to members requesting treatment for an indication that is FDA-approved for the preferred product.

Coverage for a targeted product is provided when either of the following criteria are met:

A. Member is currently receiving treatment with a targeted product, excluding when the requested targeted product is obtained as samples or via manufacturer's patient assistance programs.

B. Member has a documented inadequate response or intolerable adverse event with both of the preferred products.

Section 2: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

VELCADE (bortezomib)
bortezomib

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. Multiple myeloma
2. Mantle cell lymphoma

B. Compendial Uses
1. Systemic light chain amyloidosis
2. Waldenström's macroglobulinemia/lymphoplasmacytic lymphoma
3. Multicentric Castleman's disease
4. Adult T-cell leukemia/lymphoma
5. Antibody mediated rejection of solid organ
6. Acute lymphoblastic leukemia
7. Follicular lymphoma
8. Kaposi's sarcoma
9. Hodgkin Lymphoma
10. POEMS (polyneuropathy, organomegaly, endocrinopathy, monoclonal protein, skin changes) Syndrome

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.

B. Mantle cell lymphoma
Authorization of 12 months may be granted for the treatment of mantle cell lymphoma.

C. Multicentric Castleman's disease
Authorization of 12 months may be granted for the treatment of relapsed, refractory or progressive multicentric Castleman's disease.

D. Systemic light chain amyloidosis
Authorization of 12 months may be granted for the treatment of systemic light chain amyloidosis when the requested medication will be used in any of the following regimens:
1. In combination with dexamethasone

2. In combination with melphalan and dexamethasone
3. In combination with cyclophosphamide and dexamethasone
4. As a single agent
5. In combination with lenalidomide and dexamethasone
6. In combination with daratumumab and hyaluronidase-fihj, cyclophosphamide, and dexamethasone

E. Waldenström's macroglobulinemia/lymphoplasmacytic lymphoma
Authorization of 12 months may be granted for the treatment of Waldenström's macroglobulinemia/lymphoplasmacytic lymphoma when the requested medication will be used in any of the following regimens:
1. In combination with rituximab
2. In combination with dexamethasone
3. In combination with rituximab and dexamethasone
4. As a single agent

F. Adult T-cell Leukemia/Lymphoma
Authorization of 12 months may be granted for the treatment of adult T-cell leukemia/lymphoma when the requested medication will be used as a single agent for subsequent therapy.

G. Antibody mediated rejection of solid organ
Authorization of 12 months may be granted for the treatment of antibody mediated rejection of solid organ.

H. Acute lymphoblastic leukemia
Authorization of 12 months may be granted for the treatment of relapsed or refractory acute lymphoblastic leukemia.

I. Follicular Lymphoma
Authorization of 12 months may be granted for the treatment of relapsed or refractory follicular lymphoma.

J. Kaposi's sarcoma
Authorization of 12 months may be granted for the treatment of relapsed or refractory Kaposi's sarcoma.

K. Hodgkin Lymphoma
Authorization of 12 months may be granted for the treatment of relapsed or refractory Hodgkin Lymphoma.

L. POEMS (polyneuropathy, organomegaly, endocrinopathy, monoclonal protein, skin changes) Syndrome
Authorization of 12 months may be granted for treatment of POEMS syndrome in combination with dexamethasone.

III. 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 all indications, dosing does not exceed 1.6 mg/m^2 per dose and does not require more than 7 doses per 30 day period.

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.

CVS/caremark

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POLICY Document for BOTOX (onabotulinumtoxin A)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, and overall, clinically appropriate use. This document provides specific information to both sections of the overall policy.

Section 1: Preferred Product
- Policy information specific to preferred medications

Section 2: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 1: Preferred Product

EXCEPTIONS CRITERIA
BOTULINUM TOXINS

PREFERRED PRODUCTS: BOTOX, DYSPORT AND XEOMIN

POLICY
This policy informs prescribers of preferred products and provides an exception process for targeted products through prior authorization.

I. PLAN DESIGN SUMMARY

This program applies to the botulinum toxins products specified in this policy. Coverage for targeted products is provided based on clinical circumstances that would exclude the use of the preferred product and may be based on previous use of a product. The coverage review process will ascertain situations where a clinical exception can be made. This program applies to all members requesting treatment with the targeted product.

Each referral is reviewed based on all utilization management (UM) programs implemented for the client.

Table. Botulinum Toxins

	Product(s)
Preferred*	• **Botox** (onabotulinumtoxinA) • **Dysport** (abobotulinumtoxinA) • **Xeomin** (incobotulinumtoxinA)
Targeted	• **Myobloc** (rimabotulinumtoxinB)

*: Medications considered formulary or preferred on your plan may still require a clinical prior authorization review.

II. EXCEPTION CRITERIA

This program applies to members requesting treatment for an indication that is FDA-approved for the preferred product.

Coverage for a targeted product is provided when ANY of the following criteria is met:
A. Member has a documented inadequate response or intolerable adverse event to all of the preferred products.
B. Member is requesting Myobloc for the treatment of chronic sialorrhea and has had a documented inadequate response or an intolerable adverse event to Xeomin.

CVS/caremark

Section 2: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

BOTOX (onabotulinumtoxin A)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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 overactive bladder with symptoms of urge urinary incontinence, urgency, and frequency, in adults who have an inadequate response to or are intolerant of an anticholinergic medication
2. Treatment of urinary incontinence due to detrusor overactivity associated with a neurologic condition (e.g., spinal cord injury, multiple sclerosis) in adults or pediatric patients 5 years of age or older who have an inadequate response to or are intolerant of an anticholinergic medication
3. Prophylaxis of headaches in adult patients with chronic migraine (≥15 days per month with headache lasting 4 hours a day or longer)
4. Treatment of spasticity in patients 2 years of age and older
5. Treatment of cervical dystonia in adults, to reduce the severity of abnormal head position and neck pain
6. Treatment of severe primary axillary hyperhidrosis that is inadequately managed with topical agents. Safety and effectiveness have not been established in patients under age 18.
7. Treatment of strabismus and blepharospasm associated with dystonia, including benign essential blepharospasm or VII nerve disorders in patients 12 years of age and older

B. Compendial Uses
1. Achalasia
2. Chronic anal fissures
3. Essential tremor
4. Excessive salivation (ptyalism)
5. Hemifacial spasm
6. Spasmodic dysphonia (laryngeal dystonia)
7. Oromandibular dystonia
8. Myofascial pain syndrome
9. Focal hand dystonia
10. Facial myokymia
11. Hirschsprung disease with internal sphincter achalasia
12. Orofacial tardive dyskinesia
13. Painful bruxism
14. Palatal myoclonus
15. First bite syndrome
16. Palmar or gustatory (Frey's syndrome) hyperhidrosis

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

II. PRESCRIBER SPECIALTIES

The medication must be prescribed by, or in consultation with one of the following:

A. Blepharospasm, Strabismus: neurologist or ophthalmologist
B. Overactive bladder, urinary incontinence: neurologist or urologist
C. Spasticity, cervical dystonia, hemifacial spasm, myofascial pain syndrome, focal hand dystonia, facial myokymia: neurologist, orthopedist or physiatrist
D. Hyperhidrosis: neurologist or dermatologist
E. Migraine prophylaxis, tremor, orofacial tardive dyskinesia: neurologist
F. Chronic anal fissures, achalasia, Hirschsprung disease: gastroenterologist, proctologist or colorectal surgeon
G. Excessive salivation, spasmodic dystonia, oromandibular dystonia, bruxism, palatal myoclonus: neurologist or otolaryngologist
H. First bite syndrome: neurologist or oncologist

III. EXCLUSIONS

Coverage will not be provided for cosmetic use.

IV. CRITERIA FOR INITIAL APPROVAL

A. Blepharospasm

Authorization of 12 months may be granted for treatment of blepharospasm when all of the following are met:

1. Member is 12 years of age or older
2. Member is diagnosed with blepharospasm including blepharospasm associated with dystonia, benign essential blepharospasm or VII nerve disorder.

B. Cervical dystonia

Authorization of 12 months may be granted for the treatment of adults with cervical dystonia (e.g., torticollis) when all of the following are met:

1. There is abnormal placement of the head with limited range of motion in the neck
2. Member is 18 year of age and older.

C. Chronic migraine prophylaxis

Authorization of 6 months (two injection cycles) may be granted for treatment of chronic migraine prophylaxis when all of the following criteria are met:

1. Member experiences headaches 15 days or more per month.
2. Member experiences headaches lasting 4 hours or longer on at least 8 days per month.
3. Member completed an adequate trial of (or has a contraindication to) two oral migraine preventative therapies coming from at least 2 of the following classes with a trial of each medication at least 60 days in duration:
   a. Antidepressants (e.g., amitriptyline, venlafaxine)
   b. Antiepileptic drugs (AEDs) (e.g., divalproex sodium, topiramate, valproate sodium)
   c. Beta-adrenergic blocking agents (e.g., metoprolol, propranolol, timolol, atenolol, nadolol)
4. Member has signs and symptoms consistent with chronic migraine diagnostic criteria as defined by the International Headache Society (IHS).
5. Member is 18 years of age or older

D. Overactive bladder with urinary incontinence

Authorization of 12 months may be granted for treatment of overactive bladder with urinary incontinence, urgency, and frequency when all of the following criteria are met:

1. The member has tried and failed behavioral therapy.
2. The member has had an inadequate response or experienced intolerance to two agents from either of the following classes:

   a. Anticholinergic medication (e.g., Vesicare [solifenacin], Enablex [darifenacin], Toviaz [fesoterodine], Detrol/Detrol LA [tolterodine], Sanctura/Sanctura XR [trospium], Ditropan XL [oxybutynin]).
   b. Beta-3 adrenergic agonist (e.g., Myrbetriq [miraberon], Gemtesa [vibegron]).
3. Member is 18 years of age or older.

E. Primary axillary, palmar, and gustatory (Frey's syndrome) hyperhidrosis

Authorization of 12 months may be granted for treatment of primary axillary, palmar, or gustatory (Frey's syndrome) hyperhidrosis when all of the following criteria are met:

1. Significant disruption of professional and/or social life has occurred because of excessive sweating; and
2. Topical aluminum chloride or other extra-strength antiperspirants are ineffective or result in a severe rash.
3. Member is 18 years of age or older.

F. Strabismus

Authorization of 12 months may be granted for treatment of strabismus when all of the following are met:

1. Strabismus interference with normal visual system development is likely to occur and spontaneous recovery is unlikely.
2. Member is 12 years of age or older.

Note: Strabismus repair is considered cosmetic in adults with uncorrected congenital strabismus and no binocular fusion.

G. Upper or lower limb spasticity

Authorization of 12 months may be granted for treatment of upper or lower limb spasticity when all of the following are met:

1. Member is 2 years of age or older
2. Member has a primary diagnosis of upper or lower limb spasticity or as a symptom of a condition causing limb spasticity (including focal spasticity or equinus gait due to cerebral palsy).

H. Urinary incontinence associated with a neurologic condition (e.g., spinal cord injury, multiple sclerosis)

Authorization of 12 months may be granted for treatment of urinary incontinence associated with a neurologic condition (e.g., spinal cord injury, multiple sclerosis) when all of the following criteria are met:

1. The member has tried and failed behavioral therapy
2. The member has had an inadequate response or experienced intolerance to one agent from either of the following classes:
   a. Anticholinergic medication (e.g., Vesicare [solifenacin], Enablex [darifenacin], Toviaz [fesoterodine], Detrol/Detrol LA [tolterodine], Sanctura/Sanctura XR [trospium], Ditropan XL [oxybutynin]).
   b. Beta-3 adrenergic agonist (e.g., Myrbetriq [miraberon]
3. Member is 5 years of age or older.

I. Achalasia

Authorization of 12 months may be granted for treatment of achalasia when the member has tried and failed or is a poor candidate for conventional therapy such as pneumatic dilation and surgical myotomy.

J. Chronic anal fissures

Authorization of 12 months may be granted for treatment of chronic anal fissures when the member has not responded to first line therapy such as topical calcium channel blockers or topical nitrates.

K. Essential tremor

Authorization of 12 months may be granted for treatment of essential tremor.

L. Excessive salivation

Authorization of 12 months may be granted for treatment of excessive salivation (chronic sialorrhea or ptyalism) when the member has been refractory to pharmacotherapy (e.g., anticholinergics).

M. Hemifacial Spasm
Authorization of 12 months may be granted for treatment of hemifacial spasm.

N. Spasmodic dysphonia (laryngeal dystonia)
Authorization of 12 months may be granted for treatment of spasmodic dysphonia (laryngeal dystonia).

O. Oromandibular dystonia
Authorization of 12 months may be granted for treatment of oromandibular dystonia.

P. Myofascial Pain Syndrome
Authorization of 12 months may be granted for treatment of myofascial pain syndrome when the member has tried and failed all of the following:
1. Physical therapy
2. Injection of local anesthetics into trigger points
3. Injection of corticosteroids into trigger points

Q. Focal hand dystonia
Authorization of 12 months may be granted for the treatment of focal hand dystonias.

R. Facial myokymia
Authorization of 12 months may be granted for the treatment of facial myokymia.

S. Hirschsprung disease with internal sphincter achalasia
Authorization of 12 months may be granted for the treatment of Hirschsprung's disease with internal sphincter achalasia following endorectal pull through and the member is refractory to laxative therapy.

T. Orofacial tardive dyskinesia
Authorization of 12 months may be granted for the treatment of orofacial tardive dyskinesia when conventional therapies have been tried and failed (e.g., benzodiazepines, clozapine, or tetrabenazine).

U. Painful bruxism
Authorization of 12 months may be granted for the treatment of painful bruxism when the member has had an inadequate response to a night guard and has had an inadequate response to pharmacologic therapy such as diazepam.

V. Palatal myoclonus
Authorization of 12 months may be granted for the treatment of palatal myoclonus when the member has disabling symptoms (e.g., intrusive clicking tinnitus) who had an inadequate response to clonazepam, lamotrigine, carbamazepine or valproate.

W. First bite syndrome
Authorization of 12 months may be granted for the treatment of first bite syndrome when the member has failed relief from analgesics, antidepressants or anticonvulsants.

V. CONTINUATION OF THERAPY

A. All members (including new members) requesting authorization for continuation of therapy for approvable conditions other than migraine prophylaxis must meet ALL initial authorization criteria and be experiencing benefit from therapy.

B. Authorization of 12 months may be granted for treatment of chronic migraine prophylaxis when the member has achieved or maintained a reduction in monthly headache frequency since starting therapy with Botox.

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**.**

Adults: Dosing should not exceed a cumulative dose of 400 units every 90 days
Pediatric (patients less than 18 years of age): Dosing should not exceed the lessor of 10 units/kg or 340 units every 90 days.

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POLICY Document for BRAFTOVI (encorafenib)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, and overall, clinically appropriate use. This document provides specific information to both sections of the overall policy.

Section 1: Clinical Criteria

- Policy information specific to the clinical appropriateness for the medication

Section 2: Oncology Clinical Policy

- Policy information specific to regimen review per NCCN Guidelines.

Section 1: Clinical Criteria

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:
   a. in combination with binimetinib (Mektovi), or
   b. 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.

Section 2: Oncology Clinical Policy

Oncology Clinical Policy

Program Description

The National Comprehensive Care Network® (NCCN®) is an alliance of leading cancer centers devoted to patient care, research and education dedicated to improving the quality, effectiveness and efficiency of cancer care so patients can live better lives.[1] It is comprised of oncology experts who convene regularly to establish the best treatments for patients. NCCN develops various resources for use by stakeholders in the health care delivery system. These resources include, but are not limited to, the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®), the NCCN Drugs & Biologics Compendium (NCCN Compendium®) and the NCCN Chemotherapy Order Templates (NCCN Templates®).

NCCN templates are based on NCCN Clinical Practice Guidelines and NCCN Compendium. The NCCN Compendium lists the appropriate drugs and biologics for specific cancers using U.S. Food and Drug Administration (FDA)-approved disease indications and specific NCCN panel recommendations. Each recommendation is supported by a level of evidence category.

NCCN Categories of Evidence and Consensus

Category 1: Based on high-level evidence, there is uniform NCCN consensus that the intervention is

appropriate.
Category 2A: Based on lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2B: Based on lower-level evidence, there is NCCN consensus that the intervention is appropriate.
Category 3: Based any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

Policy for Regimen Prior Authorization

A regimen prior authorization allows submission of a single prior authorization request for all oncology drugs or biologics within an NCCN template that require prior authorization.

This policy provides coverage of a regimen review when *all* of the following criteria are met:

a. Regimen prior authorization reviews, based on NCCN templates, are initiated through the provider portal: https://provider.carefirst.com/providers/home.page
b. If the prior authorization request is submitted via phone or fax, each drug or biologic will need to be submitted and reviewed as a separate prior authorization request for review with drug-specific criteria.
c. 2. The prior authorization review is requested for an oncology drug or biologic that requires prior authorization on the medical benefit.
d. The indication is for a cancer that is eligible for regimen review. Currently, the cancer types in scope for regimen review include breast, lung, colon and rectal cancer.
e. The member is eligible for regimen review.

In addition, the following criteria must be met for approval:

a. The requested regimen for the drug(s) or biologic(s) and indication is consistent with an NCCN recommendation with a level of evidence category of 1 or 2A.
b. The NCCN template must be accepted by the provider without modification.

Authorizations may be granted for 12 months.
Further review may be indicated where the above criteria are not met.

Continuation of Therapy

To submit a request for continuation of therapy, a new regimen prior authorization review must be requested. Upon template selection, the template must be modified to include the appropriate therapies being used for maintenance treatment. The regimen request will be submitted for further review.

Dosage and Administration

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

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3. National Comprehensive Cancer Network. NCCN Guidelines website. http://www.nccn.org/professionals/physician_gls/f_guidelines.asp, accessed September 16, 2019. *(Note: An account may be required.)*
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Reference number(s)
4513-A

SPECIALTY GUIDELINE MANAGEMENT

BREYANZI (lisocabtagene maraleucel)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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
BREYANZI is a CD19-directed genetically modified autologous T-cell immunotherapy indicated for the treatment of adult patients with large B-cell lymphoma, including diffuse large B-cell lymphoma (DLBCL) not otherwise specified (NOS) (including DLBCL arising from indolent lymphoma), high grade B-cell lymphoma, primary mediastinal large B-cell lymphoma, and follicular lymphoma grade 3B who have:
1. Refractory disease to first-line chemoimmunotherapy or relapse within 12 months of first-line chemoimmunotherapy; or
2. Refractory disease to first-line chemoimmunotherapy or relapse after first-line chemoimmunotherapy and are not eligible for hematopoietic stem cell transplantation (HSCT) due to comorbidities or age; or
3. Relapsed or refractory disease after two or more lines of systemic therapy

Limitations of use: BREYANZI is not indicated for the treatment of patients with primary central nervous system lymphoma.

B. Compendial Uses
1. Human immunodeficiency virus (HIV)-related B-cell lymphomas (including HIV-related diffuse large B-cell lymphoma, primary effusion lymphoma, and human herpesvirus 8 (HHV8)-positive diffuse large B-cell lymphoma, not otherwise specified)
2. Monomorphic post-transplant lymphoproliferative disorder (B-cell type)
3. Pediatric primary mediastinal large B-cell lymphoma

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 notes, medical record documentation or claims history supporting previous lines of therapy.

III. EXCLUSIONS

Coverage will not be provided for members with any of the following exclusions:
A. Primary central nervous system lymphoma
B. Previous treatment course with the requested medication or another CD19-directed chimeric antigen receptor (CAR) T-cell therapy.
C. ECOG performance status greater than or equal to 3 (member is not ambulatory and not capable of all self-care, confined to bed or chair more than 50% of waking hours)
D. Inadequate and unstable kidney, liver, pulmonary or cardiac function

E. Active hepatitis B, active hepatitis C or any active uncontrolled infection
F. Active graft versus host disease
G. Active inflammatory disorder

IV. CRITERIA FOR INITIAL APPROVAL

A. Adult Large B-cell Lymphomas

Authorization of 3 months may be granted for treatment of B-cell lymphomas in members 18 years of age or older when either of the following criteria are met:

1. The member has received prior treatment with two or more lines of systemic therapy and has any of the following B-cell lymphoma subtypes:
   i. Diffuse large B-cell lymphoma (DLBCL) [including DLBCL NOS, follicular lymphoma grade 3, DLBCL arising from indolent lymphomas]
   ii. 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)
   iii. Primary mediastinal large B-cell lymphoma
   iv. HIV-related B-cell lymphomas (including HIV-related diffuse large B-cell lymphoma, primary effusion lymphoma, and human herpesvirus 8 (HHV8)-positive diffuse large B-cell lymphoma, not otherwise specified)
   v. Monomorphic post-transplant lymphoproliferative disorder (B-cell type)
2. The member has received prior treatment with first-line chemoimmunotherapy and has any of the following B-cell lymphoma subtypes:
   i. Diffuse large B-cell lymphoma (DLBCL) [including DLBCL NOS and follicular lymphoma grade 3]
   ii. 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)
   iii. Primary mediastinal large B-cell lymphoma
   iv. HIV-related B-cell lymphomas (including HIV-related diffuse large B-cell lymphoma, primary effusion lymphoma, and human herpesvirus 8 (HHV8)-positive diffuse large B-cell lymphoma, not otherwise specified)
   v. Monomorphic post-transplant lymphoproliferative disorder (B-cell type)

B. Pediatric Primary Mediastinal Large B-cell Lymphoma

Authorization of 3 months may be granted for treatment of primary mediastinal large B-cell lymphoma in members less than 18 years of age when the member has received prior therapy with at least two prior chemoimmunotherapy regimens and achieved partial response.

V. REFERENCES

1. Breyanzi [package insert]. Bothell, WA: Juno Therapeutics Inc.; July 2022.
2. The NCCN Drugs & Biologics Compendium® © 2023 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed April 13, 2023.
3. The NCCN Clinical Practice Guidelines in Oncology® B-Cell Lymphomas (Version 2.2023). © 2023 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed April 13, 2023.
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Reference number
1831-A

SPECIALTY GUIDELINE MANAGEMENT

BRINEURA (cerliponase 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
Brineura is indicated to slow the loss of ambulation in symptomatic pediatric patients 3 years of age and older with late infantile neuronal ceroid lipofuscinosis type 2 (CLN2), also known as tripeptidyl peptidase 1 (TPP1) 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: tripeptidyl peptidase 1 (TPP1) enzyme assay or genetic testing results supporting diagnosis.

III. CRITERIA FOR INITIAL APPROVAL

Late infantile neuronal ceroid lipofuscinosis type 2 (CLN2)
Authorization of 12 months may be granted for members with CLN2 when all of the following criteria are met:
1. Diagnosis of CLN2 was confirmed by enzyme assay demonstrating a deficiency of tripeptidyl peptidase 1 (TPP1) enzyme activity or by genetic testing; and
2. Member is 3 years of age or older; and
3. Brineura will be administered by, or under the direction of a physician knowledgeable in intraventricular administration; and
4. Dosage of Brineura will not exceed 300 mg once every other week; and
5. Member does not have acute intraventricular access device-related complications (e.g., leakage, device failure, or device-related infection) or a ventriculoperitoneal shunt.

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 following criteria are met:
A. Member has experienced no loss of ambulation or a slowed loss of ambulation from baseline; and
B. Member does not have acute intraventricular access device-related complications (e.g., leakage, device failure, or device-related infection) or ventriculoperitoneal shunts.

V. REFERENCES

1. Brineura [package insert]. Novato, CA: BioMarin Pharmaceutical, Inc.; March 2020.
2. Fietz M, AlSayed M, Burke, D, et al. Diagnosis of neuronal ceroid lipofuscinosis type 2 (CLN2 disease): Expert recommendations for early detection and laboratory diagnosis. *Molecular Genetics and Metabolism*. 2016 (11): 160-167.

POLICY Document for BRIUMVI
(ublituximab-xiiy)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, lower cost site of care and overall, clinically appropriate use. This document provides specific information to each of the three sections of the overall policy.

Section 1: Site of Care
- Policy information specific to site of care (outpatient, hospital outpatient, home infusion)

Section 2: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 1: Site of Care

CareFirst Site of Care Criteria
Administration of Intravenous Briumvi

POLICY

I. CRITERIA FOR APPROVAL FOR ADMINISTRATION IN OUTPATIENT-HOSPITAL SETTING

This policy provides coverage for administration of Briumvi in an outpatient hospital setting for up to 45 days when a member is new to therapy or is reinitiating therapy after not being on therapy for at least 6 months.

This policy provides coverage for administration of Briumvi in an outpatient hospital setting for a longer course of treatment when ANY of the following criteria are met:

A. The member has experienced an adverse reaction that did not respond to conventional interventions (e.g., acetaminophen, steroids, diphenhydramine, fluids, other pre-medications medications or slowing of infusion rate) or a severe adverse event (anaphylaxis, anaphylactoid reactions, myocardial infarction, thromboembolism, or seizures) during or immediately after an infusion.
B. The member is medically unstable (e.g., respiratory, cardiovascular, or renal conditions).
C. The member has severe venous access issues that require the use of a special interventions only available in the outpatient hospital setting.
D. The member has significant behavioral issues and/or physical or cognitive impairment that would impact the safety of the infusion therapy AND the patient does not have access to a caregiver.
E. The member is less than 14 years of age.

For situations where administration of the Briumvi does not meet the criteria for outpatient hospital infusion, coverage for the Briumvi is provided when administered in alternative sites such as physician office, home infusion or ambulatory care.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the site of care prior authorization review (where applicable):

A. Medical records supporting the member has experienced an adverse reaction that did not respond to conventional interventions or a severe adverse event during or immediately after an infusion
B. Medical records supporting the member is medically unstable
C. Medical records supporting the member has severe venous access issues that require specialized interventions only available in the outpatient hospital setting
D. Medical records supporting the member has behavioral issues and/or physical or cognitive impairment and no access to a caregiver

Section 2: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

BRIUMVI (ublituximab-xiiy)

POLICY

III. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Briumvi is indicated for the treatment of relapsing forms of multiple sclerosis, 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.

IV. PRESCRIBER SPECIALTIES

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

V. 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.

VI. CONTINUATION OF THERAPY

For all indications: Authorization of 12 months may be granted for members who are experiencing disease stability or improvement while receiving Briumvi.

VII. OTHER

A. Members will not use Briumvi 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.

REFERENCES

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SECTION 2

1. Briumvi [package insert]. Morrisville, NC: TG Therapeutics, Inc; December 2022.

Reference number(s)
4517-A

SPECIALTY GUIDELINE MANAGEMENT

CABENUVA (cabotegravir extended-release injectable suspension; rilpivirine extended-release 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 Indication
Cabenuva is indicated as a complete regimen for the treatment of human immunodeficiency virus type 1 (HIV-1) infection in adults and adolescents 12 years of age and older and weighing at least 35 kg to replace the current antiretroviral regimen in those who are virologically suppressed (HIV-1 RNA less than 50 copies per mL) on a stable antiretroviral regimen with no history of treatment failure and with no known or suspected resistance to either cabotegravir or rilpivirine.

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 initial requests, current plasma HIV-1 RNA level (viral load)

III. CRITERIA FOR INITIAL APPROVAL

Human immunodeficiency virus type 1 (HIV-1) infection
Authorization of 12 months may be granted for treatment of human immunodeficiency virus type 1 (HIV-1) infection when all of the following criteria are met:
A. Member is currently receiving a stable antiretroviral regimen.
B. Member is virologically suppressed on the current antiretroviral regimen with HIV-1 RNA less than 50 copies per mL.
C. Member has no history of treatment failure.
D. Member has no known or suspected resistance to either cabotegravir or rilpivirine.

IV. 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 not experienced a virologic failure while on the requested drug, defined as two consecutive plasma HIV-1 RNA levels greater than or equal to 200 copies per mL.

V. REFERENCES

1. Cabenuva [package insert]. Research Triangle Park, NC: ViiV Healthcare; April 2022.
2. 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/sites/default/files/guidelines/documents/AdultandAdolescentGL.pdf. Accessed November 4, 2021.

Reference number(s)
2871-A

SPECIALTY GUIDELINE MANAGEMENT

CABLIVI (caplacizumab-yhdp)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Cablivi is indicated for the treatment of adult patients with acquired thrombotic thrombocytopenic purpura (aTTP), in combination with plasma exchange and immunosuppressive 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:
For continuation of therapy: medical record documentation of signs of persistent underlying aTTP

III. CRITERIA FOR INITIAL APPROVAL

Acquired thrombotic thrombocytopenic purpura (aTTP)
Authorization of 30 days may be granted for treatment of acquired thrombotic thrombocytopenic purpura (aTTP), after the plasma exchange period in the inpatient setting, when all of the following criteria are met:
A. The member received the requested medication with plasma exchange.
B. The requested medication will be given in combination with immunosuppressive therapy.
C. The member will not receive the requested medication beyond 30 days from the cessation of plasma exchange unless the member has documented persistent aTTP.
D. The member has not experienced more than 2 recurrences of aTTP while on the requested medication. (A recurrence is when the member needs to reinitiate plasma exchange. A 28-day extension of therapy does not count as a recurrence.)

IV. CONTINUATION OF THERAPY

Authorization of 28 days may be granted for continuation of therapy for aTTP when all of the following criteria are met:
A. The request for continuation of therapy is for extension of therapy after the initial course of the requested medication (initial course: treatment with the requested medication during and 30 days after plasma exchange).
B. The member has either of the following documented signs of persistent underlying aTTP:
   1. ADAMTS13 activity level less than 10% or

2. All of the following:
    a. Microangiopathic hemolytic anemia (MAHA) documented by the presence of schistocytes on peripheral smear
    b. Thrombocytopenia (platelet count below normal per laboratory reference range), and
    c. Elevated lactate dehydrogenase (LDH) level (LDH level above normal per laboratory reference range)

C. The requested medication will be given in combination with immunosuppressive therapy.
D. The member has not received a prior 28-day extension of therapy after the initial course of the requested medication for this course of treatment.
E. The member has not experienced more than 2 recurrences of aTTP while on the requested medication. (A recurrence is when the member needs to reinitiate plasma exchange. A 28-day extension of therapy does not count as a recurrence.)

V. REFERENCES

1. Cablivi [package insert]. Cambridge, MA: Genzyme Corporation; February 2022.
2. Scully M, Cataland SR, Peyvandi F; et al. Caplacizumab treatment for acquired thrombotic thrombocytopenic purpura. *N Engl J Med*. 2019;380(4):335-346.
3. Sadler JE. Pathophysiology of thrombotic thrombocytopenic purpura. *Blood.* 2017;130(10):1181-1188.
4. Scully M, Cataland S, Coppo P, et al. Consensus on the standardization of terminology in thrombotic thrombocytopenic purpura and related thrombotic microantiopathies. *J Thromb Haemost*. 2017; 15(2):312-322.
5. Scully M, Hunt BJ, Benjamin S, et al. Guidelines on the diagnosis and management of thrombotic thrombocytopenic purpura and other thrombotic microangiopathies. *Br J Haematol*. 2012;158(3)323-335.
6. Westwood JP, Thomas M, Alwan F, et al. Rituximab prophylaxis to prevent thrombotic thrombocytopenic purpura relapse: outcome and evaluation of dosing regimens. *Blood Adv.* 2017; 1(15):1159-1166.

POLICY Document for CAMCEVI (leuprolide mesylate)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, and overall, clinically appropriate use. This document provides specific information to both sections of the overall policy.

Section 1: Preferred Product
- Policy information specific to preferred medications

Section 2: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 3: Oncology Clinical Policy
- Policy information specific to regimen review per NCCN Guidelines.

Section 1: Preferred Product

EXCEPTIONS CRITERIA
GONADOTROPIN RELEASING HORMONE AGONISTS

PREFERRED PRODUCT: ELIGARD

POLICY
This policy informs prescribers of preferred products and provides an exception process for targeted products through prior authorization.

I. PLAN DESIGN SUMMARY

This program applies to the gonadotropin releasing hormone agonist products specified in this policy. Coverage for targeted products is provided based on clinical circumstances that would exclude the use of the preferred product and may be based on previous use of a product. The coverage review process will ascertain situations where a clinical exception can be made. This program applies to all members requesting treatment with Camcevi and Lupron Depot. This program also applies to members who are new to treatment with Firmagon, Trelstar, or Zoladex for the first time.

Each referral is reviewed based on all utilization management (UM) programs implemented for the client.

Table. Gonadotropin releasing hormone agonists

	Product(s)
Preferred*	• **Eligard** (leuprolide acetate)
Targeted	• **Camcevi** (leuprolide mesylate) • **Firmagon** (degarelix) • **Lupron Depot** (leuprolide acetate for depot suspension) • **Trelstar** (triptorelin) • **Zoladex** (goserelin acetate)

*: Medications considered formulary or preferred on your plan may still require a clinical prior authorization review.

II. EXCEPTION CRITERIA

This program applies to members requesting treatment for prostate cancer.

A. Firmagon, Trelstar, and Zoladex

Coverage for the Firmagon, Trelstar, and Zoladex is provided when any of the following criteria is met:

1. Member is currently receiving treatment with the requested targeted product, excluding when the requested targeted product is obtained as samples or via manufacturer's patient assistance programs.
2. Member has a documented hypersensitivity to the preferred product.

B. Camcevi and Lupron Depot

Coverage for Camcevi and Lupron Depot is provided when the member has a documented hypersensitivity to the preferred product.

Section 2: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

CAMCEVI (leuprolide mesylate)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Camcevi 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.

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 clinical benefit to therapy (e.g., serum testosterone less than 50 ng/dL) and who have not experienced an unacceptable toxicity.

Section 3: Oncology Clinical Policy

CVS/caremark

PROGRAM DESCRIPTION

The National Comprehensive Care Network® (NCCN®) is an alliance of leading cancer centers devoted to patient care, research and education dedicated to improving the quality, effectiveness, and efficiency of cancer care so patients can live better lives.[1] It is comprised of oncology experts who convene regularly to establish the best treatments for patients. NCCN develops various resources for use by stakeholders in the health care delivery system. These resources include, but are not limited to, the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®), the NCCN Drugs & Biologics Compendium (NCCN Compendium®) and the NCCN Chemotherapy Order Templates (NCCN Templates®).

NCCN Templates® are based on NCCN Guidelines® and NCCN Compendium®. The NCCN Compendium lists the appropriate drugs and biologics as treatment options for specific cancers using U.S. Food and Drug Administration (FDA)-approved disease indications and specific NCCN panel recommendations. Each recommendation is supported by a level of evidence category.

NCCN Categories of Evidence and Consensus[2]

- Category 1: Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
- Category 2A: Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
- Category 2B: Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.
- Category 3: Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

POLICY

Policy for Regimen Prior Authorization

A regimen prior authorization allows submission of a single prior authorization request for all oncology drugs or biologics within an NCCN template that require prior authorization.

PROCEDURE

This policy provides coverage of a regimen review when all of the following criteria are met:

1. Regimen prior authorization reviews, based on NCCN templates, are initiated through the provider portal.
   - If the prior authorization request is submitted via phone or fax, each drug or biologic will need to be submitted and reviewed as a separate prior authorization request for review with drug-specific criteria.
2. The prior authorization review is requested for an oncology drug or biologic.
3. The member is eligible for regimen review.
4. The indication is for a cancer that is eligible for regimen review. Currently, the cancer types in scope for regimen review include the following:
   - Ampullary Adenocarcinoma
   - Anal Carcinoma
   - B-Cell Lymphomas
   - Basal Cell Skin Cancer
   - Biliary Tract Cancers
   - Bone Cancer
   - Breast Cancer
   - Bladder Cancer
   - Central Nervous System Cancers
   - Cervical Cancer
   - Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma
   - Chronic Myeloid leukemia

- Colon Cancer
- Dermatofibrosarcoma Protuberans
- Esophageal Cancer
- Gastric Cancer
- Gastrointestinal Stromal Tumors
- Gestational Trophoblastic Neoplasms
- Hairy Cell Leukemia
- Head and Neck Cancers
- Hodgkin Lymphoma
- Hepatocellular Carcinoma
- Kaposi Sarcoma
- Kidney Cancer
- Melanoma: Cutaneous
- Melanoma: Uveal
- Merkel Cell Carcinoma
- Mesothelioma: Peritoneal
- Mesothelioma: Pleural
- Myelodysplastic Syndromes
- Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Gene Fusions
- Myeloproliferative Neoplasms
- Neuroendocrine and Adrenal Tumors
- Non-Small Cell Lung Cancer
- Occult Primary
- Ovarian Cancer
- Pancreatic Cancer
- Penile Cancer
- Prostate Cancer
- Rectal Cancer
- Small Bowl Adenocarcinoma
- Small Cell Lung Cancer
- Soft Tissue Sarcoma
- Squamous Cell Skin Cancer
- Systemic Mastocytosis
- Systemic Light Chain Amyloidosis
- Testicular Cancer
- Thymomas and Thymic Carcinomas
- Thyroid Carcinoma
- Uterine Neoplasms
- Vulvar Cancer
- Waldenström Macroglobulinemia / Lymphoplasmacytic Lymphoma

In addition, the following criteria must be met for approval:

1. The requested regimen for the drug(s) or biologic(s) and indication is consistent with an NCCN recommendation with a level of evidence category of 1 or 2A.
2. The NCCN template must be accepted by the provider without modification.

Further review may be indicated when the above criteria are not met.

Authorizations may be granted for 12 months or as medically required, based on the member's condition and provider's assessment.

Supportive Care: Myeloid Growth Factor Therapy

Granulocyte colony stimulating factors are recommended for primary prophylaxis based on the febrile neutropenia risk of the chemotherapy regimen. Febrile neutropenia risk levels vary by NCCN Chemotherapy Order template and are listed at the top of the template. Regimens associated with a high or intermediate risk of febrile neutropenia may include a

granulocyte colony stimulating factor as part of the prior authorization.

Continuation of Therapy
To submit a request for continuation of therapy, a new regimen prior authorization review must be requested. Upon template selection, the template must be modified to include the appropriate therapies being used for maintenance treatment. The regimen request will be submitted for further review.

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

REFERENCES:

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2. Camcevi [package insert]. Durham, NC: Accord BioPharma Inc.; May 2021.
3. Firmagon [package insert]. Parsippany, NJ: Ferring Pharmaceuticals, Inc.; February 2020.
4. Lupron Depot [package insert]. North Chicago, IL: AbbVie Inc.; April 2022.
5. Trelstar [package insert]. Ewing, NJ: Verity Pharmaceuticals Inc.; December 2021.
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Reference number(s)
5268-A

SPECIALTY GUIDELINE MANAGEMENT

CAMZYOS (mavacamten)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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

Camzyos is indicated for the treatment of adults with symptomatic New York Heart Association (NYHA) class II-III obstructive hypertrophic cardiomyopathy to improve functional capacity and symptoms.

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. Imaging reports, chart notes, or medical record documentation supporting left ventricular wall thickness.
   2. Laboratory results, chart notes, or medical record documentation of familial hypertrophic cardiomyopathy or a positive genetic test (e.g., MYH7, MYBPC3, TNNI3, TNNT2, TPM1, MYL2, MYL3, ACTC1 gene variants) (if applicable).
   3. Chart notes or medical record documentation supporting baseline left ventricular ejection fraction (LVEF) ≥ 55% and baseline Valsalva left ventricular outflow tract (LVOT) peak gradient ≥ 50 mmHg.

B. Continuation requests:
   1. Chart notes or medical record documentation supporting a positive clinical response to therapy (e.g., increase in peak oxygen consumption [pVO2], NYHA class reduction).
   2. Chart notes or medical record documentation supporting left ventricular ejection fraction (LVEF) ≥ 50%.

III. CRITERIA FOR INITIAL APPROVAL

Obstructive Hypertrophic cardiomyopathy

Authorization of 3 months may be granted for treatment of obstructive hypertrophic cardiomyopathy when all of the following criteria are met:

A. Member has one of the following:
   1. Left ventricular wall thickness of greater than or equal to 15 mm anywhere in the left ventricle.
   2. Left ventricular wall thickness of greater than or equal to 13 mm anywhere in the left ventricle in members with familial hypertrophic cardiomyopathy or a positive genetic test (e.g., MYH7, MYBPC3, TNNI3, TNNT2, TPM1, MYL2, MYL3, ACTC1 gene variants).

B. Member has NYHA functional class II to class III symptoms (see Appendix).

C. Member must have a baseline left ventricular ejection fraction (LVEF) ≥ 55% and baseline Valsalva left ventricular outflow tract (LVOT) peak gradient ≥ 50 mmHg.

D. Member has experienced an inadequate response to a beta-adrenergic antagonist (e.g., atenolol, metoprolol) or non-dihydropyridine calcium channel blocker (diltiazem, verapamil) at maximally tolerated dose, or has an intolerance or contraindication to both therapies.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for obstructive hypertrophic cardiomyopathy when both of the following criteria are met:

A. The member achieved or maintained a positive clinical response to therapy (e.g., increase in pVO2, NYHA class reduction).
B. Left ventricular ejection fraction (LVEF) ≥ 50%.

V. APPENDIX

New York Heart Association (NYHA) Functional Classification

NYHA Grading	
Class I	No limitations of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, dyspnea (shortness of breath)
Class II	Slight limitation of physical activity. Comfortable at rest. Ordinary physical activity results in fatigue, palpitation, dyspnea (shortness of breath).
Class III	Marked limitation of physical activity. Comfortable at rest. Less than ordinary activity causes fatigue, palpitation, or dyspnea.
Class IV	Unable to carry on any physical activity without discomfort. Symptoms of heart failure at rest. If any physical activity is undertaken, discomfort increases.

VI. REFERENCES

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Reference number(s)
5256-A

SPECIALTY GUIDELINE MANAGEMENT

CARVYKTI (ciltacabtagene autoleucel)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Carvykti is indicated for the treatment of adult patients with relapsed or refractory multiple myeloma after four or more prior lines of therapy including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody.

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 notes, medical record documentation or claims history supporting previous lines of therapy

III. CRITERIA FOR INITIAL APPROVAL

Multiple Myeloma
Authorization of 3 months may be granted for treatment of relapsed or refractory multiple myeloma in members 18 years of age and older when all of the following criteria are met:

A. The member has received prior treatment with at least four prior lines of therapy, including at least one drug from each of the following categories:
    1. Immunomodulatory agent
    2. Proteasome inhibitor
    3. Anti-CD38 monoclonal antibody
B. The member has not received previous treatment with the requested medication, another CAR-T therapy directed at any target, or any therapy that is targeted to B-cell maturation antigen (BCMA).
C. The member has an ECOG performance status of 0 to 2.
D. The member has adequate and stable kidney, liver, pulmonary and cardiac function.
E. The member does not have known active or prior history of central nervous system (CNS) involvement, including CNS multiple myeloma.
F. The member does not have clinically significant active infection.
G. The member does not have active graft versus host disease.
H. The member does not have an active inflammatory disorder.

IV. REFERENCES

1. Carvykti [package insert]. Horsham, PA: Janssen Biotech, Inc.; March 2022.

2. Berdeja JG, Madduri D, Usmani SZ, et al. Ciltacabtagene autoleucel, a B-cell maturation antigen-directed chimeric antigen receptor T-cell therapy in patients with relapsed or refractory multiple myeloma (CARTITUDE-1): a phase 1b/2 open-label study. Lancet. 2021 Jul 24;398(10297):314-324.

POLICY Document for CEREZYME (imiglucerase)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, and overall, clinically appropriate use. This document provides specific information to both sections of the overall policy.

Section 1: Preferred Product
- Policy information specific to preferred medications

Section 2: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 1: Preferred Product

EXCEPTIONS CRITERIA
GAUCHER DISEASE AGENTS

PREFERRED PRODUCT: ELELYSO

POLICY

This policy informs prescribers of preferred products and provides an exception process for targeted products through prior authorization.

I. PLAN DESIGN SUMMARY

This program applies to the Gaucher disease products specified in this policy. Coverage for targeted products is provided based on clinical circumstances that would exclude the use of the preferred product and may be based on previous use of a product. The coverage review process will ascertain situations where a clinical exception can be made. This program applies to all members requesting treatment with a targeted product.

Each referral is reviewed based on all utilization management (UM) programs implemented for the client.

Table. Gaucher Disease Agents

	Product(s)
Preferred*	• **Elelyso** (taliglucerase alfa)
Targeted	• **Cerezyme** (imiglucerase) • **VPRIV** (velaglucerase alfa)

*: Medications considered formulary or preferred on your plan may still require a clinical prior authorization review.

II. EXCEPTION CRITERIA

This program applies to members requesting treatment for an indication that is FDA-approved for the preferred product.

Coverage for a targeted product is provided when the member has had a documented inadequate response or an intolerable adverse event with the preferred product.

CVS/caremark

Section 2: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

CEREZYME (imiglucerase)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Cerezyme is indicated for treatment of adults and pediatric patients 2 years of age and older with Type 1 Gaucher disease that results in one or more of the following conditions: anemia, thrombocytopenia, bone disease, and/or hepatomegaly or splenomegaly.

B. Compendial Uses
1. Gaucher disease type 2
2. Gaucher disease type 3

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: beta-glucocerebrosidase enzyme assay or genetic testing results supporting diagnosis.

III. CRITERIA FOR INITIAL APPROVAL

A. Gaucher disease type 1
Authorization of 12 months may be granted for treatment of Gaucher disease type 1 when the diagnosis of Gaucher disease was confirmed by enzyme assay demonstrating a deficiency of beta-glucocerebrosidase (glucosidase) enzyme activity or by genetic testing.

B. Gaucher disease type 2
Authorization of 12 months may be granted for treatment of Gaucher disease type 2 when the diagnosis of Gaucher disease was confirmed by enzyme assay demonstrating a deficiency of beta-glucocerebrosidase (glucosidase) enzyme activity or by genetic testing.

C. Gaucher disease type 3
Authorization of 12 months may be granted for treatment of Gaucher disease type 3 when the diagnosis of Gaucher disease was confirmed by enzyme assay demonstrating a deficiency of beta-glucocerebrosidase (glucosidase) enzyme activity or by genetic testing.

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.

CVS/caremark

REFERENCES:

SECTION 1

1. Elelyso [package insert]. New York, NY: Pfizer, Inc; July 2021.
2. Cerezyme [package insert]. Cambridge, MA: Genzyme Corporation; December 2021.
3. VPRIV [package insert]. Lexington, MA: Shire Human Genetic Therapies, Inc.; September 2021.

SECTION 2

1. Cerezyme [package insert]. Cambridge, MA: Genzyme Corporation; December 2021.
2. Altarescu G, Hill S, Wiggs E, et al. The efficacy of enzyme replacement therapy in patients with chronic neuronopathic Gaucher's disease. *J Pediatr.* 2001;138:539-547.
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POLICY Document for CIMZIA (certolizumab pegol)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, and overall, clinically appropriate use. This document provides specific information to both sections of the overall policy.

Section 1: Preferred Product
- Policy information specific to preferred medications

Section 2: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 1: Preferred Product

EXCEPTIONS CRITERIA
AUTOIMMUNE CONDITIONS

PREFERRED PRODUCTS: ENTYVIO, ILUMYA, SIMPONI ARIA AND STELARA IV

POLICY
This policy informs prescribers of preferred products and provides an exception process for targeted products through prior authorization.

I. PLAN DESIGN SUMMARY

This program applies to the autoimmune drug products specified in this policy. Coverage for targeted products is provided based on clinical circumstances that would exclude the use of the preferred product and may be based on previous use of a product. The coverage review process will ascertain situations where a clinical exception can be made. This program applies to all members requesting treatment with Cimzia vial. For plaque psoriasis, this program applies to all members requesting treatment with a targeted product. For all other indications, this program applies to all members who are new to treatment with a targeted product for the first time.

Each referral is reviewed based on all utilization management (UM) programs implemented for the client.

Table. Drugs for autoimmune conditions

	Product(s)
Preferred*	• **Entyvio** (vedolizumab) • **Ilumya** (tildrakizumab-asmn) • **Simponi Aria** (golimumab, intravenous) • **Stelara IV** (ustekinumab)**
Targeted	• **Actemra** (tocilizumab) • **Cimzia** (certolizumab pegol) • **Orencia** (abatacept)

Abbreviation: IV = intravenous
*: Medications considered formulary or preferred on your plan may still require a clinical prior authorization review

**Stelara IV is indicated for a one time induction dose for Crohn's disease and ulcerative colitis.

II. EXCEPTION CRITERIA

This program applies to members requesting treatment for an indication that is FDA-approved for the preferred products.

Coverage for a targeted product is provided when any of the following criteria is met:

A. For Cimzia, when any of the following criteria is met:
   1. For prefilled syringe request, member is currently receiving treatment with Cimzia prefilled syringes excluding when the requested targeted product is obtained as samples or via manufacturer's patient assistance programs, unless the request is for plaque psoriasis.
   2. Member has a documented inadequate response or intolerable adverse event with all of the preferred products (Entyvio, Ilumya, Simponi Aria, and Stelara IV) where the product's indications overlap.
   3. Member is currently pregnant or breastfeeding.

B. For all other targeted products, when any of the following criteria is met:
   1. Member is currently receiving treatment with the requested targeted product, excluding when the requested targeted product is obtained as samples or via manufacturer's patient assistance programs.
   2. Member has a documented inadequate response or intolerable adverse event with all of the preferred products (Entyvio, Ilumya, Simponi Aria, and Stelara IV) where the product's indications overlap, unless there is a documented clinical reason to avoid TNF inhibitors (see Appendix).

III. Appendix: Clinical reasons to avoid TNF inhibitors

- History of demyelinating disorder
- History of congestive heart failure
- History of hepatitis B virus infection
- Autoantibody formation/lupus-like syndrome
- History or risk of lymphoma or other malignancy
- History of being a primary non-responder to a TNF inhibitor

Section 2: Clinical Criteria

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:
      1. Member has had an inadequate response to methotrexate, leflunomide, or another conventional synthetic drug (e.g., sulfasalazine) administered at an adequate dose and duration.
      2. Member has an intolerance or contraindication to methotrexate or leflunomide (see Appendix), or another conventional synthetic drug (e.g., sulfasalazine).
      3. 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

REFERENCES:

SECTION 1

1. Actemra [package insert]. South San Francisco, CA: Genentech, Inc.; June 2022.
2. Cimzia [package insert]. Smyrna, GA: UCB, Inc.; September 2019.
3. Entyvio [package insert]. Lexington, MA: Takeda Pharmaceuticals U.S.A., Inc.; June 2022.
4. Ilumya [package insert]. Cranbury, NJ: Sun Pharma Global FZE; July 2020.
5. Orencia [package insert]. Princeton, NJ: Bristol-Meyers Squibb Company; December 2021.
6. Simponi Aria [package insert]. Horsham, PA: Janssen Biotech, Inc.; February 2021.

7. Stelara [package insert]. Horsham, PA: Janssen Biotech, Inc.; August 2022.

SECTION 2

1. Cimzia [package insert]. Smyrna, GA: UCB, Inc.; December 2022.
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POLICY Document for CINQAIR (reslizumab)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, lower cost site of care and overall, clinically appropriate use. This document provides specific information to each of the three sections of the overall policy.

Section 1: Preferred Product
- Policy information specific to preferred medications

Section 2: Site of Care
- Policy information specific to site of care (outpatient, hospital outpatient, home infusion)

Section 3: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 1: Preferred Product

EXCEPTIONS CRITERIA
ASTHMA

PREFERRED PRODUCTS: DUPIXENT, FASENRA, NUCALA, TEZSPIRE, XOLAIR

POLICY
This policy informs prescribers of preferred products and provides an exception process for targeted products through prior authorization.

I. PLAN DESIGN SUMMARY

This program applies to the asthma products specified in this policy. Coverage for targeted products is provided based on clinical circumstances that would exclude the use of the preferred product and may be based on previous use of a product. The coverage review process will ascertain situations where a clinical exception can be made. This program applies to all members requesting treatment with a targeted product.

Each referral is reviewed based on all utilization management (UM) programs implemented for the client.

Table. Asthma

	Product(s)
Preferred*	• **Dupixent** (dupilumab) • **Fasenra** (benralizumab) • **Nucala** (mepolizumab) • **Tezspire** (tezepelumab-ekko) • **Xolair** (omalizumab)
Targeted	• **Cinqair** (reslizumab)

*: Medications considered formulary or preferred on your plan may still require a clinical prior authorization review.

II. EXCEPTION CRITERIA

This program applies to members requesting treatment for an indication that is FDA-approved for the preferred product.

Coverage for a targeted product is provided when the member has a documented inadequate response or intolerable adverse event with at least three of the preferred products.

Section 2: Site of Care

CareFirst Site of Care Criteria
Administration of Intravenous Cinqair

POLICY

I. CRITERIA FOR APPROVAL FOR ADMINISTRATION IN OUTPATIENT HOSPITAL SETTING

This policy provides coverage for administration of Cinqair in an outpatient hospital setting for up to 45 days when a member is new to therapy or is reinitiating therapy after not being on therapy for at least 6 months.

This policy provides coverage for administration of Cinqair in an outpatient hospital setting for a longer course of treatment when ANY of the following criteria are met:

A. The member has experienced an adverse reaction that did not respond to conventional interventions (eg, acetaminophen, steroids, diphenhydramine, fluids or other pre-medications) or a severe adverse event (anaphylaxis, anaphylactoid reactions, myocardial infarction, thromboembolism, or seizures) during or immediately after an infusion.
B. The member is medically unstable (eg respiratory, cardiovascular, or renal conditions).
C. The member has severe venous access issues that require the use of special interventions only available in the outpatient setting.
D. The member has significant behavioral issues and/or physical or cognitive impairment that would impact the safety of the infusion therapy AND the patient does not have access to a caregiver.
E. The member is less than 14 years of age.

For situations where administration of Cinqair does not meet the criteria for outpatient hospital infusion, coverage for Cinqair is provided when administered in alternative sites such as; physician office, home infusion or ambulatory care.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the site of care prior authorization review (where applicable):

A. Medical records supporting the member has experienced an adverse reaction that did not respond to conventional interventions or a severe adverse event during or immediately after an infusion
B. Medical records supporting the member is medically unstable
C. Medical records supporting the member has severe venous access issues that requires specialized interventions only available in the outpatient hospital setting
D. Medical records supporting the member has behavioral issues and/or physical or cognitive impairment and no access to a caregiver

Section 3: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

CINQAIR (reslizumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Cinqair is indicated for the add-on maintenance treatment of patients with severe asthma aged 18 years and older with an eosinophilic phenotype.

Limitations of Use:
- Not for treatment of other eosinophilic conditions
- Not 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. For initial requests:
   1. Member's chart 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

Authorization of 6 months may be granted for treatment of asthma when all of the following criteria are met:
A. Member is 18 years of age or older.
B. Member meets either of the following criteria:
   1. Member has baseline blood eosinophil count of at least 400 cells per microliter; or
   2. Member is dependent on systemic corticosteroids
C. Member has uncontrolled asthma as demonstrated by experiencing at least one of the following within the past year:
   1. Two or more asthma exacerbations requiring oral or injectable corticosteroid treatment.
   2. One or more asthma exacerbation resulting in hospitalization or emergency medical care visit.
   3. Poor symptom control (frequent symptoms or reliever use, activity limited by asthma, night waking due to asthma).
D. Member has inadequate asthma control despite current treatment with both of the following medications at optimized doses:
   1. High dose inhaled corticosteroid
   2. Additional controller (i.e., long acting beta$_2$-agonist, long acting muscarinic antagonist, leukotriene modifier, or sustained-release theophylline)

E. Member will continue to use maintenance asthma treatments (e.g., inhaled corticosteroid, additional controller) in combination with Cinqair.
F. Member will not use Cinqair concomitantly with other biologics indicated for asthma (e.g., Dupixent, Fasenra, Nucala, Tezspire, Xolair).

V. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for treatment of asthma when all of the following criteria are met:
A. Member is 18 years of age or older.
B. Asthma control has improved on Cinqair treatment 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 Cinqair.
D. Member will not use Cinqair concomitantly with other biologics indicated for asthma (e.g., Dupixent, Fasenra, Nucala, Tezspire, Xolair).

VI. OTHER

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.

REFERENCES:

SECTION 1
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SECTION 2
1. Cinqair [package insert]. West Chester, PA: Teva Respiratory, LLC; February 2020.
2. Dupixent [package insert]. Tarrytown, NY: Regeneron Pharmaceuticals, Inc.; June 2022.
3. Fasenra [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; February 2021.
4. Nucala [package insert]. Research Triangle Park, NC: GlaxoSmithKline; January 2022.
5. Tezspire [package insert]. Thousand Oaks, CA: Amgen Inc.; December 2021.
6. Xolair [package insert]. South San Francisco, CA: Genentech, Inc.; July 2021.

SECTION 3
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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.

POLICY Document for CINRYZE (C1 esterase inhibitor [human])

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, lower cost site of care and overall, clinically appropriate use. This document provides specific information to each of the three sections of the overall policy.

Section 1: Site of Care

- Policy information specific to site of care (outpatient, hospital outpatient, home infusion)

Section 2: Clinical Criteria

- Policy information specific to the clinical appropriateness for the medication

Section 1: Site of Care

CareFirst Site of Care Criteria
Administration of Intravenous Cinryze

POLICY

I. CRITERIA FOR APPROVAL FOR ADMINISTRATION IN OUTPATIENT HOSPITAL SETTING

This policy provides coverage for administration of Cinryze in an outpatient hospital setting for up to 45 days when a member is new to therapy or is reinitiating therapy after not being on therapy for at least 6 months.

This policy provides coverage for administration of Cinryze in an outpatient hospital setting for a longer course of treatment when ANY of the following criteria are met:

A. The member has experienced an adverse reaction that did not respond to conventional interventions (eg, acetaminophen, steroids, diphenhydramine, fluids or other pre-medications) or a severe adverse event (anaphylaxis, anaphylactoid reactions, myocardial infarction, thromboembolism, or seizures) during or immediately after an infusion.
B. The member is medically unstable (eg respiratory, cardiovascular, or renal conditions).
C. The member has severe venous access issues that require the use of special interventions only available in the outpatient hospital setting.
D. The member has significant behavioral issues and/or physical or cognitive impairment that would impact the safety of the infusion therapy AND the patient does not have access to a caregiver.
E. The member is less than 14 years of age.

For situations where administration of Cinryze does not meet the criteria for outpatient hospital infusion, coverage for Cinryze is provided when administered in alternative sites such as; physician office, home infusion or ambulatory care.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the site of care prior authorization review (where applicable):

A. Medical records supporting the member has experienced an adverse reaction that did not respond to conventional interventions or a severe adverse event during or immediately after an infusion
B. Medical records supporting the member is medically unstable

C. Medical records supporting the member has severe venous access issues that requires specialized interventions only available in the outpatient hospital setting
D. Medical records supporting the member has behavioral issues and/or physical or cognitive impairment and no access to a caregiver

Section 2: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

CINRYZE (C1 esterase inhibitor [human])

POLICY

III. INDICATIONS

The indications below including FDA-approved indications and compendial 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.

IV. 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

V. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with a prescriber who specializes in the management of HAE.

VI. 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.

VII. 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.

REFERENCES

SECTION 1

1. Cinryze [package insert]. Lexington, MA: Takeda Pharmaceuticals U.S.A.,Inc.; February 2023.

SECTION 2

1. Cinryze [package insert]. Lexington, MA: ViroPharma Biologics; April 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.
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4. 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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17. Veronez CL, Csuka D, Sheik FR, et al. The expanding spectrum of mutations in hereditary angioedema. *J Allergy Clin Immunol Pract.* 2021;S2213-2198(21)00312-3.

Reference number(s)
1942-A

SPECIALTY GUIDELINE MANAGEMENT

COAGADEX (coagulation Factor X [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 Indications
Coagadex is indicated in adults and children with hereditary Factor X deficiency for:
A. Routine prophylaxis to reduce the frequency of bleeding episodes.
B. On-demand treatment and control of bleeding episodes.
C. Perioperative management of bleeding in patients with mild, moderate, and severe hereditary Factor X deficiency.

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

II. CRITERIA FOR INITIAL APPROVAL

Hereditary Factor X Deficiency
A. Authorization of 12 months may be granted for prophylaxis to reduce the frequency of bleeding episodes.
B. Authorization of 12 months may be granted for on-demand treatment and control of bleeding episodes.
C. Authorization of 1 month may be granted for perioperative management of bleeding in members with mild, moderate, or severe hereditary Factor X deficiency.

III. CONTINUATION OF THERAPY

A. Perioperative management of bleeding
All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

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 when the member is experiencing benefit from therapy (e.g., reduced frequency or severity of bleeds).

IV. REFERENCES

1. Coagadex [package insert]. Durham, NC: Bio Products Laboratory USA, Inc.; April 2023.
2. National Hemophilia Foundation. MASAC Recommendations Concerning Products Licensed for the Treatment of Hemophilia and Selected Disorders of the Coagulation System. Revised August 2023.

MASAC Document #280. https://www.hemophilia.org/healthcare-professionals/guidelines-on-care/masac-documents/masac-document-280-masac-recommendations-concerning-products-licensed-for-the-treatment-of-hemophilia-and-selected-disorders-of-the-coagulation-system. Accessed October 4, 2023.

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Reference number(s)
2987-A

SPECIALTY GUIDELINE MANAGEMENT

CORIFACT (coagulation Factor XIII concentrate [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
Corifact is indicated in adult and pediatric patients with congenital Factor XIII deficiency for routine prophylactic treatment and peri-operative management of surgical bleeding.

B. Compendial Use
Acquired factor XIII deficiency

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

II. CRITERIA FOR INITIAL APPROVAL

Factor XIII Deficiency
Authorization of 12 months may be granted for treatment of factor XIII deficiency.

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. REFERENCES

1. Corifact [package insert]. Kankakee, IL: CSL Behring LLC; September 2020.
2. National Hemophilia Foundation. MASAC recommendations concerning products licensed for the treatment of hemophilia and other bleeding disorders. Revised April 2022. MASAC Document #272. https://www.hemophilia.org/sites/default/files/document/files/272_Treatment.pdf. Accessed September 26, 2022.
3. Mumford AD, Ackroyd S, Alikhan R, et al. Guideline for the diagnosis and management of the rare coagulation disorders: a United Kingdom Haemophilia Centre Doctors' Organization guideline on behalf of the British Committee for Standards in Haematology. *Br J Haematol*. 2014;167(3):304-26.
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Reference number(s)
4528-A

SPECIALTY GUIDELINE MANAGEMENT

COSELA (trilaciclib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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
COSELA is indicated to decrease the incidence of chemotherapy-induced myelosuppression in adult patients when administered prior to a platinum/etoposide-containing regimen or topotecan-containing regimen for extensive-stage small cell lung cancer (ES-SCLC).

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

II. CRITERIA FOR INITIAL APPROVAL

Extensive-stage Small Cell Lung Cancer
Authorization of 6 months may be granted to decrease the incidence of chemotherapy-induced myelosuppression in adult patients with extensive-stage small cell lung cancer when all of the following criteria are met:

A. The member will be receiving either of the following chemotherapeutic regimens:
   1. A platinum/etoposide-containing regimen.
   2. A topotecan-containing regimen.
B. The requested medication will be given within 4 hours prior to the start of chemotherapy on each day chemotherapy is administered.
C. The requested medication will not be used with granulocyte colony-stimulating factors (G-CSFs) and/or erythropoiesis-stimulating agents (ESAs) as primary prophylaxis during cycle 1.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

1. Cosela [package insert]. Durham, NC: G1 Therapeutics, Inc; February 2021.

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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POLICY Document for CRYSVITA (burosumab-twza)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, lower cost site of care and overall, clinically appropriate use. This document provides specific information to each of the three sections of the overall policy.

Section 1: Site of Care
- Policy information specific to site of care (outpatient, hospital outpatient, home infusion)

Section 2: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 1: Site of Care

CareFirst Site of Care Criteria
Administration of Subcutaneous Crysvita

POLICY

I. CRITERIA FOR APPROVAL FOR ADMINISTRATION IN OUTPATIENT HOSPITAL SETTING

This policy provides coverage for administration of Crysvita in an outpatient hospital setting for 45 days when a member is new to therapy or is reinitiating therapy after not being on therapy for at least 6 months.

This policy provides coverage for administration of Crysvita in an outpatient hospital setting for a longer course of treatment when ANY of the following criteria are met:

A. The member has experienced an adverse reaction that did not respond to conventional interventions (eg, acetaminophen, steroids, diphenhydramine, fluids or other pre-medications) or a severe adverse event (anaphylaxis, anaphylactoid reactions, myocardial infarction, thromboembolism, or seizures) during or immediately after drug administration.
B. The member is medically unstable (eg respiratory, cardiovascular, or renal conditions).
C. The member has significant behavioral issues and/or physical or cognitive impairment that would impact the safety of drug administration AND the patient does not have access to a caregiver.
D. The member is less than 14 years of age.

For situations where administration of Crysvita does not meet the criteria for outpatient hospital administration, coverage for Crysvita is provided when administered in alternative sites such as; physician office, home infusion or ambulatory care.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the site of care prior authorization review (where applicable):

A. Medical records supporting the member has experienced an adverse reaction that did not respond to conventional interventions or a severe adverse event during or immediately after drug administration
B. Medical records supporting the member is medically unstable
C. Medical records supporting the member has behavioral issues and/or physical or cognitive impairment and no access to a caregiver

CVS/caremark

Section 2: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

CRYSVITA (burosumab-twza)

POLICY

III. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Crysvita is indicated for the treatment of:
1. X-linked hypophosphatemia (XLH) in adult and pediatric patients 6 months of age and older.
2. FGF23-related hypophosphatemia in tumor-induced osteomalacia (TIO) associated with phosphaturic mesenchymal tumors that cannot be curatively resected or localized in adult and pediatric patients 2 years of age and older.

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

IV. DOCUMENTATION

A. X-linked hypophosphatemia
Submission of the following information is necessary to initiate the prior authorization review for X-linked hypophosphatemia (XLH):
1. Initial requests:
   a. Radiographic evidence of rickets or other bone disease attributed to XLH
   b. At least one of the following:
      i. Genetic testing results confirming the member has a PHEX (phosphate regulating gene with homology to endopeptidases located on the X chromosome) mutation
      ii. Genetic testing results confirming a PHEX mutation in a directly related family member with appropriate X-linked inheritance
      iii. Lab test results confirming the member's serum fibroblast growth factor 23 (FGF23) level is above the upper limit of normal or abnormal for the assay.
2. Continuation of therapy requests: documentation (e.g., chart notes, lab test results) of a response to therapy (e.g., increase or normalization in serum phosphate, improvement in bone and joint pain, reduction in fractures, improvement in skeletal deformities).

B. Tumor induced osteomalacia
Submission of the following information is necessary to initiate the prior authorization review for tumor induced osteomalacia (TIO):
1. Initial requests:
   a. Lab test results confirming the member's serum fibroblast growth factor 23 (FGF23) level is above the upper limit of normal or abnormal for the assay.
   b. Fasting serum phosphorus levels less than 2.5 mg/dL

c. Ratio of renal tubular maximum reabsorption rate of phosphate to glomerular filtration rate (TmP/GFR) less than 2.5 mg/dL

2. Continuation of therapy requests: documentation (e.g., chart notes, lab test results) of a response to therapy (e.g., increase or normalization in serum phosphate, improvement in bone and joint pain, reduction in fractures, improvement in skeletal deformities).

V. CRITERIA FOR INITIAL APPROVAL

A. X-linked hypophosphatemia (XLH)

Authorization of 12 months may be granted for treatment of X-linked hypophosphatemia (XLH) when both of the following criteria is met:

1. The member meets one of the following:
   a. Genetic testing was conducted to confirm a PHEX mutation in the member and genetic testing results were submitted confirming diagnosis.
   b. Genetic testing was conducted to confirm a PHEX mutation in a directly related family member with appropriate X-linked inheritance and genetic testing results were submitted confirming diagnosis.
   c. Member's FGF23 level is above the upper limit of normal or abnormal for the assay and lab test results were submitted confirming diagnosis.
2. Member has radiographic evidence of rickets or other bone disease attributed to XLH.

B. Tumor-induced osteomalacia (TIO)

Authorization of 12 months may be granted for treatment of tumor-induced osteomalacia (TIO) when the following criteria is met:

1. Member's diagnosis is confirmed by ALL of the following and lab test results were submitted confirming diagnosis:
   a. FGF23 level is above the upper limit of normal or abnormal for the assay.
   b. Fasting serum phosphorus levels are less than 2.5 mg/dL
   c. Ratio of renal tubular maximum reabsorption rate of phosphate to glomerular filtration rate (TmP/GFR) is less than 2.5 mg/dL
2. Member's disease is associated with phosphaturic mesenchymal tumors that cannot be curatively resected or localized.

VI. 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 and who are experiencing benefit from therapy as evidenced by disease improvement or disease stability (e.g., increase or normalization in serum phosphate, improvement in bone and joint pain, reduction in fractures, improvement in skeletal deformities).

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POLICY Document for CYRAMZA (ramucirumab)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, and overall, clinically appropriate use. This document provides specific information to both sections of the overall policy.

Section 1: Clinical Criteria

- Policy information specific to the clinical appropriateness for the medication

Section 2: Oncology Clinical Policy

- Policy information specific to regimen review per NCCN Guidelines.

Section 1: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

CYRAMZA (ramucirumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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. Gastric Cancer: Cyramza as a single agent, or in combination with paclitaxel, is indicated for the treatment of patients with advanced or metastatic, gastric or gastro-esophageal junction (GEJ) adenocarcinoma with disease progression on or after prior fluoropyrimidine-or platinum-containing chemotherapy.
2. Non-Small Cell Lung Cancer (NSCLC):
    a. Cyramza, in combination with docetaxel, is indicated for the treatment of patients with metastatic NSCLC with disease progression on or after platinum-based chemotherapy. Patients with epidermal growth factor receptor (EGFR) or anaplastic lymphoma kinase (ALK) genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving Cyramza.
    b. Cyramza, in combination with erlotinib, is indicated for the first-line treatment of patients with metastatic NSCLC whose tumors have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 (L858R) substitution mutations.
3. Colorectal Cancer: Cyramza, in combination with FOLFIRI (irinotecan, folinic acid, and fluorouracil), is indicated for the treatment of patients with metastatic colorectal cancer (mCRC) with disease progression on or after prior therapy with bevacizumab, oxaliplatin, and a fluoropyrimidine.
4. Hepatocellular Carcinoma: Cyramza as a single agent, is indicated for the treatment of patients with hepatocellular carcinoma (HCC) who have an alpha fetoprotein (AFP) of ≥400 ng/mL and have been treated with sorafenib.

B. Compendial Uses
~~1.~~ Esophageal adenocarcinoma
2. Colorectal cancer, advanced, including anal adenocarcinoma and appendiceal adenocarcinoma
3. NSCLC, EGFR mutation positive, recurrent, advanced

4. Mesothelioma

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: EGFR mutation testing results and alpha fetoprotein (AFP) level results (where applicable).

III. CRITERIA FOR INITIAL APPROVAL

A. Gastric, Gastro-esophageal Junction (GEJ), Esophagogastric Junction (EGJ), and Esophageal Adenocarcinoma
Authorization of 12 months may be granted for treatment of gastric, gastro-esophageal junction (GEJ), esophagogastric junction (EGJ), and esophageal adenocarcinoma for members who are not surgical candidates or who have unresectable locally advanced, recurrent or metastatic disease, when used as subsequent therapy as a single agent, in combination with paclitaxel, or in combination with irinotecan with or without fluorouracil.

B. Non-Small Cell Lung Cancer (NSCLC)
Authorization of 12 months may be granted for treatment of recurrent, advanced or metastatic NSCLC when either of the following criteria is met:
1. Used in combination with docetaxel as subsequent therapy.
2. Used in combination with erlotinib for EGFR exon 19 deletion or exon 21 (L858R) substitution mutation positive disease.

C. Colorectal Cancer (CRC)
Authorization of 12 months may be granted for treatment of advanced or metastatic colorectal cancer, including anal adenocarcinoma and appendiceal adenocarcinoma, in combination with FOLFIRI (irinotecan, folinic acid, and 5-fluorouracil) or irinotecan.

D. Hepatocellular Carcinoma (HCC)
Authorization of 12 months may be granted for subsequent treatment of progressive hepatocellular carcinoma as a single agent in members who have an alpha fetoprotein (AFP) of greater than or equal to 400 ng/mL.

E. Mesothelioma
Authorization of 12 months may be granted for the subsequent treatment of pleural mesothelioma, pericardial mesothelioma, or tunica vaginalis testis mesothelioma when used in combination with gemcitabine.

IV. CONTINUATION OF THERAPY

A. NSCLC
Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for NSCLC when either of the following criteria is met:
1. There is no evidence of unacceptable toxicity or disease progression while on the current regimen, or
2. Disease is T790M negative and there is no evidence of unacceptable toxicity

B. All other indications

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.

Section 2: Oncology Clinical Policy

PROGRAM DESCRIPTION

The National Comprehensive Care Network® (NCCN®) is an alliance of leading cancer centers devoted to patient care, research and education dedicated to improving the quality, effectiveness, and efficiency of cancer care so patients can live better lives.[1] It is comprised of oncology experts who convene regularly to establish the best treatments for patients. NCCN develops various resources for use by stakeholders in the health care delivery system. These resources include, but are not limited to, the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®), the NCCN Drugs & Biologics Compendium (NCCN Compendium®) and the NCCN Chemotherapy Order Templates (NCCN Templates®).

NCCN Templates® are based on NCCN Guidelines® and NCCN Compendium®. The NCCN Compendium lists the appropriate drugs and biologics as treatment options for specific cancers using U.S. Food and Drug Administration (FDA)-approved disease indications and specific NCCN panel recommendations. Each recommendation is supported by a level of evidence category.

NCCN Categories of Evidence and Consensus[2]

- Category 1: Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
- Category 2A: Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
- Category 2B: Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.
- Category 3: Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

POLICY

Policy for Regimen Prior Authorization
A regimen prior authorization allows submission of a single prior authorization request for all oncology drugs or biologics within an NCCN template that require prior authorization.

PROCEDURE

This policy provides coverage of a regimen review when all of the following criteria are met:
1. Regimen prior authorization reviews, based on NCCN templates, are initiated through the provider portal.
   - If the prior authorization request is submitted via phone or fax, each drug or biologic will need to be submitted and reviewed as a separate prior authorization request for review with drug-specific criteria.
2. The prior authorization review is requested for an oncology drug or biologic.
3. The member is eligible for regimen review.
4. The indication is for a cancer that is eligible for regimen review. Currently, the cancer types in scope for regimen review include the following:
   - Ampullary Adenocarcinoma
   - Anal Carcinoma
   - B-Cell Lymphomas
   - Basal Cell Skin Cancer
   - Biliary Tract Cancers

- Bone Cancer
- Breast Cancer
- Bladder Cancer
- Central Nervous System Cancers
- Cervical Cancer
- Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma
- Chronic Myeloid leukemia
- Colon Cancer
- Dermatofibrosarcoma Protuberans
- Esophageal Cancer
- Gastric Cancer
- Gastrointestinal Stromal Tumors
- Gestational Trophoblastic Neoplasms
- Hairy Cell Leukemia
- Head and Neck Cancers
- Hodgkin Lymphoma
- Hepatocellular Carcinoma
- Kaposi Sarcoma
- Kidney Cancer
- Melanoma: Cutaneous
- Melanoma: Uveal
- Merkel Cell Carcinoma
- Mesothelioma: Peritoneal
- Mesothelioma: Pleural
- Myelodysplastic Syndromes
- Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Gene Fusions
- Myeloproliferative Neoplasms
- Neuroendocrine and Adrenal Tumors
- Non-Small Cell Lung Cancer
- Occult Primary
- Ovarian Cancer
- Pancreatic Cancer
- Penile Cancer
- Prostate Cancer
- Rectal Cancer
- Small Bowl Adenocarcinoma
- Small Cell Lung Cancer
- Soft Tissue Sarcoma
- Squamous Cell Skin Cancer
- Systemic Mastocytosis
- Systemic Light Chain Amyloidosis
- Testicular Cancer
- Thymomas and Thymic Carcinomas
- Thyroid Carcinoma
- Uterine Neoplasms
- Vulvar Cancer
- Waldenström Macroglobulinemia / Lymphoplasmacytic Lymphoma

In addition, the following criteria must be met for approval:

1. The requested regimen for the drug(s) or biologic(s) and indication is consistent with an NCCN recommendation with a level of evidence category of 1 or 2A.
2. The NCCN template must be accepted by the provider without modification.

Further review may be indicated when the above criteria are not met.

Authorizations may be granted for 12 months or as medically required, based on the member's condition and provider's assessment.

Supportive Care: Myeloid Growth Factor Therapy
Granulocyte colony stimulating factors are recommended for primary prophylaxis based on the febrile neutropenia risk of the chemotherapy regimen. Febrile neutropenia risk levels vary by NCCN Chemotherapy Order template and are listed at the top of the template. Regimens associated with a high or intermediate risk of febrile neutropenia may include a granulocyte colony stimulating factor as part of the prior authorization.

Continuation of Therapy
To submit a request for continuation of therapy, a new regimen prior authorization review must be requested. Upon template selection, the template must be modified to include the appropriate therapies being used for maintenance treatment. The regimen request will be submitted for further review.

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

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Reference number(s)
1615-A

SPECIALTY GUIDELINE MANAGEMENT

DARZALEX (daratumumab)

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
Darzalex is indicated for the treatment of adult patients with multiple myeloma:
1. in combination with lenalidomide and dexamethasone in newly diagnosed patients who are ineligible for autologous stem cell transplant and in patients with relapsed or refractory multiple myeloma who have received at least one prior therapy.
2. in combination with bortezomib, melphalan and prednisone in newly diagnosed patients who are ineligible for autologous stem cell transplant.
3. in combination with bortezomib, thalidomide, and dexamethasone in newly diagnosed patients who are eligible for autologous stem cell transplant.
4. in combination with bortezomib and dexamethasone in patients who have received at least one prior therapy.
5. in combination with carfilzomib and dexamethasone in patients with relapsed or refractory multiple myeloma who have received one to three prior lines of therapy.
6. in combination with pomalidomide and dexamethasone in patients who have received at least two prior therapies including lenalidomide and a proteasome inhibitor.
7. as monotherapy, in patients who have received at least three prior lines of therapy including a proteasome inhibitor (PI) and an immunomodulatory agent or who are double-refractory to a PI and an immunomodulatory agent.

B. Compendial Uses
1. Multiple myeloma
2. Systemic light chain amyloidosis

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

II. CRITERIA FOR INITIAL APPROVAL

A. Multiple Myeloma

1. Authorization of 12 months may be granted for the treatment of multiple myeloma when used in combination with cyclophosphamide, bortezomib, and dexamethasone

2. Authorization of 12 months may be granted for the treatment of multiple myeloma as primary therapy when any of the following criteria is met:
    a. The member is ineligible for a transplant and the requested medication will be used in combination with either:
        i. Lenalidomide and dexamethasone

ii. Bortezomib, melphalan, and prednisone

b. The member is eligible for transplant and the requested medication will be used in combination with any of the following:
   i. Bortezomib, thalidomide, and dexamethasone for a maximum of 16 doses
   ii. Bortezomib, lenalidomide, and dexamethasone
   iii. Carfilzomib, lenalidomide, and dexamethasone

3. Authorization of 12 months may be granted for the treatment of previously treated multiple myeloma when any of the following criteria is met:
   a. The requested medication will be used in combination with lenalidomide and dexamethasone in members who have received at least one prior therapy
   b. The requested medication will be used in combination with bortezomib and dexamethasone in members who have received at least one prior therapy
   c. The requested medication will be used in combination with carfilzomib and dexamethasone in members who have received at least one prior therapy
   d. The requested medication will be used in combination with pomalidomide and dexamethasone in members who have received at least one prior therapy including a proteasome inhibitor (PI) and an immunomodulatory agent
   e. The requested medication will be used in combination with selinexor and dexamethasone
   f. The requested medication will be used as a single agent in members who have received at least three prior therapies, including a PI and an immunomodulatory agent
   g. The requested medication will be used as a single agent in members who are double refractory to a PI and an immunomodulatory agent

4. Authorization of 12 months may be granted for the single-agent maintenance therapy of symptomatic multiple myeloma for transplant candidates.

B. Systemic Light Chain Amyloidosis

Authorization of 12 months may be granted for the treatment of systemic light chain amyloidosis when the member has relapsed or 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 either of the following regimen or indication-specific criteria is met:

A. All members (including new members) requesting the requested medication in combination with bortezomib, thalidomide, and dexamethasone for multiple myeloma must meet all initial criteria.
B. For all other regimens and indications listed in Section II, there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

IV. REFERENCES

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Reference number(s)
3854-A

SPECIALTY GUIDELINE MANAGEMENT

DARZALEX FASPRO (daratumumab and hyaluronidase-fihj)

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. Darzalex Faspro is indicated for the treatment of adult patients with multiple myeloma:
   a. in combination with bortezomib, melphalan and prednisone in newly diagnosed patients who are ineligible for autologous stem cell transplant.
   b. in combination with lenalidomide and dexamethasone in newly diagnosed patients who are ineligible for autologous stem cell transplant and in patients with relapsed or refractory multiple myeloma who have received at least one prior therapy.
   c. in combination with bortezomib, thalidomide, and dexamethasone in newly diagnosed patients who are eligible for autologous stem cell transplant.
   d. in combination with bortezomib and dexamethasone in patients who have received at least one prior therapy.
   e. in combination with pomalidomide and dexamethasone in patients who have received at least one prior line of therapy including lenalidomide and a proteasome inhibitor.
   f. in combination with carfilzomib and dexamethasone in patients with relapsed or refractory multiple myeloma who have received one to three prior lines of therapy.
   g. as monotherapy, in patients who have received at least three prior lines of therapy including a proteasome inhibitor (PI) and an immunomodulatory agent or who are double-refractory to a PI and an immunomodulatory agent.

2. Darzalex Faspro is indicated for the treatment of adult patients with newly diagnosed light chain amyloidosis in combination with bortezomib, cyclophosphamide and dexamethasone.

B. Compendial Uses
1. For multiple myeloma, may be used as a single agent or in combination with other systemic therapies where intravenous daratumumab is recommended
2. For light chain amyloidosis, may be used for relapsed/refractory disease

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

II. CRITERIA FOR INITIAL APPROVAL

A. Multiple Myeloma
1. Authorization of 12 months may be granted for the treatment of multiple myeloma when used in combination with cyclophosphamide, bortezomib, and dexamethasone

2. Authorization of 12 months may be granted for the treatment of multiple myeloma as primary therapy when any of the following criteria is met:
    a. The member is ineligible for a transplant and the requested medication will be used in combination with either:
        i. Lenalidomide and dexamethasone
        ii. Bortezomib, melphalan, and prednisone
    b. The member is eligible for transplant and the requested medication will be used in combination with any of the following:
        i. Bortezomib, thalidomide, and dexamethasone for a maximum of 16 doses
        ii. Bortezomib, lenalidomide, and dexamethasone
        iii. Carfilzomib, lenalidomide, and dexamethasone

3. Authorization of 12 months may be granted for the treatment of previously treated multiple myeloma when any of the following criteria is met:
    a. The requested medication will be used in combination with lenalidomide and dexamethasone in members who have received at least one prior therapy
    b. The requested medication will be used in combination with bortezomib and dexamethasone in members who have received at least one prior therapy
    c. The requested medication will be used in combination with carfilzomib and dexamethasone in members who have received at least one prior therapy
    d. The requested medication will be used in combination with pomalidomide and dexamethasone in members who have received at least one prior therapy including a proteasome inhibitor (PI) and an immunomodulatory agent.
    e. The requested medication will be used in combination with selinexor and dexamethasone
    f. The requested medication will be used as a single agent in members who have received at least three prior therapies, including a PI and an immunomodulatory agent
    g. The requested medication will be used as a single agent in members who are double refractory to a PI and an immunomodulatory agent

4. Authorization of 12 months may be granted for the single-agent maintenance therapy of symptomatic multiple myeloma for transplant candidates

B. Light Chain Amyloidosis

Authorization of 12 months may be granted for the treatment of light chain amyloidosis in either of the following settings:

1. For newly diagnosed members when used in combination with bortezomib, cyclophosphamide and dexamethasone.
2. For relapsed or 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 any of the following criteria are met:

A. All members (including new members) requesting the requested medication in combination with bortezomib, thalidomide, and dexamethasone for multiple myeloma must meet all initial criteria.
B. For members requesting reauthorization for newly diagnosed light chain amyloidosis, the maximum treatment duration is 24 months and there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

C. For all other regimens and indications listed in Section II, there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

IV. REFERENCES

1. Darzalex Faspro [package insert]. Horsham, PA: Janssen Biotech, Inc.; April 2022.
2. The NCCN Drugs & Biologics Compendium® ©2022 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed October 11, 2022.
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Reference number
2288-A

SPECIALTY GUIDELINE MANAGEMENT

DACOGEN (decitabine)
decitabine

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Myelodysplastic syndromes (MDS): Dacogen (decitabine) is indicated for treatment of adult patients with myelodysplastic syndromes (MDS) including previously treated and untreated, *de novo* and secondary MDS of all French-American-British subtypes (refractory anemia, refractory anemia with ringed sideroblasts, refractory anemia with excess blasts, refractory anemia with excess blasts in transformation, and chronic myelomonocytic leukemia) and intermediate-1, intermediate-2, and high-risk International Prognostic Scoring System groups.

B. Compendial Uses
1. Acute myeloid leukemia (AML)
2. Accelerated phase or blast phase myelofibrosis
3. Lower risk myelodysplastic syndromes (MDS) associated with thrombocytopenia, neutropenia, symptomatic anemia, or increased marrow blasts
4. Blastic plasmacytoid dendritic cell neoplasm (BPDCN)
5. Myelodysplastic syndrome/myeloproliferative neoplasm (MDS/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/myeloproliferative neoplasm (MDS/MPN) overlap neoplasms

Authorization of 12 months may be granted for the treatment of MDS/MPN overlap neoplasms (i.e. chronic myelomonocytic leukemia (CMML), 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.

IV. REFERENCES

1. Dacogen [package insert]. Rockville, MD: Otsuka America Pharmaceutical, Inc.; November 2021.
2. National Comprehensive Cancer Network. The NCCN Drugs & Biologics Compendium. http://www.nccn.org. Accessed January 7, 2022.

Reference number(s)
1620-A

SPECIALTY GUIDELINE MANAGEMENT

DESFERAL (deferoxamine)
deferoxamine 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 Indication
Chronic iron overload due to transfusion-dependent anemias

B. Compendial Uses
1. Aluminum toxicity in patients undergoing dialysis
2. 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:

Chronic iron overload due to transfusion-dependent anemias:
A. Initial requests: pretreatment serum ferritin level
B. Continuation requests: current serum ferritin level

III. CRITERIA FOR INITIAL APPROVAL

A. Chronic Iron Overload due to Transfusion-Dependent Anemias
Authorization of 6 months may be granted for treatment of chronic iron overload due to transfusion-dependent anemias when the pretreatment serum ferritin level is consistently greater than 1000 mcg/L.

B. Aluminum toxicity in Members Undergoing Dialysis
Authorization of 6 months may be granted for treatment of aluminum toxicity in members undergoing dialysis.

C. 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. Chronic Iron Overload due to Transfusion-Dependent Anemias
Authorization of 6 months may be granted for continued treatment in members requesting reauthorization for chronic iron overload due to transfusion-dependent anemias when member is experiencing benefit from therapy as evidenced by a decrease in serum ferritin levels as compared to pretreatment baseline.

B. Aluminum toxicity in Members Undergoing Dialysis
Authorization of 6 months may be granted for continued treatment in members requesting reauthorization for aluminum toxicity while undergoing dialysis when member is experiencing benefit from therapy as evidenced by any of the following:
1. Decreased serum aluminum concentrations
2. Symptomatic improvement (e.g., neurological symptom improvement, decreased bone pain)

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.

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3. Micromedex Solutions [database online]. Truven Health Analytics, Inc. Ann Arbor, MI. Available at: www.micromedexsolutions.com. Accessed October 1, 2022.
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POLICY Document for TAXOTERE (docetaxel) docetaxel

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, and overall, clinically appropriate use. This document provides specific information to both sections of the overall policy.

Section 1: Clinical Criteria

- Policy information specific to the clinical appropriateness for the medication

Section 2: Oncology Clinical Policy

- Policy information specific to regimen review per NCCN Guidelines.

Section 1: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

TAXOTERE (docetaxel)
docetaxel

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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 (BC)
   a. Docetaxel is indicated for the treatment of patients with locally advanced or metastatic breast cancer after failure of prior chemotherapy.
   b. Docetaxel in combination with doxorubicin and cyclophosphamide is indicated for the adjuvant treatment of patients with operable node-positive breast cancer.
2. Non-Small Cell Lung Cancer (NSCLC)
   a. Docetaxel as a single agent is indicated for the treatment of patients with locally advanced or metastatic NSCLC after failure of prior platinum-based chemotherapy.
   b. Docetaxel in combination with cisplatin is indicated for the treatment of patients with unresectable, locally advanced or metastatic NSCLC who have not previously received chemotherapy for this condition.
3. Prostate Cancer
   Docetaxel in combination with prednisone is indicated for the treatment of patients with metastatic castration-resistant prostate cancer.
4. Gastric Adenocarcinoma (GC)
   Docetaxel in combination with cisplatin and fluorouracil is indicated for the treatment of patients with advanced gastric adenocarcinoma, including adenocarcinoma of the gastroesophageal junction, who have not received prior chemotherapy for advanced disease.
5. Head and Neck Cancer
   Docetaxel in combination with cisplatin and fluorouracil is indicated for the induction treatment of patients with locally advanced squamous cell carcinoma of the head and neck (SCCHN).

B. Compendial Uses
1. Anal cancer
2. Bladder cancer, primary carcinoma of the urethra, upper genitourinary (GU) tract tumors, and urothelial carcinoma of the prostate
3. Bone cancer: Ewing's sarcoma and osteosarcoma
4. Breast cancer
5. Esophageal and esophagogastric junction cancers
6. Gastric cancer
7. Head and neck cancer (including very advanced head and neck cancer and cancers of the lip (mucosa), oral cavity, salivary gland, oropharynx, hypopharynx, nasopharynx, glottic larynx, or supraglottic larynx)
8. Non-small cell lung cancer
9. Occult primary tumors (cancer of unknown primary)
10. Ovarian cancer/fallopian tube cancer/primary peritoneal cancer: epithelial ovarian cancer, fallopian tube cancer, primary peritoneal cancer, malignant germ cell tumors, malignant sex cord-stromal tumors, carcinosarcoma (malignant mixed Müllerian tumors), clear cell carcinoma of the ovary, mucinous carcinoma of the ovary, low-grade serious carcinoma/ovarian borderline epithelial tumor (low malignant potential), and grade 1 endometrioid carcinoma.
11. Prostate cancer
12. Small cell lung cancer
13. Soft tissue sarcoma (including angiosarcoma, extremity/body wall, head/neck, retroperitoneal/intra-abdominal, pleomorphic rhabdomyosarcoma, dermatofibrosarcoma protuberans (DFSP) with fibrosarcomatous transformation, and solitary fibrous tumor)
14. Thyroid carcinoma: anaplastic carcinoma
15. Uterine neoplasms: endometrial carcinoma and uterine sarcoma
16. Small bowel adenocarcinoma

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

II. CRITERIA FOR INITIAL APPROVAL

A. Anal Cancer
Authorization of 6 months may be granted for treatment of metastatic or unresectable locally recurrent anal squamous cell carcinoma.

B. Bladder Cancer, Primary Carcinoma of the Urethra, Upper Genitourinary Tract Tumors, and Urothelial Carcinoma of the Prostate

1. Bladder Cancer
Authorization of 6 months may be granted for treatment of bladder cancer.

2. Primary Carcinoma of the Urethra
Authorization of 6 months may be granted for treatment of recurrent or metastatic primary carcinoma of the urethra.

3. Upper Genitourinary Tract Tumors and Urothelial Carcinoma of the Prostate
Authorization of 6 months may be granted for treatment of metastatic upper genitourinary tract tumors or urothelial carcinoma of the prostate.

C. Bone Cancer

1. Ewing's Sarcoma

Authorization of 6 months may be granted for treatment of relapsed, progressive, or metastatic Ewing's sarcoma.

2. **Osteosarcoma**
   Authorization of 6 months may be granted for treatment of relapsed, refractory, or metastatic osteosarcoma.

D. Breast Cancer
Authorization of 6 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 no response to preoperative systemic therapy, as a single agent or in combination with capecitabine.
2. Member has human epidermal growth factor receptor 2 (HER2)-positive recurrent unresectable or metastatic disease or no response to preoperative systemic therapy, and the requested medication will be used in one of the following regimens:
   a. In combination with pertuzumab and trastuzumab.
   b. In combination with trastuzumab.
3. The requested medication will be used as adjuvant therapy.
4. The requested medication will be used as preoperative therapy.
5. The requested medication will be used as a substitute for other taxanes (e.g., paclitaxel or albumin-bound paclitaxel) in select patients due to medical necessity.

E. Esophageal and Esophagogastric Junction Cancers
Authorization of 6 months may be granted for treatment of esophageal or esophagogastric junction cancer.

F. Gastric Cancer
Authorization of 6 months may be granted for treatment of gastric cancer.

G. Head and Neck Cancer
Authorization of 6 months may granted for treatment of head and neck cancer (including very advanced head and neck cancer, cancers of the lip (mucosa), oral cavity, salivary gland, oropharynx, hypopharynx, nasopharynx, glottic larynx, and supraglottic larynx).

H. Non-Small Cell Lung Cancer (NSCLC)
Authorization of 6 months may be granted for treatment of non-small cell lung cancer.

I. Occult Primary Tumors (cancer of unknown primary)
Authorization of 6 months may be granted for treatment of occult primary cancer.

J. Ovarian Cancer, Fallopian Tube Cancer, and Primary Peritoneal Cancer
Authorization of 6 months may be granted for treatment of 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 carcinoma/ovarian borderline epithelial tumor (low malignant potential), mucinous carcinoma of the ovary, malignant sex-cord stromal tumors, or malignant germ cell tumor residual disease.

K. Prostate Cancer
Authorization of 6 months may be granted for treatment of prostate cancer.

L. Small Cell Lung Cancer (SCLC)
Authorization of 6 months may be granted for treatment of small cell lung cancer.

M. Soft Tissue Sarcoma

Authorization of 6 months may be granted for treatment of soft tissue sarcoma (including angiosarcoma, extremity/body wall, head/neck, retroperitoneal/intra-abdominal, pleomorphic rhabdomyosarcoma, dermatofibrosarcoma protuberans (DFSP) with fibrosarcomatous transformation, and solitary fibrous tumor.

N. Thyroid Carcinoma – Anaplastic Carcinoma[4]
Authorization of 6 months may be granted for treatment of thyroid carcinoma-anaplastic carcinoma.

O. Uterine Neoplasms
Authorization of 6 months may be granted for treatment of uterine neoplasms (including endometrial carcinoma and uterine sarcoma).

P. Small Bowel Adenocarcinoma
Authorization of 6 months may be granted for treatment of advanced or metastatic small bowel adenocarcinoma.

III. CONTINUATION OF THERAPY

Authorization of 6 months may be granted for continued treatment in members requesting reauthorization for an indication in Section II when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

Section 2: Oncology Clinical Policy

PROGRAM DESCRIPTION

The National Comprehensive Care Network® (NCCN®) is an alliance of leading cancer centers devoted to patient care, research and education dedicated to improving the quality, effectiveness, and efficiency of cancer care so patients can live better lives.[1] It is comprised of oncology experts who convene regularly to establish the best treatments for patients. NCCN develops various resources for use by stakeholders in the health care delivery system. These resources include, but are not limited to, the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®), the NCCN Drugs & Biologics Compendium (NCCN Compendium®) and the NCCN Chemotherapy Order Templates (NCCN Templates®).

NCCN Templates® are based on NCCN Guidelines® and NCCN Compendium®. The NCCN Compendium lists the appropriate drugs and biologics as treatment options for specific cancers using U.S. Food and Drug Administration (FDA)-approved disease indications and specific NCCN panel recommendations. Each recommendation is supported by a level of evidence category.

NCCN Categories of Evidence and Consensus[2]

- Category 1: Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
- Category 2A: Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
- Category 2B: Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.
- Category 3: Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

POLICY

Policy for Regimen Prior Authorization
A regimen prior authorization allows submission of a single prior authorization request for all oncology drugs or biologics within an NCCN template that require prior authorization.

PROCEDURE

This policy provides coverage of a regimen review when all of the following criteria are met:
1. Regimen prior authorization reviews, based on NCCN templates, are initiated through the provider portal.
    - If the prior authorization request is submitted via phone or fax, each drug or biologic will need to be submitted and reviewed as a separate prior authorization request for review with drug-specific criteria.
2. The prior authorization review is requested for an oncology drug or biologic.
3. The member is eligible for regimen review.
4. The indication is for a cancer that is eligible for regimen review. Currently, the cancer types in scope for regimen review include the following:
    - Ampullary Adenocarcinoma
    - Anal Carcinoma
    - B-Cell Lymphomas
    - Basal Cell Skin Cancer
    - Biliary Tract Cancers
    - Bone Cancer
    - Breast Cancer
    - Bladder Cancer
    - Central Nervous System Cancers
    - Cervical Cancer
    - Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma
    - Chronic Myeloid leukemia
    - Colon Cancer
    - Dermatofibrosarcoma Protuberans
    - Esophageal Cancer
    - Gastric Cancer
    - Gastrointestinal Stromal Tumors
    - Gestational Trophoblastic Neoplasms
    - Hairy Cell Leukemia
    - Head and Neck Cancers
    - Hodgkin Lymphoma
    - Hepatocellular Carcinoma
    - Kaposi Sarcoma
    - Kidney Cancer
    - Melanoma: Cutaneous
    - Melanoma: Uveal
    - Merkel Cell Carcinoma
    - Mesothelioma: Peritoneal
    - Mesothelioma: Pleural
    - Myelodysplastic Syndromes
    - Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Gene Fusions
    - Myeloproliferative Neoplasms
    - Neuroendocrine and Adrenal Tumors
    - Non-Small Cell Lung Cancer
    - Occult Primary
    - Ovarian Cancer
    - Pancreatic Cancer
    - Penile Cancer
    - Prostate Cancer
    - Rectal Cancer
    - Small Bowl Adenocarcinoma

- Small Cell Lung Cancer
- Soft Tissue Sarcoma
- Squamous Cell Skin Cancer
- Systemic Mastocytosis
- Systemic Light Chain Amyloidosis
- Testicular Cancer
- Thymomas and Thymic Carcinomas
- Thyroid Carcinoma
- Uterine Neoplasms
- Vulvar Cancer
- Waldenström Macroglobulinemia / Lymphoplasmacytic Lymphoma

In addition, the following criteria must be met for approval:

1. The requested regimen for the drug(s) or biologic(s) and indication is consistent with an NCCN recommendation with a level of evidence category of 1 or 2A.
2. The NCCN template must be accepted by the provider without modification.

Further review may be indicated when the above criteria are not met.

Authorizations may be granted for 12 months or as medically required, based on the member's condition and provider's assessment.

Supportive Care: Myeloid Growth Factor Therapy
Granulocyte colony stimulating factors are recommended for primary prophylaxis based on the febrile neutropenia risk of the chemotherapy regimen. Febrile neutropenia risk levels vary by NCCN Chemotherapy Order template and are listed at the top of the template. Regimens associated with a high or intermediate risk of febrile neutropenia may include a granulocyte colony stimulating factor as part of the prior authorization.

Continuation of Therapy
To submit a request for continuation of therapy, a new regimen prior authorization review must be requested. Upon template selection, the template must be modified to include the appropriate therapies being used for maintenance treatment. The regimen request will be submitted for further review.

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

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SECTION 1

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SECTION 2

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5. National Comprehensive Cancer Network. NCCN Chemotherapy Order Templates (NCCN Templates) website. https://www.nccn.org/compendia-templates/nccn-templates-main/browse-by-cancer-type, accessed June 6, 2023. (Note: A subscription may be required.)

Reference number(s)
3029-A

SPECIALTY GUIDELINE MANAGEMENT

DUOPA (carbidopa and levodopa enteral 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
Duopa is indicated for the treatment of motor fluctuations in patients with advanced Parkinson's disease.

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

II. EXCLUSIONS

Coverage will not be provided for 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 treatment of motor fluctuations in members with advanced Parkinson's disease when all of the following criteria are met:
A. Member is levodopa responsive with clearly defined "on" periods; *and*
B. The member has off periods greater than 3 hours per day despite optimization efforts; and
C. The member must have had an inadequate response or intolerable adverse event with oral carbidopa-levodopa (IR or CR) and one of the following anti-Parkinson agents:
    1. Catechol-O-methyl transferase (COMT) inhibitor (e.g., entacapone)
    2. Monoamine oxidase B (MAO)-B inhibitor (e.g., oral selegiline, Azilect)
    3. Dopamine agonists (e.g., pramipexole, ropinirole, Neupro)

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for Parkinson's disease who have demonstrated a positive clinical response to Duopa therapy.

V. REFERENCES

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POLICY Document for DUPIXENT (dupilumab)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, and overall, clinically appropriate use. This document provides specific information to both sections of the overall policy.

Section 1: Preferred Product
- Policy information specific to preferred medications

Section 2: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 1: Preferred Product

EXCEPTIONS CRITERIA
ASTHMA

PREFERRED PRODUCTS: DUPIXENT, FASENRA, NUCALA, TEZSPIRE, XOLAIR

POLICY
This policy informs prescribers of preferred products and provides an exception process for targeted products through prior authorization.

I. PLAN DESIGN SUMMARY

This program applies to the asthma products specified in this policy. Coverage for targeted products is provided based on clinical circumstances that would exclude the use of the preferred product and may be based on previous use of a product. The coverage review process will ascertain situations where a clinical exception can be made. This program applies to all members requesting treatment with a targeted product.

Each referral is reviewed based on all utilization management (UM) programs implemented for the client.

Table. Asthma

	Product(s)
Preferred*	• **Dupixent** (dupilumab) • **Fasenra** (benralizumab) • **Nucala** (mepolizumab) • **Tezspire** (tezepelumab-ekko) • **Xolair** (omalizumab)
Targeted	• **Cinqair** (reslizumab)

*: Medications considered formulary or preferred on your plan may still require a clinical prior authorization review.

II. EXCEPTION CRITERIA

This program applies to members requesting treatment for an indication that is FDA-approved for the preferred product.

Coverage for a targeted product is provided when the member has a documented inadequate response or intolerable adverse event with at least three of the preferred products.

Section 2: Clinical Criteria

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

A. For initial requests:
   1. Member's chart or medical record showing pretreatment blood eosinophil count (where 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.

C. Chronic rhinosinusitis with nasal polyposis

A. For initial requests:
   1. 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).

2. Chart notes, medical record documentation, or claims history supporting previous medications tried. If therapy is not advisable, documentation of clinical reason to avoid therapy.

B. For continuation requests: Chart notes or medical record documentation supporting positive clinical response.

D. **Eosinophilic esophagitis**

A. For initial requests:
1. Member's chart or medical record showing endoscopic biopsy details including intraepithelial esophageal eosinophil count.
2. Chart notes, medical record documentation, or claims history supporting previous medications tried. If therapy is not advisable, documentation of clinical reason to avoid therapy.

B. For continuation requests: Chart notes or medical record documentation supporting positive clinical response.

E. **Prurigo Nodularis**

A. For initial requests:
1. Member's chart or medical record of symptoms (e.g., pruritus, nodular lesions).
2. 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.

B. 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%
	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%

Potency	Drug	Dosage form	Strength
	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%
	Hydrocortisone acetate	Cream, Ointment	0.5%
		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)

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POLICY Document for DYSPORT (abobotulinumtoxin A)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, and overall, clinically appropriate use. This document provides specific information to both sections of the overall policy.

Section 1: Preferred Product
- Policy information specific to preferred medications

Section 2: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 1: Preferred Product

EXCEPTIONS CRITERIA
BOTULINUM TOXINS

PREFERRED PRODUCTS: BOTOX, DYSPORT AND XEOMIN

POLICY
This policy informs prescribers of preferred products and provides an exception process for targeted products through prior authorization.

I. PLAN DESIGN SUMMARY

This program applies to the botulinum toxins products specified in this policy. Coverage for targeted products is provided based on clinical circumstances that would exclude the use of the preferred product and may be based on previous use of a product. The coverage review process will ascertain situations where a clinical exception can be made. This program applies to all members requesting treatment with the targeted product.

Each referral is reviewed based on all utilization management (UM) programs implemented for the client.

Table. Botulinum Toxins

	Product(s)
Preferred*	• **Botox** (onabotulinumtoxinA) • **Dysport** (abobotulinumtoxinA) • **Xeomin** (incobotulinumtoxinA)
Targeted	• **Myobloc** (rimabotulinumtoxinB)

*: Medications considered formulary or preferred on your plan may still require a clinical prior authorization review.

II. EXCEPTION CRITERIA

This program applies to members requesting treatment for an indication that is FDA-approved for the preferred product.

Coverage for a targeted product is provided when ANY of the following criteria is met:
A. Member has a documented inadequate response or intolerable adverse event to all of the preferred products.
B. Member is requesting Myobloc for the treatment of chronic sialorrhea and has had a documented inadequate response or an intolerable adverse event to Xeomin.

CVS/caremark

Section 2: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

DYSPORT (abobotulinumtoxin A)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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 cervical dystonia in adults
   2. Treatment of spasticity in patients 2 years of age and older

B. Compendial Uses
   1. Blepharospasm
   2. Hemifacial spasm
   3. Chronic anal fissures
   4. Excessive salivation
   5. Primary axillary hyperhidrosis

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

II. PRESCRIBER SPECIALTIES

The medication must be prescribed by, or in consultation with one of the following:

A. Cervical dystonia, spasticity, hemifacial spasm: neurologist, orthopedist or physiatrist
B. Blepharospasm: neurologist or ophthalmologist
C. Chronic anal fissures: gastroenterologist, proctologist or colorectal surgeon
D. Excessive salivation: neurologist or otolaryngologist
E. Primary axillary hyperhidrosis: neurologist or dermatologist

III. EXCLUSIONS

Coverage will not be provided for cosmetic use.

IV. CRITERIA FOR INITIAL APPROVAL

A. Cervical dystonia

Authorization of 12 months may be granted for treatment of adults with cervical dystonia (e.g., torticollis) when all of the following are met:

1. Member is 18 years of age or older
2. Member has abnormal placement of the head with limited range of motion in the neck.

B. Upper or lower limb spasticity

Authorization of 12 months may be granted for treatment of upper or lower limb spasticity when all of the following are met:

1. Member is 2 years of age or older

2. Member has a primary diagnosis of upper or lower limb spasticity or as a symptom of a condition (including focal spasticity or equinus gait due to cerebral palsy)

C. Blepharospasm
Authorization of 12 months may be granted for treatment of blepharospasm, including blepharospasm associated with dystonia and benign essential blepharospasm.

D. Hemifacial spasm
Authorization of 12 months may be granted for treatment of hemifacial spasm.

E. Chronic anal fissures
Authorization of 12 months may be granted for treatment of chronic anal fissures when the member has not responded to first-line therapy such as topical calcium channel blockers or topical nitrates.

F. Excessive salivation
Authorization of 12 months may be granted for treatment of excessive salivation (chronic sialorrhea) when the member has been refractory to pharmacotherapy (e.g., anticholinergics).

G. Primary axillary hyperhidrosis
Authorization of 12 months may be granted for treatment of primary axillary hyperhidrosis when all of the following criteria are met:
1. Significant disruption of professional and/or social life has occurred because of excessive sweating; and
2. Topical aluminum chloride or other extra-strength antiperspirants are ineffective or result in a severe rash.

V. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria and be experiencing benefit from therapy.

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Reference number(s)
5670-A

SPECIALTY GUIDELINE MANAGEMENT

ELAHERE (mirvetuximab soravtansine-gynx)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Elahere is indicated for the treatment of adult patients with folate receptor-alpha positive, platinum-resistant epithelial ovarian, fallopian tube, or primary peritoneal cancer, who have received one to three prior systemic treatment regimens.

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 testing or laboratory results confirming folate receptor-alpha status, where applicable.

III. CRITERIA FOR INITIAL APPROVAL

Epithelial Ovarian, Fallopian Tube, or Primary Peritoneal Cancer
Authorization of 12 months may be granted for treatment of epithelial ovarian, fallopian tube, or primary peritoneal cancer when all of the following criteria are met:
1. Member has folate receptor-alpha positive disease
2. Member has platinum-resistant disease
3. Member has received at least one prior systemic 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. Elahere [package insert]. Waltham, MA: ImmunoGen, Inc.; November 2022.

POLICY Document for ELAPRASE (idursulfase)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, lower cost site of care and overall, clinically appropriate use. This document provides specific information to each of the three sections of the overall policy.

Section 1: Site of Care
- Policy information specific to site of care (outpatient, hospital outpatient, home infusion)

Section 2: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 1: Site of Care

Care First Site of Care Criteria
Administration of Intravenous Elaprase

POLICY

I. CRITERIA FOR APPROVAL FOR ADMINISTRATION IN OUTPATIENT HOSPITAL SETTING

This policy provides coverage for administration of Elaprase in an outpatient hospital setting for up to 54 days when a member is new to therapy or is reinitiating therapy after not being on therapy for at least 6 months.

This policy provides coverage for administration of Elaprase in an outpatient hospital setting for a longer course of treatment when ANY of the following criteria are met:

A. The member has experienced an adverse reaction to the drug that did not respond to conventional interventions (eg, acetaminophen, steroids, diphenhydramine, fluids, other pre-medications or slowing of infusion rate) or a severe adverse event (anaphylaxis, anaphylactoid reactions, myocardial infarction, thromboembolism, or seizures) during or immediately after (up to 24 hours post infusion) an infusion.
B. The member has developed idursulfase IgG antibodies which increases the risk for infusion related reactions.
C. The member is medically unstable (eg respiratory, cardiovascular, or renal conditions).
D. The member has severe venous access issues that require the use of special interventions only available in the outpatient hospital setting.
E. The member has significant behavioral issues and/or physical or cognitive impairment that would impact the safety of the infusion therapy AND the patient does not have access to a caregiver.
F. The member is less than 14 years of age.

For situations where administration of Elaprase does not meet the criteria for outpatient hospital infusion, coverage for Elaprase is provided when administered in alternative sites such as; physician office, home infusion or ambulatory care.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the site of care prior authorization review (where applicable):

A. Medical records supporting the member has experienced an adverse reaction that did not respond to conventional interventions or a severe adverse event during or immediately after an infusion
B. Medical records supporting the member has developed idursulfase IgG antibodies
C. Medical records supporting the member is medically unstable
D. Medical records supporting the member has severe venous access issues that requires specialized interventions only available in the outpatient hospital setting
E. Medical records supporting the member has behavioral issues and/or physical or cognitive impairment and no access to a caregiver

Section 2: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

ELAPRASE (idursulfase)

POLICY

III. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Elaprase is indicated for patients with Hunter syndrome (Mucopolysaccharidosis II, MPS II). Elaprase has been shown to improve walking capacity in patients 5 years and older. In patients 16 months to 5 years of age, no data are available to demonstrate improvement in disease-related symptoms or long term clinical outcome; however, treatment with Elaprase has reduced spleen volume similarly to that of adults and children 5 years of age and older. The safety and efficacy of Elaprase have not been established in pediatric patients less than 16 months of age.

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

IV. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
A. Initial requests: iduronate 2-sulfatase enzyme assay or genetic testing results supporting diagnosis.
B. Continuation requests: chart notes documenting a clinically positive response to therapy, which shall include improvement, stabilization, or slowing of disease progression.

V. CRITERIA FOR INITIAL APPROVAL

Mucopolysaccharidosis II (MPS II)
Authorization of 12 months may be granted for treatment of MPS II when the diagnosis of MPS II was confirmed by enzyme assay demonstrating a deficiency of iduronate 2-sulfatase enzyme activity or by genetic testing.

VI. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for mucopolysaccharidosis II (MPS II) who have a clinically positive response to therapy, which shall include improvement, stabilization, or slowing of disease progression.

REFERENCES

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SECTION 2

1. Elaprase [package insert]. Lexington, MA: Shire Human Genetic Therapies, Inc.; November 2018.
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POLICY Document for ELFABRIO
(pegunigalsidase alfa-iwxj)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, lower cost site of care and overall, clinically appropriate use. This document provides specific information to each of the three sections of the overall policy.

Section 1: Site of Care
- Policy information specific to site of care (outpatient, hospital outpatient, home infusion)

Section 2: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 1: Site of Care

CareFirst Site of Care Criteria
Administration of Intravenous Elfabrio

POLICY

I. CRITERIA FOR APPROVAL FOR ADMINISTRATION IN OUTPATIENT HOSPITAL SETTING

This policy provides coverage for administration of Elfabrio in an outpatient hospital setting for up to 106 days when a member is new to therapy or is reinitiating therapy after not being on therapy for at least 6 months.

This policy provides coverage for administration of Elfabrio in an outpatient hospital setting for a longer course of treatment when ANY of the following criteria are met:

A. The member has experienced an adverse reaction to the drug that did not respond to conventional interventions (eg, acetaminophen, steroids, diphenhydramine, fluids, pre-medications or slowing of infusion rate) or a severe adverse event (anaphylaxis, anaphylactoid reactions, myocardial infarction, thromboembolism, or seizures) during or immediately after an infusion.
B. The member has developed IgG or IgE anti-drug antibodies which increases the risk for infusion related reactions.
C. The member is medically unstable (eg respiratory, cardiovascular, or renal conditions).
D. The member has severe venous access issues that require the use of special interventions only available in the outpatient hospital setting.
E. The member has significant behavioral issues and/or physical or cognitive impairment that would impact the safety of the infusion therapy AND the patient does not have access to a caregiver.
F. The member is less than 14 years of age.

For situations where administration of Elfabrio does not meet the criteria for outpatient hospital infusion, coverage for Elfabrio is provided when administered in alternative sites such as; physician office, home infusion or ambulatory care.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the site of care prior authorization review (where applicable):

A. Medical records supporting the member has experienced an adverse reaction that did not respond to conventional interventions or a severe adverse event during or immediately after an infusion

B. Medical records supporting the member has developed IgG or IgE anti-drug antibodies
C. Medical records supporting the member is medically unstable
D. Medical records supporting the member has severe venous access issues that requires specialized interventions only available in the outpatient hospital setting
E. Medical records supporting the member has behavioral issues and/or physical or cognitive impairment and no access to a caregiver

Section 2: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

ELFABRIO (pegunigalsidase alfa-iwxj)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Elfabrio is indicated for the treatment of adults with confirmed Fabry 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. Initial requests: alpha-galactosidase enzyme assay or genetic testing results supporting diagnosis. In the case of obligate carriers, the documentation must be submitted for the parent.
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
Authorization of 12 months may be granted for treatment of Fabry disease when both of the following criteria are met:
A. The diagnosis of Fabry disease was confirmed by enzyme assay demonstrating a deficiency of alpha-galactosidase enzyme activity or by genetic testing, or the member is a symptomatic obligate carrier; and
B. The requested medication will not be used in combination with Galafold.

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).

REFERENCES

SECTION 1

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SECTION 2

1. Elfabrio [package insert]. Cary, NC: Chiesi USA, Inc.; May 2023.
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POLICY Document for ELELYSO (taliglucerase alfa)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, and overall, clinically appropriate use. This document provides specific information to both sections of the overall policy.

Section 1: Preferred Product
- Policy information specific to preferred medications

Section 2: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 1: Preferred Product

EXCEPTIONS CRITERIA
GAUCHER DISEASE AGENTS

PREFERRED PRODUCT: ELELYSO

POLICY

This policy informs prescribers of preferred products and provides an exception process for targeted products through prior authorization.

I. PLAN DESIGN SUMMARY

This program applies to the Gaucher disease products specified in this policy. Coverage for targeted products is provided based on clinical circumstances that would exclude the use of the preferred product and may be based on previous use of a product. The coverage review process will ascertain situations where a clinical exception can be made. This program applies to all members requesting treatment with a targeted product.

Each referral is reviewed based on all utilization management (UM) programs implemented for the client.

Table. Gaucher Disease Agents

	Product(s)
Preferred*	• **Elelyso** (taliglucerase alfa)
Targeted	• **Cerezyme** (imiglucerase) • **VPRIV** (velaglucerase alfa)

*: Medications considered formulary or preferred on your plan may still require a clinical prior authorization review.

II. EXCEPTION CRITERIA

This program applies to members requesting treatment for an indication that is FDA-approved for the preferred product.

Coverage for a targeted product is provided when the member has had a documented inadequate response or an intolerable adverse event with the preferred product.

CVS/caremark

Section 2: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

ELELYSO (taliglucerase 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
Elelyso is indicated for the treatment of patients 4 years and older with a confirmed diagnosis of Type 1 Gaucher disease.

B. Compendial Uses
1. Gaucher disease type 2
2. Gaucher disease type 3

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: beta-glucocerebrosidase enzyme assay or genetic testing results supporting diagnosis

III. CRITERIA FOR INITIAL APPROVAL

A. Gaucher disease type 1
Authorization of 12 months may be granted for treatment of Gaucher disease type 1 when the diagnosis of Gaucher disease was confirmed by enzyme assay demonstrating a deficiency of beta-glucocerebrosidase (glucosidase) enzyme activity or by genetic testing.

B. Gaucher disease type 2
Authorization of 12 months may be granted for treatment of Gaucher disease type 2 when the diagnosis of Gaucher disease was confirmed by enzyme assay demonstrating a deficiency of beta-glucocerebrosidase (glucosidase) enzyme activity or by genetic testing.

C. Gaucher disease type 3
Authorization of 12 months may be granted for treatment of Gaucher disease type 3 when the diagnosis of Gaucher disease was confirmed by enzyme assay demonstrating a deficiency of beta-glucocerebrosidase (glucosidase) enzyme activity or by genetic testing.

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.

Reference number(s)
6032-A

SPECIALTY GUIDELINE MANAGEMENT

ELEVIDYS (delandistrogene moxeparvovec-rokl)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Elevidys is indicated for the treatment of ambulatory pediatric patients aged 4 through 5 years with Duchenne muscular dystrophy (DMD) with a confirmed mutation in the *DMD* gene.

This indication is approved under accelerated approval based on expression of Elevidys micro-dystrophin in skeletal muscle observed in patients treated with Elevidys. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

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. Genetic test results confirming the DMD diagnosis.
B. Medical records (e.g., chart notes, lab reports) documenting the member's ambulation status.

III. EXCLUSIONS

Coverage will not be provided for members with any of the following exclusions:
A. Member has a deletion in exon 8 and/or exon 9 in the *DMD* gene.
B. Elevidys will not be used in combination with exon-skipping therapies (casimersen, eteplirsen, golodirsen, viltolarsen).

IV. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with a physician who specializes in the treatment of Duchenne muscular dystrophy (DMD).

V. CRITERIA FOR INITIAL APPROVAL

Duchenne muscular dystrophy
Authorization of 1 month for one dose total may be granted for treatment of Duchenne muscular dystrophy when all of the following criteria are met:

A. Member is 4 to 5 years of age (inclusive).
B. Member is ambulatory (e.g., able to walk with or without assistance, not wheelchair dependent).
C. Member has a definitive diagnosis of DMD confirmed via genetic testing.
D. Member has anti-recombinant adeno-associated virus serotype rh74 (anti-AAVrh74) total binding antibody titers of < 1:400.
E. Member has not received treatment with Elevidys previously.

VI. REFERENCES

1. Elevidys [package insert]. Cambridge, MA: Sarepta Therapeutics, Inc.; June 2023.

CVS/caremark

REFERENCES:

SECTION 1

1. Elelyso [package insert]. New York, NY: Pfizer, Inc; July 2021.
2. Cerezyme [package insert]. Cambridge, MA: Genzyme Corporation; December 2021.
3. VPRIV [package insert]. Lexington, MA: Shire Human Genetic Therapies, Inc.; September 2021.

SECTION 2

1. Elelyso [package insert]. New York, NY: Pfizer, Inc; July 2021.
2. Zimran A, Brill-Almon E, Chertkoff R, et al. Pivotal trial with plant cell-expressed recombinant glucocerebrosidase, taliglucerase alfa, a novel enzyme replacement therapy for Gaucher disease. *Blood*. 2011;118:5767-5773.
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4. Kaplan P, Baris H, De Meirleir L, et al. Revised recommendations for the management of Gaucher disease in children. *Eur J Pediatr.* 2013;172:447-458.
5. Vellodi A, Tylki-Szymanska A, Davies EH, et al. Management of neuronopathic Gaucher disease: revised recommendations. European Working Group on Gaucher Disease. *J Inherit Metab Dis*. 2009;32(5):660.
6. National Organization for Rare Disorders. (2003). NORD guide to rare disorders. Philadelphia: Lippincott Williams & Wilkins.

POLICY Document for ELIGARD (leuprolide acetate)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, and overall, clinically appropriate use. This document provides specific information to both sections of the overall policy.

Section 1: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 2: Oncology Clinical Policy
- Policy information specific to regimen review per NCCN Guidelines.

Section 1: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

ELIGARD (leuprolide 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
Palliative treatment of advanced prostate cancer

B. Compendial Uses
1. Prostate cancer
2. Recurrent androgen receptor positive salivary gland tumors
3. Gender Dysphoria (also known as gender non-conforming or transgender persons)

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

II. PRESCRIBER SPECIALTIES

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 patients less than 18 years of age.

III. CRITERIA FOR INITIAL APPROVAL

A. Prostate cancer
Authorization of 12 months may be granted for treatment of prostate cancer.

B. Gender dysphoria

1. Authorization of 12 months may be granted for pubertal hormonal suppression in an adolescent member when all of the following criteria are met:
   i. The member has a diagnosis of gender dysphoria.
   ii. The member has reached Tanner stage 2 of puberty or greater.
   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 transition when all of the following criteria are met:
   i. The member has a diagnosis of gender dysphoria.
   ii. The member will receive Eligard concomitantly with gender-affirming hormones.
   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.

C. 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.

IV. CONTINUATION OF THERAPY

A. Salivary gland tumors

Authorization of 12 months may be granted for continued treatment of salivary gland tumors in members requesting reauthorization who are experiencing clinical benefit to therapy and who have not experienced an unacceptable toxicity.

B. Prostate cancer

Authorization of 12 months may be granted for continued treatment of prostate cancer in members requesting reauthorization who are experiencing clinical benefit to therapy (e.g., serum testosterone less than 50 ng/dL) and who have not experienced an unacceptable toxicity.

C. Gender Dysphoria

1. Authorization of 12 months may be granted for continued treatment for pubertal hormonal suppression in adolescent members requesting reauthorization when all of the following criteria are met:
   a. The member has a diagnosis of gender dysphoria.
   b. The member has previously reached Tanner stage 2 of puberty or greater.
   c. The member's comorbid conditions are reasonably controlled.
   d. The member has been educated on any contraindications and side effects to therapy.
   e. 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 transition in members requesting reauthorization when all of the following criteria are met:
   a. The member has a diagnosis of gender dysphoria.
   b. The member will receive Eligard concomitantly with gender-affirming hormones.
   c. The member's comorbid conditions are reasonably controlled.
   d. The member has been educated on any contraindications and side effects to therapy.

   Before the start of therapy, the member has been informed of fertility preservation options.

Section 2: Oncology Clinical Policy

Oncology Clinical Policy

Program Description

The National Comprehensive Care Network® (NCCN®) is an alliance of leading cancer centers devoted to patient care, research and education dedicated to improving the quality, effectiveness and efficiency of cancer care so patients can live better lives.[1] It is comprised of oncology experts who convene regularly to establish the best treatments for patients. NCCN develops various resources for use by stakeholders in the health care delivery system. These resources include, but are not limited to, the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®), the NCCN Drugs & Biologics Compendium (NCCN Compendium®) and the NCCN Chemotherapy Order Templates (NCCN Templates®).

NCCN templates are based on NCCN Clinical Practice Guidelines and NCCN Compendium. The NCCN Compendium lists the appropriate drugs and biologics for specific cancers using U.S. Food and Drug Administration (FDA)-approved disease indications and specific NCCN panel recommendations. Each recommendation is supported by a level of evidence category.

NCCN Categories of Evidence and Consensus

Category 1: Based on high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2A: Based on lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2B: Based on lower-level evidence, there is NCCN consensus that the intervention is appropriate.
Category 3: Based any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

Policy for Regimen Prior Authorization

A regimen prior authorization allows submission of a single prior authorization request for all oncology drugs or biologics within an NCCN template that require prior authorization.

This policy provides coverage of a regimen review when *all* of the following criteria are met:

a. Regimen prior authorization reviews, based on NCCN templates, are initiated through the provider portal: https://provider.carefirst.com/providers/home.page
b. If the prior authorization request is submitted via phone or fax, each drug or biologic will need to be submitted and reviewed as a separate prior authorization request for review with drug-specific criteria.
c. 2. The prior authorization review is requested for an oncology drug or biologic that requires prior authorization on the medical benefit.
d. The indication is for a cancer that is eligible for regimen review. Currently, the cancer types in scope for regimen review include breast, lung, colon and rectal cancer.
e. The member is eligible for regimen review.

In addition, the following criteria must be met for approval:

a. The requested regimen for the drug(s) or biologic(s) and indication is consistent with an NCCN recommendation with a level of evidence category of 1 or 2A.
b. The NCCN template must be accepted by the provider without modification.

Authorizations may be granted for 12 months.
Further review may be indicated where the above criteria are not met.

Continuation of Therapy

To submit a request for continuation of therapy, a new regimen prior authorization review must be requested. Upon template selection, the template must be modified to include the appropriate therapies being used for maintenance treatment. The regimen request will be submitted for further review.

Dosage and Administration

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

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2. National Comprehensive Cancer Network. NCCN Categories of Evidence and Consensus website. https://www.nccn.org/professionals/physician_gls/categories_of_consensus.aspx, accessed September 16, 2019.
3. National Comprehensive Cancer Network. NCCN Guidelines website. http://www.nccn.org/professionals/physician_gls/f_guidelines.asp, accessed September 16, 2019. *(Note: An account may be required.)*
4. National Comprehensive Cancer Network. NCCN Drugs and Biologics Compendium® website. http://www.nccn.org/professionals/drug_compendium/content/contents.asp, accessed September 16, 2019. *(Note: A subscription may be required.)*
5. National Comprehensive Cancer Network. NCCN Chemotherapy Order Templates (NCCN Templates) website. https://www.nccn.org/professionals/OrderTemplates/Default.aspx, accessed September 16, 2019. *(Note: A subscription may be required.)*

Reference number(s)
2831-A

SPECIALTY GUIDELINE MANAGEMENT

ELZONRIS (tagraxofusp-erzs)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Elzonris is a CD123-directed cytotoxin indicated for the treatment of blastic plasmacytoid dendritic cell neoplasm (BPDCN) in adults and in pediatric patients 2 years and older.

B. Compendial Use
Blastic plasmacytoid dendritic cell neoplasm (BPDCN)

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 confirming the member is positive for CD123 expression

III. CRITERIA FOR INITIAL APPROVAL

Blastic plasmacytoid dendritic cell neoplasm (BPDCN)
Authorization of 12 months may be granted for treatment of blastic plasmacytoid dendritic cell neoplasm (BPDCN) when the member's disease is positive for CD123 expression and 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. Elzonris [package insert]. New York, NY: Stemline Therapeutics, Inc.; November 2022.
2. The NCCN Drugs & Biologics Compendium® © 2023 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed January 6, 2023.

B. Member has a documented inadequate response or intolerable adverse event with one of the preferred products.

Section 2: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

EMPAVELI (pegcetacoplan)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Empaveli is indicated for the treatment of adult patients with paroxysmal nocturnal hemoglobinuria (PNH).

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 new requests for treatment of:

A. For initial requests: flow cytometry used to show results of glycosylphosphatidylinositol-anchored proteins (GPI-APs) deficiency.
B. For continuation requests: Chart notes or medical record documentation supporting positive clinical response.

III. CRITERIA FOR INITIAL APPROVAL

Paroxysmal nocturnal hemoglobinuria
Authorization of 6 months may be granted for treatment of paroxysmal nocturnal hemoglobinuria (PNH) when all of the following criteria are met:

A. The diagnosis of PNH was confirmed by detecting a deficiency of glycosylphosphatidylinositol-anchored proteins (GPI-APs) as demonstrated by either of the following:
   1. At least 5% PNH cells
   2. At least 51% of GPI-AP deficient poly-morphonuclear cells
B. Flow cytometry is used to demonstrate GPI-APs deficiency

IV. CONTINUATION OF THERAPY

Paroxysmal nocturnal hemoglobinuria
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 and demonstrate a positive response to therapy (e.g., improvement in hemoglobin levels, normalization of lactate dehydrogenase [LDH] levels).

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.

Reference number(s)
2230-A

SPECIALTY GUIDELINE MANAGEMENT

EMPLICITI (elotuzumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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. Empliciti is indicated in combination with lenalidomide and dexamethasone for the treatment of adult patients with multiple myeloma who have received one to three prior therapies.
   2. Empliciti is indicated in combination with pomalidomide and dexamethasone for the treatment of adult patients with multiple myeloma who have received at least two prior therapies including lenalidomide and a proteasome inhibitor.

B. Compendial Uses
   Therapy for previously treated multiple myeloma for relapsed or progressive disease in combination with bortezomib and dexamethasone

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 lenalidomide and dexamethasone in members who have received at least one prior therapy
2. The requested medication will be used in combination with bortezomib and dexamethasone in members who have received at least one prior therapy
3. The requested medication will be used in combination with pomalidomide and dexamethasone in members who have received at least two prior therapies, including an immunomodulatory agent and a proteasome inhibitor

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. Empliciti [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; March 2022.

2. The NCCN Drugs & Biologics Compendium 2022 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed October 7, 2022.
3. The NCCN Clinical Practice Guidelines in Oncology Multiple Myeloma (Version 1.2023) 2022 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed October 7, 2022.

POLICY Document for ENHERTU (fam-trastuzumab deruxtecan-nxki)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, and overall, clinically appropriate use. This document provides specific information to both sections of the overall policy.

Section 1: Clinical Criteria

- Policy information specific to the clinical appropriateness for the medication

Section 2: Oncology Clinical Policy

- Policy information specific to regimen review per NCCN Guidelines.

Section 1: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

ENHERTU (fam-trastuzumab deruxtecan-nxki)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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. HER2-positive Breast Cancer
   Enhertu is indicated for the treatment of adult patients with unresectable or metastatic human epidermal growth factor receptor 2 (HER2)-positive breast cancer who have received a prior anti-HER2 based regimen either:
   i. in the metastatic setting, or
   ii. in the neoadjuvant or adjuvant setting and have developed disease recurrence during or within six months of completing therapy.
2. HER2-low Breast Cancer
   Enhertu is indicated for the treatment of adult patients with unresectable or metastatic HER2-low [immunohistochemistry score (IHC) 1+ or IHC 2+/ in situ hybridization test (ISH) negative] breast cancer, as determined by an FDA-approved test, who have received a prior chemotherapy in the metastatic setting or developed disease recurrence during or within 6 months of completing adjuvant chemotherapy.
3. Gastric or Gastroesophageal Junction Adenocarcinoma
   Enhertu is indicated for the treatment of adult patients with locally advanced or metastatic HER2-positive gastric or gastroesophageal junction adenocarcinoma who have received a prior trastuzumab-based regimen.
4. Non-Small Cell Lung Cancer (NSCLC)
   Enhertu is indicated for the treatment of adult patients with unresectable or metastatic non-small cell lung cancer (NSCLC) whose tumors have activating HER2 (ERBB2) mutations, as detected by an FDA-approved test, and who have received a prior systemic therapy.

B. Compendial Uses
1. HER2-positive breast cancer, treatment of recurrent disease
2. HER2-low breast cancer, treatment of recurrent disease
3. Non-small cell lung cancer with HER2 mutations, treatment of recurrent and advanced disease
4. HER2-amplified and RAS and BRAF wild-type colorectal cancer (including appendiceal and anal adenocarcinoma)
5. HER2-positive esophageal cancer
6. HER2-positive cervical cancer
7. HER2-positive endometrial carcinoma
8. HER2-positive salivary gland tumor

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: human epidermal growth factor receptor 2 (HER2) status (e.g., immunohistochemistry (IHC) score, in situ hybridization (ISH) test), RAS mutation status (where applicable), BRAF mutation status (where applicable)

III. CRITERIA FOR INITIAL APPROVAL

A. Breast cancer
Authorization of 12 months may be granted for treatment of breast cancer when either of the following criteria are met:
1. Member has HER2-positive breast cancer and meets all of the following criteria:
   i. The disease had no response to preoperative systemic therapy, or the disease is recurrent, metastatic, or unresectable
   ii. The requested medication will be used as a single agent.
2. Member has HER2-low (IHC 1+ or IHC 2+/ISH-) breast cancer and meets all of the following criteria:
   i. The disease had no response to preoperative systemic therapy, or the disease is recurrent, metastatic or unresectable
   ii. The member has tried at least one prior chemotherapy in the metastatic setting or developed recurrence during or within 6 months of completing adjuvant chemotherapy
   iii. The requested medication will be used as a single agent

B. Non-small cell lung cancer
Authorization of 12 months may be granted for subsequent treatment of non-small cell lung cancer with HER2 (ERBB2) mutations when both of the following criteria are met:
1. The disease is recurrent, advanced, metastatic or unresectable
2. The requested medication will be used as a single agent

C. Colorectal Cancer
Authorization of 12 months may be granted for treatment of colorectal cancer (including appendiceal and anal adenocarcinoma) with HER2-amplified and RAS and BRAF wild-type disease as a single agent when the requested medication will be used as subsequent therapy for progression of advanced or metastatic disease.

D. Esophageal, Gastric or Gastroesophageal Junction Adenocarcinoma
Authorization of 12 months may be granted for subsequent treatment of HER2-positive locally advanced, recurrent or metastatic esophageal, gastric or gastroesophageal junction adenocarcinoma as a single agent.

E. Cervical Cancer

Authorization of 12 months may be granted for subsequent treatment of recurrent or metastatic HER2-positive (IHC 3+ or 2+) cervical cancer when used as a single agent.

F. Endometrial Carcinoma
Authorization of 12 months may be granted for subsequent treatment of recurrent HER2-positive (IHC 3+ or 2+) endometrial carcinoma when used as a single agent.

G. Salivary Gland Tumor
Authorization of 12 months may be granted for treatment of recurrent HER2-positive salivary gland tumor 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.

Section 2: Oncology Clinical Policy

PROGRAM DESCRIPTION

The National Comprehensive Care Network® (NCCN®) is an alliance of leading cancer centers devoted to patient care, research and education dedicated to improving the quality, effectiveness, and efficiency of cancer care so patients can live better lives.[1] It is comprised of oncology experts who convene regularly to establish the best treatments for patients. NCCN develops various resources for use by stakeholders in the health care delivery system. These resources include, but are not limited to, the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®), the NCCN Drugs & Biologics Compendium (NCCN Compendium®) and the NCCN Chemotherapy Order Templates (NCCN Templates®).

NCCN Templates® are based on NCCN Guidelines® and NCCN Compendium®. The NCCN Compendium lists the appropriate drugs and biologics as treatment options for specific cancers using U.S. Food and Drug Administration (FDA)-approved disease indications and specific NCCN panel recommendations. Each recommendation is supported by a level of evidence category.

NCCN Categories of Evidence and Consensus[2]

- Category 1: Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
- Category 2A: Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
- Category 2B: Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.
- Category 3: Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

POLICY

Policy for Regimen Prior Authorization
A regimen prior authorization allows submission of a single prior authorization request for all oncology drugs or biologics within an NCCN template that require prior authorization.

PROCEDURE

This policy provides coverage of a regimen review when all of the following criteria are met:
1. Regimen prior authorization reviews, based on NCCN templates, are initiated through the provider portal.
    - If the prior authorization request is submitted via phone or fax, each drug or biologic will need to be submitted and reviewed as a separate prior authorization request for review with drug-specific criteria.
2. The prior authorization review is requested for an oncology drug or biologic.
3. The member is eligible for regimen review.
4. The indication is for a cancer that is eligible for regimen review. Currently, the cancer types in scope for regimen review include the following:
    - Ampullary Adenocarcinoma
    - Anal Carcinoma
    - B-Cell Lymphomas
    - Basal Cell Skin Cancer
    - Biliary Tract Cancers
    - Bone Cancer
    - Breast Cancer
    - Bladder Cancer
    - Central Nervous System Cancers
    - Cervical Cancer
    - Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma
    - Chronic Myeloid leukemia
    - Colon Cancer
    - Dermatofibrosarcoma Protuberans
    - Esophageal Cancer
    - Gastric Cancer
    - Gastrointestinal Stromal Tumors
    - Gestational Trophoblastic Neoplasms
    - Hairy Cell Leukemia
    - Head and Neck Cancers
    - Hodgkin Lymphoma
    - Hepatocellular Carcinoma
    - Kaposi Sarcoma
    - Kidney Cancer
    - Melanoma: Cutaneous
    - Melanoma: Uveal
    - Merkel Cell Carcinoma
    - Mesothelioma: Peritoneal
    - Mesothelioma: Pleural
    - Myelodysplastic Syndromes
    - Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Gene Fusions
    - Myeloproliferative Neoplasms
    - Neuroendocrine and Adrenal Tumors
    - Non-Small Cell Lung Cancer
    - Occult Primary
    - Ovarian Cancer
    - Pancreatic Cancer
    - Penile Cancer
    - Prostate Cancer
    - Rectal Cancer
    - Small Bowl Adenocarcinoma
    - Small Cell Lung Cancer
    - Soft Tissue Sarcoma
    - Squamous Cell Skin Cancer
    - Systemic Mastocytosis
    - Systemic Light Chain Amyloidosis

- Testicular Cancer
- Thymomas and Thymic Carcinomas
- Thyroid Carcinoma
- Uterine Neoplasms
- Vulvar Cancer
- Waldenström Macroglobulinemia / Lymphoplasmacytic Lymphoma

In addition, the following criteria must be met for approval:

1. The requested regimen for the drug(s) or biologic(s) and indication is consistent with an NCCN recommendation with a level of evidence category of 1 or 2A.
2. The NCCN template must be accepted by the provider without modification.

Further review may be indicated when the above criteria are not met.

Authorizations may be granted for 12 months or as medically required, based on the member's condition and provider's assessment.

Supportive Care: Myeloid Growth Factor Therapy
Granulocyte colony stimulating factors are recommended for primary prophylaxis based on the febrile neutropenia risk of the chemotherapy regimen. Febrile neutropenia risk levels vary by NCCN Chemotherapy Order template and are listed at the top of the template. Regimens associated with a high or intermediate risk of febrile neutropenia may include a granulocyte colony stimulating factor as part of the prior authorization.

Continuation of Therapy
To submit a request for continuation of therapy, a new regimen prior authorization review must be requested. Upon template selection, the template must be modified to include the appropriate therapies being used for maintenance treatment. The regimen request will be submitted for further review.

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

REFERENCES:

SECTION 1

1. Enhertu [package insert]. Basking Ridge, NJ: Daiichi Sankyo Inc.; August 2022.
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): Anal Carcinoma. Version 2.2022. Accessed December 12, 2022. https://www.nccn.org/professionals/physician_gls/pdf/anal.pdf

SECTION 2

1. National Comprehensive Cancer Network. About NCCN website. https://www.nccn.org/home/about, accessed June 6, 2023.
2. National Comprehensive Cancer Network. NCCN Categories of Evidence and Consensus website, https://www.nccn.org/guidelines/guidelines-process/development-and-update-of-guidelines, accessed June 6, 2023.
3. National Comprehensive Cancer Network. NCCN Guidelines website. https://www.nccn.org/guidelines/category_1, accessed June 6, 2023. (Note: An account may be required.)
4. National Comprehensive Cancer Network. NCCN Drugs and Biologics Compendium website https://www.nccn.org/compendia-templates/compendia/drugs-and-biologics-compendia, accessed June 6, 2023. (Note: A subscription may be required.)

5. National Comprehensive Cancer Network. NCCN Chemotherapy Order Templates (NCCN Templates) website. https://www.nccn.org/compendia-templates/nccn-templates-main/browse-by-cancer-type, accessed June 6, 2023. (Note: A subscription may be required.)

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.

POLICY Document for ENJAYMO

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, lower cost site of care and overall, clinically appropriate use. This document provides specific information to each of the three sections of the overall policy.

Section 1: Site of Care

- Policy information specific to site of care (outpatient, hospital outpatient, home infusion)

Section 2: Clinical Criteria

- Policy information specific to the clinical appropriateness for the medication

Section 1: Site of Care

CareFirst Site of Care Criteria
Administration of Intravenous Enjaymo

POLICY

I. CRITERIA FOR APPROVAL FOR ADMINISTRATION IN OUTPATIENT HOSPITAL SETTING

This policy provides coverage for administration of Enjaymo in an outpatient hospital setting for up to 45 days when a member is new to therapy or is reinitiating therapy after not being on therapy for at least 6 months.

This policy provides coverage for administration of Enjaymo in an outpatient hospital setting for a longer course of treatment when ANY of the following criteria are met:

A. The member has experienced an adverse reaction to the drug that did not respond to conventional interventions (eg, acetaminophen, steroids, diphenhydramine, fluids or other pre-medications) or a severe adverse event (anaphylaxis, anaphylactoid reactions, myocardial infarction, thromboembolism, or seizures) during or immediately after an infusion.
B. The member is medically unstable (eg respiratory, cardiovascular, or renal conditions).
C. The member has severe venous access issues that require the use of special interventions only available in the outpatient hospital setting.
D. The member has significant behavioral issues and/or physical or cognitive impairment that would impact the safety of the infusion therapy AND the patient does not have access to a caregiver.
E. The member is less than 14 years of age.

For situations where administration of Enjaymo does not meet the criteria for outpatient hospital infusion, coverage for Enjaymo is provided when administered in alternative sites such as physician office, home infusion or ambulatory care.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the site of care prior authorization review (where applicable):

A. Medical records supporting the member has experienced an adverse reaction that did not respond to conventional interventions or a severe adverse event during or immediately after an infusion
B. Medical records supporting the member is medically unstable

C. Medical records supporting the member has severe venous access issues that requires specialized interventions only available in the outpatient hospital setting
D. Medical records supporting the member has behavioral issues and/or physical or cognitive impairment and no access to a caregiver

Section 2: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

ENJAYMO (sutimlimab-jome)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Enjaymo is indicated for the treatment of hemolysis in adults with cold agglutinin disease (CAD).

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: chart notes, medical records or test results documenting:
   1. Lactate dehydrogenase (LDH) level above the upper limit of normal and haptoglobin level below the lower limit of normal
   2. Positive polyspecific direct antiglobulin test (DAT) result
   3. Monospecific DAT result strongly positive for C3d
   4. Cold agglutinin titer of 1:64 or higher measured at 4°C
   5. DAT result for IgG of 1+ or less
   6. Secondary CAD has been ruled out (e.g., cold agglutinin syndrome secondary to infection, rheumatologic disease, or active hematologic malignancy)
B. For continuation requests: Chart notes or medical record documentation supporting positive clinical response.

III. CRITERIA FOR INITIAL APPROVAL

Cold Agglutinin Disease (CAD)
Authorization of 6 months may be granted for the treatment of cold agglutinin disease (CAD) when all of the following criteria are met:
A. Confirmed diagnosis of primary cold agglutinin disease (CAD) based on all of the following:
   1. Evidence of hemolysis as indicated by both of the following:
      i. Lactate dehydrogenase (LDH) level above the upper limit of normal
      ii. Haptoglobin level below the lower limit of normal
   2. Positive polyspecific direct antiglobulin test (DAT) result

3. Monospecific DAT result strongly positive for C3d
4. Cold agglutinin titer of 1:64 or higher measured at 4°C
5. DAT result for IgG of 1+ or less

B. Secondary CAD has been ruled out (e.g., cold agglutinin syndrome secondary to infection, rheumatologic disease, or active hematologic malignancy)

IV. CONTINUATION OF THERAPY

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 and member demonstrates a positive response to therapy (e.g., improvement in hemoglobin levels, improvement in markers of hemolysis [e.g., bilirubin, haptoglobin, lactate dehydrogenase [LDH], reticulocyte count], a reduction in blood transfusions).

REFERENCES

SECTION 1

1. Enjaymo [package insert]. Waltham, MA: Bioverativ USA Inc.; March 2023.

SECTION 2

1. Enjaymo [package insert]. Waltham, MA: Bioverativ USA Inc.; January 2023.
2. Röth A, Barcellini W, D'Sa S, Miyakawa Y, Broome CM, Michel M, Kuter DJ, Jilma B, Tvedt THA, Fruebis J, et al. Sutimlimab in cold agglutinin disease. N Engl J Med. 2021;384(14):1323–34.
3. Jäger U, Barcellini W, Broome CM, et al. Diagnosis and treatment of autoimmune hemolytic anemia in adults: Recommendations from the First International Consensus Meeting. Blood Rev. 2020;41:100648.

POLICY Document for ENTYVIO (vedolizumab)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, lower cost site of care and overall, clinically appropriate use. This document provides specific information to each of the three sections of the overall policy.

Section 1: Site of Care

- Policy information specific to site of care (outpatient, hospital outpatient, home infusion)

Section 2: Clinical Criteria

- Policy information specific to the clinical appropriateness for the medication

Section 1: Site of Care

CareFirst Site of Care Criteria
Administration of Intravenous Entyvio

POLICY

I. CRITERIA FOR APPROVAL FOR ADMINISTRATION IN OUTPATIENT HOSPITAL SETTING

This policy provides coverage for administration of Entyvio in an outpatient hospital setting for 3 months when a member is new to therapy or reinitiating therapy after not being on therapy for at least 6 months.

This policy provides coverage for administration of Entyvio in an outpatient hospital setting for a longer course of treatment when ANY of the following criteria are met:

A. The member has experienced an adverse reaction that did not respond to conventional interventions (eg, acetaminophen, steroids, diphenhydramine, fluids or other pre-medications) or a severe adverse event (anaphylaxis, anaphylactoid reactions, myocardial infarction, thromboembolism, or seizures) during or immediately after an infusion.
B. The member is medically unstable (eg respiratory, cardiovascular, or renal conditions).
C. The member has severe venous access issues that require the use of special interventions only available in the outpatient hospital setting.
D. The member has significant behavioral issues and/or physical or cognitive impairment that would impact the safety of the infusion therapy AND the patient does not have access to a caregiver.
E. The member is less than 14 years of age.

For situations where administration of Entyvio does not meet the criteria for outpatient hospital infusion, coverage for Entyvio is provided when administered in alternative sites such as; physician office, home infusion or ambulatory care.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the site of care prior authorization review (where applicable):

A. Medical records supporting the member has experienced an adverse reaction that did not respond to conventional interventions or a severe adverse event during or immediately after an infusion

B. Medical records supporting the member is medically unstable
C. Medical records supporting the member has severe venous access issues that require specialized interventions only available in the outpatient hospital setting
D. Medical records supporting the member has behavioral issues and/or physical or cognitive impairment and no access to a caregiver

Section 2: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

ENTYVIO (vedolizumab)

POLICY

III. INDICATIONS

The indications below including FDA-approved indications and compendial 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 ulcerative colitis (UC)
   2. Adult patients with moderately to severely active Crohn's disease (CD)

B. Compendial Uses
   Immune checkpoint inhibitor-related toxicity

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

IV. DOCUMENTATION

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

A. 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.

B. Crohn's disease (CD)
   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 supporting diagnosis of fistulizing Crohn's disease (if applicable).

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

C. 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.

V. PRESCRIBER SPECIALTIES

The medication must be prescribed by or in consultation with one of the following:
A. Crohn's disease and ulcerative colitis: gastroenterologist
B. Immune checkpoint inhibitor-related toxicity: hematologist or oncologist

VI. CRITERIA FOR INITIAL APPROVAL

A. Ulcerative colitis (UC)

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

2. Authorization of 12 months may be granted for the treatment of moderately to severely active UC for adult members who had an inadequate response, intolerance or contraindication to at least one conventional therapy option (See Appendix A).

3. Authorization of 12 months may be granted for adult members who have been hospitalized for acute, severe UC (e.g., continuous bleeding, severe toxic symptoms, including fever and anorexia).

B. Crohn's disease (CD)

1. Authorization of 12 months may be granted for adult members who have previously received a biologic indicated for the treatment of moderately to severely active Crohn's disease.

2. Authorization of 12 months may be granted for the treatment of moderately to severely active CD in adult members who had an inadequate response, intolerance or contraindication to at least one conventional therapy option (See Appendix B).

3. Authorization of 12 months may be granted for the treatment of fistulizing CD in adult members.

C. Immune checkpoint inhibitor-related toxicity

Authorization of 1 month 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 systemic corticosteroids.

VII. CONTINUATION OF THERAPY

A. 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. Endoscopic appearance of the mucosa
   vii. Improvement on a disease activity scoring tool (e.g., Ulcerative Colitis Endoscopic Index of Severity [UCEIS], Mayo score)

B. 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 or fistulizing 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 or fistulizing 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. Endoscopic appearance of the mucosa
   vii. Improvement on a disease activity scoring tool (e.g., Crohn's Disease Activity Index [CDAI] score)

C. Immune checkpoint inhibitor-related toxicity

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

VIII. OTHER

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

IX. DOSAGE AND ADMINISTRATION

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

X. APPENDICES

Appendix A: Examples of Conventional Therapy Options for UC

1. Mild to moderate disease – induction of remission:
   a. Oral mesalamine (e.g., Asacol, Asacol HD, Lialda, Pentasa), balsalazide, olsalazine

b. Rectal mesalamine (e.g., Canasa, Rowasa)
c. Rectal hydrocortisone (e.g., Colocort, Cortifoam)
d. Alternatives: prednisone, azathioprine, mercaptopurine, sulfasalazine

2. Mild to moderate disease – maintenance of remission:
   a. Oral mesalamine, balsalazide, olsalazine, rectal mesalamine
   b. Alternatives: azathioprine, mercaptopurine, sulfasalazine
3. Severe disease – induction of remission:
   a. Prednisone, hydrocortisone IV, methylprednisolone IV
   b. Alternatives: cyclosporine IV, tacrolimus, sulfasalazine
4. Severe disease – maintenance of remission:
   a. Azathioprine, mercaptopurine
   b. Alternative: sulfasalazine

Appendix B: Examples of Conventional Therapy Options for CD

1. Mild to moderate disease – induction of remission:
   a. Oral budesonide
   b. Alternatives: metronidazole, ciprofloxacin, rifaximin
2. Mild to moderate disease – maintenance of remission:
   a. Azathioprine, mercaptopurine
   b. Alternatives: oral budesonide, methotrexate intramuscular (IM) or subcutaneous (SC), sulfasalazine
3. Moderate to severe disease – induction of remission:
   a. Prednisone, methylprednisolone intravenously (IV)
   b. Alternatives: methotrexate IM or SC
4. Moderate to severe disease – maintenance of remission:
   a. Azathioprine, mercaptopurine
   b. Alternative: methotrexate IM or SC
5. Perianal and fistulizing disease – induction of remission: Metronidazole ± ciprofloxacin, tacrolimus
6. Perianal and fistulizing disease – maintenance of remission
   a. Azathioprine, mercaptopurine
   b. Alternative: methotrexate IM or SC

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Reference number(s)
6002-A

SPECIALTY GUIDELINE MANAGEMENT

EPKINLY (epcoritamab- bysp)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Epkinly 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 indolent lymphoma, and high-grade B–cell lymphoma (HGBL), after two or more lines of systemic therapy.

B. Compendial Uses
B-Cell Lymphomas:
1. Diffuse Large B-Cell Lymphomas
2. High Grade B-Cell Lymphomas
3. Histologic Transformation of Indolent Lymphomas to Diffuse Large B-Cell Lymphoma
4. Human Immunodeficiency Virus (HIV)- Related B-Cell Lymphomas
   a. HIV-related diffuse large B-cell lymphoma
   b. Primary effusion lymphoma
   c. Human Herpes Virus Type 8 (HHV8)-positive diffuse large B-cell lymphoma, not otherwise specified
5. Monomorphic Post-Transplant Lymphoproliferative Disorders

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

II. CRITERIA FOR INITIAL APPROVAL

B-Cell Lymphomas
Authorization of 12 months may be granted for treatment of B-cell lymphoma after at least 2 prior lines of systemic therapy when the member has partial response, no response, progressive, relapsed or refractory disease with any of the following subtypes::
A. Diffuse Large B-Cell Lymphoma (DLBCL)
B. High Grade B- Cell Lymphoma
C. Histologic Transformation of Indolent Lymphoma to DLBCL
D. HIV-Related B- Cell Lymphoma including HIV-related DLBCL, primary effusion lymphoma, and HHV8-positive DLBCL, not otherwise specified when the requested medication is used as a single agent
E. Monomorphic Post-Transplant Lymphoproliferative Disorder 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

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POLICY Document for
EPOGEN, PROCRIT, RETACRIT (epoetin alfa)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, and overall, clinically appropriate use. This document provides specific information to both sections of the overall policy.

Section 1: Preferred Product
- Policy information specific to preferred medications

Section 2: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 1: Preferred Product

EXCEPTIONS CRITERIA
ERYTHROPOIESIS STIMULATING AGENTS
PREFERRED PRODUCTS: ARANESP AND RETACRIT

POLICY
This policy informs prescribers of preferred products and provides an exception process for targeted products through prior authorization.

I. PLAN DESIGN SUMMARY

This program applies to the erythropoiesis stimulating agents specified in this policy. Coverage for targeted products is provided based on clinical circumstances that would exclude the use of the preferred products and may be based on previous use of a product. The coverage review process will ascertain situations where a clinical exception can be made. This program applies to all members who are requesting treatment with the targeted products, Epogen or Procrit. This program also applies to members who are new to treatment with the targeted product, Mircera, for the first time.

Each referral is reviewed based on all utilization management (UM) programs implemented for the client.

Table. Erythropoiesis stimulating agents

	Product(s)
Preferred*	• **Aranesp** (darbepoetin alfa) • **Retacrit** (epoetin alfa-epbx)
Targeted	• **Epogen** (epoetin alfa) • **Mircera** (methoxy polyethylene glycol-epoetin beta) • **Procrit** (epoetin alfa)

*: Medications considered formulary or preferred on your plan may still require a clinical prior authorization review.

II. EXCEPTION CRITERIA

This program applies to members requesting treatment for an indication that is FDA-approved for the preferred products.

A. Mircera

Coverage for the targeted product is provided when the member meets either of the following criteria:

1. Member is currently receiving treatment with a targeted product, excluding when the requested targeted product is obtained as samples or via manufacturer's patient assistance programs.
2. Member has a documented inadequate response or intolerable adverse event with both of the preferred products, Retacrit and Aranesp.

B. Epogen or Procrit

Coverage for the targeted products are provided when both of the following criteria are met:

1. Member has had a documented intolerable adverse event with the preferred product, Retacrit, and the adverse event was not an expected adverse event attributed to the active ingredient as described in the prescribing information.
2. Member has experienced a documented inadequate response or intolerable adverse event with the preferred product, Aranesp, when prescribed for the treatment of anemia due to chronic kidney disease or the treatment of anemia due to myelosuppressive chemotherapy in cancer.

Section 2: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

EPOGEN, PROCRIT, RETACRIT (epoetin 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. Epoetin alfa is indicated for the treatment of anemia due to chronic kidney disease (CKD), including patients on dialysis and not on dialysis to decrease the need for red blood cell (RBC) transfusion.
2. Epoetin alfa is indicated for the treatment of anemia due to zidovudine administered at ≤ 4200 mg/week in HIV-infected patients with endogenous serum erythropoietin levels of ≤ 500 mUnits/mL.
3. Epoetin alfa is indicated for the 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.
4. Epoetin alfa is indicated to reduce the need for allogeneic RBC transfusions among patients with perioperative hemoglobin > 10 to ≤ 13 g/dL who are at high risk for perioperative blood loss from elective, noncardiac, nonvascular surgery. Epoetin alfa is not indicated for patients who are willing to donate autologous blood preoperatively.

B. Compendial Uses

1. Symptomatic anemia in patients with myelodysplastic syndromes (MDS)
2. Anemia in congestive heart failure
3. Anemia in rheumatoid arthritis
4. Anemia due to hepatitis C treatment with ribavirin in combination with either interferon alfa or peginterferon alfa
5. Anemia in patients whose religious beliefs forbid blood transfusions
6. Symptomatic anemia in patients with primary myelofibrosis, post-polycythemia vera myelofibrosis, or post-essential thrombocythemia myelofibrosis
7. 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 Epogen/Procrit/Retacrit. Members may not use Epogen/Procrit/Retacrit 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 < 500 mU/mL.

D. Reduction of Allogeneic Red Blood Cell Transfusion in Patients Undergoing Elective, Noncardiac, Nonvascular Surgery
Authorization of 30 days may be granted for reduction of allogenic red blood cell transfusion in members scheduled to have an elective, noncardiac, nonvascular surgery with pretreatment hemoglobin ≤ 13 g/dL.

E. Anemia in Congestive Heart Failure (CHF)
Authorization of 12 weeks may be granted for treatment of anemia in congestive heart failure in members with pretreatment hemoglobin < 9 g/dL.

F. Anemia in Rheumatoid Arthritis (RA)
Authorization of 12 weeks may be granted for treatment of anemia in rheumatoid arthritis in members with pretreatment hemoglobin < 10 g/dL.

G. Anemia Due to Hepatitis C Treatment
Authorization of 12 weeks may be granted for treatment of anemia due to Hepatitis C treatment in members with pretreatment hemoglobin < 10 g/dL who are receiving ribavirin in combination with either interferon alfa or peginterferon alfa.

H. Anemia Due to Zidovudine in HIV-infected Patients
Authorization of 12 weeks may be granted for treatment of anemia due to zidovudine in HIV-infected members currently receiving zidovudine with pretreatment hemoglobin < 10 g/dL whose pretreatment serum EPO level is < 500 mU/mL.

I. 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.

J. 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

K. 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 current 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 Epogen/Procrit/Retacrit. Members may not use Epogen/Procrit/Retacrit 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 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 the 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 is < 12 g/dL

D. Anemia in Congestive Heart Failure (CHF) or Rheumatoid Arthritis (RA)
Authorization of 12 weeks may be granted for continued treatment of anemia in congestive heart failure or anemia in rheumatoid arthritis with current hemoglobin < 12 g/dL.

E. Anemia Due to Hepatitis C Treatment
Authorization of 12 weeks may be granted for continued treatment of anemia due to Hepatitis C treatment in members who meet ALL of the following criteria:
1. The member is receiving ribavirin in combination with either interferon alfa or peginterferon alfa.
2. The current hemoglobin is < 12 g/dL.

F. Anemia Due to Zidovudine in HIV-infected Patients
Authorization of 12 weeks may be granted for continued treatment of anemia due to zidovudine in HIV-infected members receiving zidovudine with current hemoglobin < 12 g/dL.

G. 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.

H. 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 with current hemoglobin < 12 g/dL.

I. 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.

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Reference number(s)
1642-A

SPECIALTY GUIDELINE MANAGEMENT

Flolan (epoprostenol injection)
Veletri (epoprostenol injection)
epoprostenol 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
Flolan/Veletri/epoprostenol is indicated for the treatment of pulmonary arterial hypertension (PAH) (World Health Organization [WHO] Group I) to improve exercise capacity. Studies establishing effectiveness included predominantly patients with New York Heart Association (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)
Indefinite authorization 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

Indefinite authorization 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

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POLICY Document for ERBITUX® (cetuximab)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, and overall, clinically appropriate use. This document provides specific information to both sections of the overall policy.

Section 1: Clinical Criteria

- Policy information specific to the clinical appropriateness for the medication

Section 2: Oncology Clinical Policy

- Policy information specific to regimen review per NCCN Guidelines.

Section 1: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

ERBITUX® (cetuximab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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. Squamous Cell Carcinoma of the Head and Neck (SCCHN)
   Erbitux is indicated:
   a. In combination with radiation therapy for the initial treatment of locally or regionally advanced squamous cell carcinoma of the head and neck (SCCHN).
   b. In combination with platinum-based therapy with fluorouracil for the first-line treatment of patients with recurrent locoregional disease or metastatic SCCHN.
   c. As a single agent for the treatment of patients with recurrent or metastatic SCCHN for whom prior platinum-based therapy has failed.

2. K-Ras Wild-type, EGFR-expressing Colorectal Cancer (CRC)
   Erbitux is indicated for the treatment of K-Ras wild-type, epidermal growth factor receptor (EGFR)-expressing, metastatic colorectal cancer (mCRC) as determined by an FDA-approved test:
   a. In combination with FOLFIRI (irinotecan, fluorouracil, leucovorin) for first-line treatment,
   b. In combination with irinotecan in patients who are refractory to irinotecan-based chemotherapy,
   c. As a single agent in patients who have failed oxaliplatin- and irinotecan-based chemotherapy or who are intolerant to irinotecan.

   Limitations of Use:
   Erbitux is not indicated for treatment of Ras-mutant colorectal cancer or when the results of the Ras mutation tests are unknown.

3. BRAF V600E Mutation-Positive Metastatic Colorectal Cancer (CRC)

Erbitux is indicated, in combination with encorafenib, 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.

B. Compendial Uses
1. Colorectal cancer
2. Squamous cell carcinoma of the head and neck
3. Occult primary head and neck cancer
4. Penile cancer
5. Squamous cell skin cancer
6. 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:
A. Documentation of RAS wild-type status or KRAS G12C mutation, where applicable.
B. Documentation of BRAF mutation status, where applicable.
C. Documentation of EGFR expression, where applicable.

III. CRITERIA FOR INITIAL APPROVAL

A. Colorectal Cancer
Authorization of 6 months may be granted for treatment of colorectal cancer, including appendiceal adenocarcinoma and anal adenocarcinoma, for unresectable/inoperable, advanced, or metastatic disease and the member has not previously experienced clinical failure on panitumumab when either of the following criteria are met:
1. The member meets all of the following criteria:
   i. The *RAS (KRAS* and *NRAS)* mutation status is negative (wild-type)
   ii. If the tumor is positive for BRAF V600E mutation, the requested medication will be used in combination with encorafenib (Braftovi)
   iii. For colon cancer, the tumor is left-sided only, or
2. The member meets all of the following criteria:
   i. The disease is KRAS G12C mutation positive
   ii. The requested medication will be used in combination with sotorasib (Lumakras) or adagrasib (Krazati)
   iii. The member previously received treatment with chemotherapy

B. Squamous Cell Carcinoma of the Head and Neck
Authorization of 6 months may be granted for treatment of squamous cell carcinoma of the head and neck when any of the following criteria is met:
1. Disease is locally or regionally advanced, unresectable, recurrent, persistent, or metastatic.
2. Member is unfit for surgery.
3. The requested medication will be used in combination with radiation.

C. Occult Primary Head and Neck Cancer
Authorization of 6 months may be granted as a single agent for treatment of occult primary head and neck cancer for chemoradiation.

D. Penile Cancer
Authorization of 6 months may be granted as a single agent for subsequent treatment of metastatic penile cancer.

E. Squamous Cell Skin Cancer
Authorization of 6 months may be granted as a single agent for treatment of squamous cell skin cancer in unresectable/inoperable/incompletely resected, locally advanced, regional, recurrent, or distant metastatic disease.

F. Non-Small Cell Lung Cancer (NSCLC)
Authorization of 6 months may be granted for subsequent treatment of recurrent, advanced or metastatic NSCLC when all of the following criteria are met:
1. The requested medication will be used in combination with afatinib (Gilotrif).
2. The requested medication will be used in members with a known sensitizing EGFR mutation (e.g., EGFR exon 19 deletion or L858R mutation, or EGFR S768I, L861Q, and/or G719X mutation) following disease progression on EGFR tyrosine kinase inhibitor therapy.

IV. CONTINUATION OF THERAPY
Authorization of 6 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.

Section 2: Oncology Clinical Policy

PROGRAM DESCRIPTION

The National Comprehensive Care Network® (NCCN®) is an alliance of leading cancer centers devoted to patient care, research and education dedicated to improving the quality, effectiveness, and efficiency of cancer care so patients can live better lives.[1] It is comprised of oncology experts who convene regularly to establish the best treatments for patients. NCCN develops various resources for use by stakeholders in the health care delivery system. These resources include, but are not limited to, the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®), the NCCN Drugs & Biologics Compendium (NCCN Compendium®) and the NCCN Chemotherapy Order Templates (NCCN Templates®).

NCCN Templates® are based on NCCN Guidelines® and NCCN Compendium®. The NCCN Compendium lists the appropriate drugs and biologics as treatment options for specific cancers using U.S. Food and Drug Administration (FDA)-approved disease indications and specific NCCN panel recommendations. Each recommendation is supported by a level of evidence category.

NCCN Categories of Evidence and Consensus[2]
- Category 1: Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
- Category 2A: Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
- Category 2B: Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.
- Category 3: Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

POLICY

Policy for Regimen Prior Authorization
A regimen prior authorization allows submission of a single prior authorization request for all oncology drugs or biologics within an NCCN template that require prior authorization.

PROCEDURE

This policy provides coverage of a regimen review when all of the following criteria are met:
1. Regimen prior authorization reviews, based on NCCN templates, are initiated through the provider portal.
    - If the prior authorization request is submitted via phone or fax, each drug or biologic will need to be submitted and reviewed as a separate prior authorization request for review with drug-specific criteria.
2. The prior authorization review is requested for an oncology drug or biologic.
3. The member is eligible for regimen review.
4. The indication is for a cancer that is eligible for regimen review. Currently, the cancer types in scope for regimen review include the following:
    - Ampullary Adenocarcinoma
    - Anal Carcinoma
    - B-Cell Lymphomas
    - Basal Cell Skin Cancer
    - Biliary Tract Cancers
    - Bone Cancer
    - Breast Cancer
    - Bladder Cancer
    - Central Nervous System Cancers
    - Cervical Cancer
    - Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma
    - Chronic Myeloid leukemia
    - Colon Cancer
    - Dermatofibrosarcoma Protuberans
    - Esophageal Cancer
    - Gastric Cancer
    - Gastrointestinal Stromal Tumors
    - Gestational Trophoblastic Neoplasms
    - Hairy Cell Leukemia
    - Head and Neck Cancers
    - Hodgkin Lymphoma
    - Hepatocellular Carcinoma
    - Kaposi Sarcoma
    - Kidney Cancer
    - Melanoma: Cutaneous
    - Melanoma: Uveal
    - Merkel Cell Carcinoma
    - Mesothelioma: Peritoneal
    - Mesothelioma: Pleural
    - Myelodysplastic Syndromes
    - Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Gene Fusions
    - Myeloproliferative Neoplasms
    - Neuroendocrine and Adrenal Tumors
    - Non-Small Cell Lung Cancer
    - Occult Primary
    - Ovarian Cancer
    - Pancreatic Cancer
    - Penile Cancer
    - Prostate Cancer
    - Rectal Cancer
    - Small Bowl Adenocarcinoma
    - Small Cell Lung Cancer
    - Soft Tissue Sarcoma
    - Squamous Cell Skin Cancer
    - Systemic Mastocytosis

- o Systemic Light Chain Amyloidosis
- o Testicular Cancer
- o Thymomas and Thymic Carcinomas
- o Thyroid Carcinoma
- o Uterine Neoplasms
- o Vulvar Cancer
- o Waldenström Macroglobulinemia / Lymphoplasmacytic Lymphoma

In addition, the following criteria must be met for approval:

1. The requested regimen for the drug(s) or biologic(s) and indication is consistent with an NCCN recommendation with a level of evidence category of 1 or 2A.
2. The NCCN template must be accepted by the provider without modification.

Further review may be indicated when the above criteria are not met.

Authorizations may be granted for 12 months or as medically required, based on the member's condition and provider's assessment.

Supportive Care: Myeloid Growth Factor Therapy
Granulocyte colony stimulating factors are recommended for primary prophylaxis based on the febrile neutropenia risk of the chemotherapy regimen. Febrile neutropenia risk levels vary by NCCN Chemotherapy Order template and are listed at the top of the template. Regimens associated with a high or intermediate risk of febrile neutropenia may include a granulocyte colony stimulating factor as part of the prior authorization.

Continuation of Therapy
To submit a request for continuation of therapy, a new regimen prior authorization review must be requested. Upon template selection, the template must be modified to include the appropriate therapies being used for maintenance treatment. The regimen request will be submitted for further review.

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

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POLICY Document for TARCEVA (erlotinib)
erlotinib

The overall objective of this policy is to support the appropriate and cost-effective use of the medication. This document provides specific information to each section of the overall policy.

Section 1: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 2: Oncology Clinical Policy
- Policy information specific to regimen review per NCCN Guidelines.

Section 1: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT
TARCEVA (erlotinib)
erlotinib

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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)
   Tarceva is indicated for the 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 receiving first-line, maintenance, or second or greater line treatment after progression following at least one prior chemotherapy regimen.

   Limitations of use:
   a. Safety and efficacy of Tarceva have not been established in patients with NSCLC whose tumors have other EGFR mutations.
   b. Tarceva is not recommended for use in combination with platinum-based chemotherapy.

2. Pancreatic cancer
   Tarceva in combination with gemcitabine is indicated for the first-line treatment of patients with locally advanced, unresectable or metastatic pancreatic cancer.

B. Compendial Uses
1. NSCLC, recurrent, advanced or metastatic sensitizing EGFR mutation-positive
2. Recurrent bone cancer – recurrent chordoma
3. Renal cell carcinoma, relapsed or stage IV disease with non-clear cell histology
4. Brain metastases from EGFR sensitizing mutation-positive NSCLC
5. Recurrent pancreatic 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: EGFR mutation testing results (where applicable).

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 NSCLC (including brain metastases from NSCLC) when the member has sensitizing EGFR mutation-positive disease as a single agent or in combination with ramucirumab or bevacizumab.

B. Pancreatic cancer
Authorization of 12 months may be granted for treatment of locally advanced, unresectable, recurrent or metastatic pancreatic cancer in combination with gemcitabine.

C. Renal cell carcinoma (RCC)
Authorization of 12 months may be granted for treatment of relapsed or stage IV renal cell carcinoma with non-clear cell histology as a single agent or in combination with bevacizumab.

D. Chordoma
Authorization of 12 months may be granted for treatment of recurrent chordoma 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 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.

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.

Section 2: Oncology Clinical Policy

Oncology Clinical Policy

Program Description

The National Comprehensive Care Network® (NCCN®) is an alliance of leading cancer centers devoted to patient care, research and education dedicated to improving the quality, effectiveness and efficiency of cancer care so patients can live better lives.[1] It is comprised of oncology experts who convene regularly to establish the best treatments for patients. NCCN develops various resources for use by stakeholders in the health care delivery system. These resources include,

but are not limited to, the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®), the NCCN Drugs & Biologics Compendium (NCCN Compendium®) and the NCCN Chemotherapy Order Templates (NCCN Templates®).

NCCN templates are based on NCCN Clinical Practice Guidelines and NCCN Compendium. The NCCN Compendium lists the appropriate drugs and biologics for specific cancers using U.S. Food and Drug Administration (FDA)-approved disease indications and specific NCCN panel recommendations. Each recommendation is supported by a level of evidence category.

NCCN Categories of Evidence and Consensus[2]
Category 1: Based on high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2A: Based on lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2B: Based on lower-level evidence, there is NCCN consensus that the intervention is appropriate.
Category 3: Based any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

Policy for Regimen Prior Authorization

A regimen prior authorization allows submission of a single prior authorization request for all oncology drugs or biologics within an NCCN template that require prior authorization.

This policy provides coverage of a regimen review when *all* of the following criteria are met:
a. Regimen prior authorization reviews, based on NCCN templates, are initiated through the provider portal: https://provider.carefirst.com/providers/home.page
b. If the prior authorization request is submitted via phone or fax, each drug or biologic will need to be submitted and reviewed as a separate prior authorization request for review with drug-specific criteria.
2. The prior authorization review is requested for an oncology drug or biologic that requires prior authorization on the medical benefit.
3. The indication is for a cancer that is eligible for regimen review. Currently, the cancer types in scope for regimen review include breast, lung, colon and rectal cancer.
4. The member is eligible for regimen review.

In addition, the following criteria must be met for approval:
1. The requested regimen for the drug(s) or biologic(s) and indication is consistent with an NCCN recommendation with a level of evidence category of 1 or 2A.
2. The NCCN template must be accepted by the provider without modification. Authorizations may be granted for 12 months. Further review may be indicated where the above criteria are not met.

Continuation of Therapy

To submit a request for continuation of therapy, a new regimen prior authorization review must be requested. Upon template selection, the template must be modified to include the appropriate therapies being used for maintenance treatment. The regimen request will be submitted for further review.

Dosage and Administration

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

REFERENCES

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Reference number
2292-A

SPECIALTY GUIDELINE MANAGEMENT

ERWINAZE (asparaginase *Erwinia chrysanthemi*)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Erwinaze is indicated as a component of a multi-agent chemotherapeutic regimen for the treatment of patients with acute lymphoblastic leukemia (ALL) who have developed hypersensitivity to *E. coli*-derived asparaginase.

B. Compendial Uses
1. Extranodal natural killer/T-cell lymphoma: as a component of multi-agent chemotherapeutic regimen
2. Lymphoblastic lymphoma (managed in the same manner as ALL)
3. Acute lymphoblastic leukemia (ALL) as induction therapy for adults aged 65 years and older as a component of multi-agent chemotherapeutic regimen, or as a substitute for pegaspargase in cases of systemic allergic reaction or anaphylaxis due to pegaspargase hypersensitivity
4. Pediatric acute lymphoblastic leukemia (ALL) as a substitute for pegaspargase in cases of systemic allergic reaction or anaphylaxis due to pegaspargase hypersensitivity
5. Acute myeloid leukemia (AML)

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

II. CRITERIA FOR INITIAL APPROVAL

A. Acute Lymphoblastic Leukemia (ALL) and Lymphoblastic Lymphoma
Authorization of 12 months may be granted for the treatment of ALL or lymphoblastic lymphoma when the requested medication will be used in conjunction with multi-agent chemotherapy and any of the following criteria is met:
1. The member has previously received and developed hypersensitivity to an E. coli-derived asparaginase (e.g., pegaspargase).
2. The requested medication will be used as induction therapy for members age 65 years and older.

B. Extranodal Natural Killer/T-cell Lymphoma
Authorization of 12 months may be granted for the treatment of extranodal natural killer/T-cell lymphoma when both of the following criteria are met:
1. The member has previously received and developed hypersensitivity to an E. coli-derived asparaginase (e.g., pegaspargase).
2. The requested medication is used in conjunction with multi-agent chemotherapy.

C. Acute Myeloid Leukemia (AML)
Authorization of 12 months may be granted for the treatment of AML when both of the following criteria are met:

1. The member has previously received and developed hypersensitivity to an E. coli-derived asparaginase (e.g., pegaspargase).
2. The requested medication is used in conjunction with 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 disease progression or an unacceptable toxicity while on the current regimen.

IV. REFERENCES

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3. Erwinaze. Micromedex® (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed June 2, 2022.

Reference number(s)
2921-A

SPECIALTY GUIDELINE MANAGEMENT

EVENITY (romosozumab-aqqg)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Evenity is indicated for the treatment of osteoporosis in postmenopausal women 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.

Limitations of Use: Limit duration of use to 12 monthly doses. If osteoporosis therapy remains warranted, continued therapy with an anti-resorptive agent should be considered.

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 fragility fractures, T-score, and FRAX fracture probability as applicable to section III.

III. CRITERIA FOR INITIAL APPROVAL

Postmenopausal osteoporosis treatment
Authorization of a total of 12 months may be granted to postmenopausal members with osteoporosis when ANY of the following criteria are met:

A. Member has a history of fragility fractures
B. 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:
    1. 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)
    2. Member has failed prior treatment with or is intolerant to previous injectable osteoporosis therapy (e.g., zoledronic acid [Reclast], teriparatide [Forteo, Bonsity], denosumab [Prolia], abaloparatide [Tymlos])
    3. 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)

IV. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria AND have received less than 12 monthly doses of Evenity.

V. 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.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.

VI. REFERENCES

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POLICY Document for AFINITOR (everolimus) AFINITOR DISPERZ (everolimus) everolimus (generic)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication. This document provides specific information to each section of the overall policy.

Section 1: Clinical Criteria
Policy information specific to the clinical appropriateness for the medication
Section 2: Oncology Clinical Policy
Policy information specific to regimen review per NCCN Guidelines.

Section 1: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

AFINITOR (everolimus)
AFINITOR DISPERZ (everolimus)
everolimus (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. Hormone Receptor-Positive, HER2-Negative Breast Cancer
Afinitor is indicated for the treatment of postmenopausal women with advanced hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative breast cancer in combination with exemestane, after failure of treatment with letrozole or anastrozole.
2. Neuroendocrine Tumors (NET)
   a. Afinitor is indicated for the treatment of adult patients with progressive neuroendocrine tumors of pancreatic origin (PNET) with unresectable, locally advanced or metastatic disease.
   b. Afinitor is indicated for the treatment of adult patients with progressive, well-differentiated, non-functional neuroendocrine tumors (NET) of gastrointestinal (GI) or lung origin with unresectable, locally advanced or metastatic disease.
3. Renal Cell Carcinoma (RCC)
Afinitor is indicated for the treatment of adult patients with advanced renal cell carcinoma (RCC) after failure of treatment with sunitinib or sorafenib.
4. Tuberous Sclerosis Complex (TSC)-Associated Renal Angiomyolipoma
Afinitor is indicated for the treatment of adult patients with renal angiomyolipoma and tuberous sclerosis complex (TSC), not requiring immediate surgery.
5. Tuberous Sclerosis Complex (TSC)-Associated Subependymal Giant Cell Astrocytoma (SEGA)

Afinitor and Afinitor Disperz are indicated in adult and pediatric patients aged 1 year and older with tuberous sclerosis complex (TSC) for the treatment of subependymal giant cell astrocytoma (SEGA) that requires therapeutic intervention but cannot be curatively resected.

6. Tuberous Sclerosis Complex (TSC)-Associated Partial-Onset Seizures
   Afinitor Disperz is indicated for the adjunctive treatment of adult and pediatric patients aged 2 years and older with TSC-associated partial-onset seizures.

B. Compendial Uses
   1. Relapsed or stage IV renal cell carcinoma
   2. Soft tissue sarcoma subtypes:
      a. Perivascular epithelioid cell tumors (PEComa)
      b. Angiomyolipoma
      c. Lymphangioleiomyomatosis
   3. Gastrointestinal stromal tumors (GIST)
   4. Neuroendocrine tumors:
      a. Neuroendocrine tumors of the gastrointestinal tract, lung and thymus (carcinoid tumors)
      b. Neuroendocrine tumors of the pancreas
      c. Well differentiated Grade 3 neuroendocrine tumors
   5. Thymomas and thymic carcinomas
   6. Classic Hodgkin lymphoma
   7. Central nervous system cancers:
      a. Meningiomas
      b. Glioma
      c. Subependymal giant cell astrocytoma (SEGA)
   8. Thyroid carcinoma (papillary carcinoma, Hürthle cell carcinoma, and follicular carcinoma)
   9. Waldenström's macroglobulinemia/lymphoplasmacytic lymphoma
   10. Endometrial carcinoma
   11. HR+/HER2- breast cancer, recurrent unresectable or stage IV (M1)
   12. Tuberous sclerosis complex
   13. 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:

1. Documentation of the presence of phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha (PIK3CA) mutation (where applicable)
2. Hormone receptor (HR) and human epidermal growth factor receptor 2 (HER2) status (where applicable)

III. CRITERIA FOR INITIAL APPROVAL

A. Breast Cancer

Authorization of 12 months may be granted for subsequent treatment of hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative recurrent unresectable, advanced, or metastatic breast cancer when prescribed in combination with exemestane, fulvestrant, or tamoxifen.

B. Renal Cell Carcinoma
Authorization of 12 months may be granted for treatment of relapsed, advanced, or stage IV renal cell carcinoma when any of the following criteria are met:
1. The requested medication is given as a single agent or in combination with lenvatinib as subsequent therapy for clear cell histology; OR
2. The requested medication is given as single-agent or in combination with lenvatinib or bevacizumab for non-clear cell histology.

C. Neuroendocrine Tumors
Authorization of 12 months may be granted for the treatment of the following neuroendocrine tumors:
1. Neuroendocrine tumors of the gastrointestinal tract, lung, and thymus (carcinoid tumors)
2. Neuroendocrine tumors of the pancreas
3. Well differentiated Grade 3 neuroendocrine tumors

D. Tuberous Sclerosis Complex (TSC)
Authorization of 12 months may be granted for treatment of TSC.

E. Soft Tissue Sarcoma
Authorization of 12 months may be granted for treatment of any of the following subtypes of soft tissue sarcoma as single agent therapy: locally advanced unresectable or metastatic perivascular epithelioid cell tumor (PEComa), recurrent angiomyolipoma, or recurrent lymphangioleiomyomatosis.

F. Gastrointestinal Stromal Tumor (GIST)
Authorization of 12 months may be granted for treatment of unresectable, recurrent/progressive, or metastatic GIST in combination with either imatinib, sunitinib, or regorafenib for members who have failed at least four FDA-approved therapies (e.g., imatinib, sunitinib, regorafenib, ripretinib)

G. Thymoma and Thymic Carcinoma
Authorization of 12 months may be granted for treatment of thymoma or thymic carcinoma as a single agent.

H. Classic Hodgkin Lymphoma
Authorization of 12 months may be granted for treatment of relapsed or refractory classic Hodgkin lymphoma for third-line or subsequent systemic therapy as a single agent.

I. Waldenström's Macroglobulinemia/Lymphoplasmacytic Lymphoma
Authorization of 12 months may be granted for treatment of Waldenström's macroglobulinemia/lymphoplasmacytic lymphoma as a single-agent therapy for previously treated disease.

J. 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.

K. Endometrial Carcinoma
Authorization of 12 months may be granted for treatment of endometrial carcinoma in combination with letrozole.

L. Central Nervous System Cancers
Authorization of 12 months may be granted for treatment of the following central nervous system cancers:
1. Glioma (including glioblastoma) or meningioma
2. Adjuvant treatment of subependymal giant cell astrocytoma (SEGA) as a single agent

M. 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 phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha (PIK3CA) mutation:
1. Symptomatic or relapsed/refractory Erdheim-Chester Disease (ECD)
2. Symptomatic or relapsed/refractory Rosai-Dorfman Disease
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 in Section III when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

Section 2: Oncology Clinical Policy

Oncology Clinical Policy

Program Description
The National Comprehensive Care Network® (NCCN®) is an alliance of leading cancer centers devoted to patient care, research and education dedicated to improving the quality, effectiveness and efficiency of cancer care so patients can live better lives.[1] It is comprised of oncology experts who convene regularly to establish the best treatments for patients. NCCN develops various resources for use by stakeholders in the health care delivery system. These resources include, but are not limited to, the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®), the NCCN Drugs & Biologics Compendium (NCCN Compendium®) and the NCCN Chemotherapy Order Templates (NCCN Templates®).

NCCN templates are based on NCCN Clinical Practice Guidelines and NCCN Compendium. The NCCN Compendium lists the appropriate drugs and biologics for specific cancers using U.S. Food and Drug Administration (FDA)-approved disease indications and specific NCCN panel recommendations. Each recommendation is supported by a level of evidence category.

NCCN Categories of Evidence and Consensus[2]
Category 1: Based on high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2A: Based on lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2B: Based on lower-level evidence, there is NCCN consensus that the intervention is appropriate.
Category 3: Based any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

Policy for Regimen Prior Authorization
A regimen prior authorization allows submission of a single prior authorization request for all oncology drugs or biologics within an NCCN template that require prior authorization.

This policy provides coverage of a regimen review when *all* of the following criteria are met:

a. Regimen prior authorization reviews, based on NCCN templates, are initiated through the provider portal: https://provider.carefirst.com/providers/home.page

b. If the prior authorization request is submitted via phone or fax, each drug or biologic will need to be submitted and reviewed as a separate prior authorization request for review with drug-specific criteria.

2. The prior authorization review is requested for an oncology drug or biologic that requires prior authorization on the medical benefit.
3. The indication is for a cancer that is eligible for regimen review. Currently, the cancer types in scope for regimen review include breast, lung, colon and rectal cancer.
4. The member is eligible for regimen review.

In addition, the following criteria must be met for approval:
1. The requested regimen for the drug(s) or biologic(s) and indication is consistent with an NCCN recommendation with a level of evidence category of 1 or 2A.
2. The NCCN template must be accepted by the provider without modification. Authorizations may be granted for 12 months. Further review may be indicated where the above criteria are not met.

Continuation of Therapy

To submit a request for continuation of therapy, a new regimen prior authorization review must be requested. Upon template selection, the template must be modified to include the appropriate therapies being used for maintenance treatment. The regimen request will be submitted for further review.

Dosage and Administration

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

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SECTION 1

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SECTION 2

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3. National Comprehensive Cancer Network. NCCN Guidelines website. http://www.nccn.org/professionals/physician_gls/f_guidelines.asp, accessed September 16, 2019. (Note: An account may be required.)
4. National Comprehensive Cancer Network. NCCN Drugs and Biologics Compendium® website. http://www.nccn.org/professionals/drug_compendium/content/contents.asp, accessed September 16, 2019. (Note: A subscription may be required.)
5. National Comprehensive Cancer Network. NCCN Chemotherapy Order Templates (NCCN Templates) website. https://www.nccn.org/professionals/OrderTemplates/Default.aspx, accessed September 16, 2019. (Note: A subscription may be required.)

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POLICY Document for EVKEEZA (evinacumab-dgnb)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, lower cost site of care and overall, clinically appropriate use. This document provides specific information to each of the three sections of the overall policy.

Section 1: Site of Care

- Policy information specific to site of care (outpatient, hospital outpatient, home infusion)

Section 2: Clinical Criteria

- Policy information specific to the clinical appropriateness for the medication

Section 1: Site of Care

CareFirst Site of Care Criteria
Administration of Intravenous Evkeeza

POLICY

I. CRITERIA FOR APPROVAL FOR ADMINISTRATION IN OUTPATIENT HOSPITAL SETTING

This policy provides coverage for administration of Evkeeza in an outpatient hospital setting for up to 45 days when a member is new to therapy or is reinitiating therapy after not being on therapy for at least 6 months.

This policy provides coverage for administration of Evkeeza in an outpatient hospital setting for a longer course of treatment when ANY of the following criteria are met:

A. The member has experienced an adverse reaction to the drug that did not respond to conventional interventions (eg, acetaminophen, steroids, diphenhydramine, fluids, other pre-medications or slowing of infusion rate) or a severe adverse event (anaphylaxis, anaphylactoid reactions, myocardial infarction, thromboembolism, or seizures) during or immediately after an infusion.
B. The member is medically unstable (eg respiratory, cardiovascular, or renal conditions).
C. The member has severe venous access issues that require the use of special interventions only available in the outpatient hospital setting.
D. The member has significant behavioral issues and/or physical or cognitive impairment that would impact the safety of the infusion therapy AND the patient does not have access to a caregiver.
E. The member is less than 14 years of age.

For situations where administration of Evkeeza does not meet the criteria for outpatient hospital infusion, coverage for Evkeeza is provided when administered in alternative sites such as physician office, home infusion or ambulatory care.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the site of care prior authorization review (where applicable):

A. Medical records supporting the member has experienced an adverse reaction that did not respond to conventional interventions or a severe adverse event during or immediately after an infusion
B. Medical records supporting the member is medically unstable

C. Medical records supporting the member has severe venous access issues that requires specialized interventions only available in the outpatient hospital setting
D. Medical records supporting the member has behavioral issues and/or physical or cognitive impairment and no access to a caregiver

Section 2: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

EVKEEZA (evinacumab-dgnb)

POLICY

III. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Evkeeza is indicated as an adjunct to other low-density lipoprotein-cholesterol (LDL-C) lowering therapies for the treatment of adult and pediatric patients, aged 12 years and older, with homozygous familial hypercholesterolemia (HoFH).

Limitations of Use:
- The safety and effectiveness of Evkeeza have not been established in patients with other causes of hypercholesterolemia, including those with heterozygous familial hypercholesterolemia (HeFH).
- The effects of Evkeeza on cardiovascular morbidity and mortality have not been determined.

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

IV. 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 maximally tolerated lipid lowering therapy for both initial requests and continuation requests

V. 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 has 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])
2. Member is receiving stable treatment with at least 3 lipid-lowering therapies (e.g., statins, ezetimibe, proprotein convertase subtilisin/kexin type 9 (PCSK9) directed therapy) at the maximally tolerated dose

C. Member will continue to receive concomitant lipid-lowering therapy
D. Member is 12 years of age or older

VI. 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 is currently receiving concomitant lipid-lowering therapy at the maximally tolerated dose
C. The member is receiving benefit from therapy. Benefit is defined as either of the following:
1. LDL-C is now at goal
2. Member has had at least 30% reduction of LDL-C from baseline

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SECTION 2

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POLICY Document for EXONDYS 51 (eteplirsen)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, lower cost site of care and overall, clinically appropriate use. This document provides specific information to each of the three sections of the overall policy.

Section 1: Site of Care

- Policy information specific to site of care (outpatient, hospital outpatient, home infusion)

Section 2: Clinical Criteria

- Policy information specific to the clinical appropriateness for the medication

Section 1: Site of Care

CareFirst Site of Care Criteria
Administration of Intravenous Exondys 51

POLICY

I. CRITERIA FOR APPROVAL FOR ADMINISTRATION IN OUTPATIENT HOSPITAL SETTING

This policy provides coverage for administration of Exondys 51 in an outpatient hospital setting for up to 45 days when a member is new to therapy or reinitiating therapy after not being on therapy for at least 6 months.

This policy provides coverage for administration of Exondys 51 in an outpatient hospital setting for a longer course of treatment when ANY of the following criteria are met:

A. The member has experienced an adverse reaction to the drug that did not respond to conventional interventions (eg, acetaminophen, steroids, diphenhydramine, fluids, other pre-medications or slowing of infusion rate) or a severe adverse event (anaphylaxis, anaphylactoid reactions, myocardial infarction, thromboembolism, or seizures) during or immediately after an infusion.
B. The member is medically unstable (eg respiratory, cardiovascular, or renal conditions).
C. The member has severe venous access issues that require the use of special interventions only available in the outpatient hospital setting.
D. The member has significant behavioral issues and/or physical or cognitive impairment that would impact the safety of the infusion therapy AND the patient does not have access to a caregiver.
E. The member is less than 14 years of age.

For situations where administration of Exondys 51 does not meet the criteria for outpatient hospital infusion, coverage for Exondys 51 is provided when administered in alternative sites such as; physician office, home infusion or ambulatory care.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the site of care prior authorization review (where applicable):

A. Medical records supporting the member has experienced an adverse reaction that did not respond to conventional interventions or a severe adverse event during or immediately after an infusion
B. Medical records supporting the member is medically unstable
C. Medical records supporting the member has severe venous access issues that requires specialized interventions only available in the outpatient hospital setting

D. Medical records supporting the member has behavioral issues and/or physical or cognitive impairment and no access to a caregiver

Section 2: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

EXONDYS 51 (eteplirsen)

POLICY

III. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Exondys 51 is indicated for the treatment of Duchenne muscular dystrophy (DMD) in patients who have a confirmed mutation of the DMD gene that is amenable to exon 51 skipping.

This indication is approved under accelerated approval based on an increase in dystrophin in skeletal muscle observed in some patients treated with Exondys 51. Continued approval for this indication may be contingent upon verification of a clinical benefit in confirmatory trials.

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

IV. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
A. Initial requests: laboratory confirmation of Duchenne muscular dystrophy (DMD) diagnosis with a *DMD* gene mutation that is amenable to exon 51 skipping (refer to examples in Appendix).
B. Continuation of therapy requests: documentation (e.g., chart notes) of response to therapy.

V. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with a physician who specializes in treatment of Duchenne muscular dystrophy (DMD).

VI. 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:
1. Genetic testing was conducted to confirm the diagnosis of DMD and to identify the specific type of *DMD* gene mutation.
2. The *DMD* gene mutation is amenable to exon 51 skipping (refer to examples in Appendix).
3. Treatment with Exondys 51 is initiated before the age of 14.
4. Member is able to achieve an average distance of at least 180 meters while walking independently over 6 minutes.

5. Member will not exceed a dose of 30 mg/kg once weekly.

VII. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for members requesting continuation of therapy when both of the following criteria are met:

A. The member has demonstrated a response to therapy as evidenced by remaining ambulatory (e.g., able to walk with or without assistance, not wheelchair dependent).
B. The member will not exceed a dose of 30 mg/kg once weekly.

VIII. APPENDIX

Examples of *DMD* gene mutations (exon deletions) amenable to exon 51 skipping (not an all-inclusive list):

1. Deletion of exon 50
2. Deletion of exon 52
3. Deletion of exons 45-50
4. Deletion of exons 47-50
5. Deletion of exons 48-50
6. Deletion of exons 49-50

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SECTION 2

1. Exondys 51 [package insert]. Cambridge, MA: Sarepta Therapeutics, Inc.; January 2022.
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III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment of an indication listed in Section II for members who have demonstrated a positive clinical response to therapy (e.g., improvement or maintenance in best corrected visual acuity [BCVA] or visual field, or a reduction in the rate of vision decline or the risk of more severe vision loss).

REFERENCES:

SECTION 1

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POLICY Document for EYLEA (aflibercept)
EYLEA HD (aflibercept)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, and overall, clinically appropriate use. This document provides specific information to both sections of the overall policy.

Section 1: Preferred Product
- Policy information specific to preferred medications

Section 2: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 1: Preferred Product

EXCEPTIONS CRITERIA
VEGF INHIBITORS FOR OCULAR INDICATIONS

PREFERRED PRODUCTS: AVASTIN, BYOOVIZ

POLICY
This policy informs prescribers of preferred products and provides an exception process for targeted products through prior authorization.

I. PLAN DESIGN SUMMARY

This program applies to the VEGF inhibitor ocular products specified in this policy. Coverage for targeted products is provided based on clinical circumstances that would exclude the use of the preferred product and may be based on previous use of a product. The coverage review process will ascertain situations where a clinical exception can be made. For Lucentis, this program applies to all members requesting treatment with a targeted product. For Eylea, this program applies to members who are new to treatment with a targeted product for the first time for an ocular indication.

Each referral is reviewed based on all utilization management (UM) programs implemented for the client.

Table. VEGF Inhibitors for Ocular indications

	Product(s)
Preferred*	• **Avastin** (bevacizumab) • **Byooviz** (ranibizumab-nuna)
Targeted	• **Eylea** (aflibercept) • **Lucentis** (ranibizumab)

*: Medications considered formulary or preferred on your plan may still require a clinical prior authorization review.

II. EXCEPTION CRITERIA

This program applies to members requesting treatment for ocular indications.

A. Eylea

Coverage of the targeted product Eylea is provided when any of the following criteria is met:

1. Member is currently receiving treatment with a targeted product, excluding when the requested targeted product is obtained as samples or via manufacturer's patient assistance programs.
2. Member has a documented inadequate response or intolerable adverse event with both preferred products, Avastin and Byooviz.

B. Lucentis

Coverage for the targeted product Lucentis is provided when both of the following criteria are met:

1. Member has failed treatment with the preferred product Byooviz due to a documented intolerable adverse event that was NOT an expected adverse event attributed to the active ingredient as described in the prescribing information (i.e., known adverse reaction for both products).
2. Member has a documented inadequate response or intolerable adverse event with the preferred product, Avastin.

Section 2: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

EYLEA (aflibercept)
EYLEA HD (aflibercept)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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

Eylea is indicated for the treatment of:

A. Diabetic macular edema
B. Diabetic retinopathy
C. Neovascular (wet) age-related macular degeneration
D. Macular edema following retinal vein occlusion
E. Retinopathy of Prematurity

Eylea HD is indicated for the treatment of:

A. Diabetic macular edema
B. Diabetic retinopathy
C. Neovascular (wet) age-related macular degeneration

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

II. CRITERIA FOR INITIAL APPROVAL

A. Diabetic Macular Edema

Authorization of 6 months may be granted for treatment of diabetic macular edema.

B. Diabetic Retinopathy

Authorization of 6 months may be granted for treatment of diabetic retinopathy.

C. Neovascular (Wet) Age-Related Macular Degeneration
Authorization of 6 months may be granted for treatment of neovascular (wet) age-related macular degeneration.

D. Macular Edema Following Retinal Vein Occlusion
Authorization of 6 months may be granted for treatment of macular edema following retinal vein occlusion.

E. Retinopathy of Prematurity
Authorization of 6 months may be granted for treatment of retinopathy of prematurity.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment of an indication listed in Section II for members who have demonstrated a positive clinical response to therapy (e.g., improvement or maintenance in best corrected visual acuity [BCVA] or visual field, or a reduction in the rate of vision decline or the risk of more severe vision loss).

REFERENCES:

SECTION 1
1. Avastin [package insert]. South San Francisco, CA: Genentech, Inc.; December 2020.
2. Eylea [package insert]. Tarrytown, NY: Regeneron Pharmaceuticals, Inc.; August 2022.
3. Lucentis [package insert]. San Francisco, CA: Genentech, Inc.; March 2018.
4. Byooviz (ranibizumab) [package insert]. Cambridge, MA: Biogen Inc; June 2022

SECTION 2
1. Eylea [package insert]. Tarrytown, NY: Regeneron Pharmaceuticals; February 2023.
2. Eylea HD [package insert]. Tarrytown, NY: Regeneron Pharmaceuticals; August 2023.
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POLICY Document for FABRAZYME (agalsidase beta)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, lower cost site of care and overall, clinically appropriate use. This document provides specific information to each of the three sections of the overall policy.

Section 1: Site of Care

- Policy information specific to site of care (outpatient, hospital outpatient, home infusion)

Section 2: Clinical Criteria

- Policy information specific to the clinical appropriateness for the medication

Section 1: Site of Care

CareFirst Site of Care Criteria
Administration of Intravenous Fabrazyme

POLICY

I. CRITERIA FOR APPROVAL FOR ADMINISTRATION IN OUTPATIENT HOSPITAL SETTING

This policy provides coverage for administration of Fabrazyme in an outpatient hospital setting for up to 106 days when a member is new to therapy or is reinitiating therapy after not being on therapy for at least 6 months.

This policy provides coverage for administration of Fabrazyme in an outpatient hospital setting for a longer course of treatment when ANY of the following criteria are met:

A. The member has experienced an adverse reaction to the drug that did not respond to conventional interventions (eg, acetaminophen, steroids, diphenhydramine, fluids, pre-medications or slowing of infusion rate) or a severe adverse event (anaphylaxis, anaphylactoid reactions, myocardial infarction, thromboembolism, or seizures) during or immediately after an infusion.
B. The member has developed fabrazyme IgE antibodies which increases the risk for infusion related reactions.
C. The member is medically unstable (eg respiratory, cardiovascular, or renal conditions).
D. The member has severe venous access issues that require the use of special interventions only available in the outpatient hospital setting.
E. The member has significant behavioral issues and/or physical or cognitive impairment that would impact the safety of the infusion therapy AND the patient does not have access to a caregiver.
F. The member is less than 14 years of age.

For situations where administration of Fabrazyme does not meet the criteria for outpatient hospital infusion, coverage for Fabrazyme is provided when administered in alternative sites such as; physician office, home infusion or ambulatory care.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the site of care prior authorization review (where applicable):

A. Medical records supporting the member has experienced an adverse reaction that did not respond to conventional interventions or a severe adverse event during or immediately after an infusion
B. Medical records supporting the member has developed fabrazyme IgE antibodies
C. Medical records supporting the member is medically unstable
D. Medical records supporting the member has severe venous access issues that requires specialized interventions only available in the outpatient hospital setting
E. Medical records supporting the member has behavioral issues and/or physical or cognitive impairment and no access to a caregiver

Section 2: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

FABRAZYME (agalsidase 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 Indication
Fabrazyme is indicated for the treatment of adult and pediatric patients 2 years of age and older with confirmed Fabry 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. Initial requests: alpha-galactosidase enzyme assay or genetic testing results supporting diagnosis. In the case of obligate carriers, the documentation must be submitted for the parent.
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
Authorization of12 months may be granted for treatment of Fabry disease when both of the following criteria are met:
A. The diagnosis of Fabry disease was confirmed by enzyme assay demonstrating a deficiency of alpha-galactosidase enzyme activity or by genetic testing, or the member is a symptomatic obligate carrier; and
B. Fabrazyme will not be used in combination with Galafold.

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,

REFERENCES

SECTION 1

1. Fabrazyme [package insert]. Cambridge, MA: Genzyme Corporation.; March 2021.
2. Cousins A, Lee P, Rorman D, et al. Home-based infusion therapy for patients with Fabry disease. *Br J Nurs.* 2008;17(10):653-657.
3. Wilcox WR, Banikazemi M, Guffon N, et al. Long-term safety and efficacy of enzyme replacement therapy for Fabry disease. *Am J Hum Genet.* 2004;75(1):65-74.
4. Banikazemi M, Bultas J, Waldek S, et al. Agalsidase-beta therapy for advanced Fabry disease: a randomized trial. *Ann Intern Med.* 2007;146(2):77-86.

SECTION 2

1. Fabrazyme [package insert]. Cambridge, MA: Genzyme Corporation; March 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.

POLICY Document for
REBINYN (coagulation factor IX [recombinant], glycoPEGylated)

IDELVION (coagulation factor IX [recombinant], albumin fusion protein)

ALPROLIX (coagulation factor IX [recombinant], Fc fusion protein)

BENEFIX, IXINITY, RIXUBIS (coagulation factor IX [recombinant])

ALPHANINE SD (coagulation factor IX [human])

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, and overall, clinically appropriate use. This document provides specific information to both sections of the overall policy.

Section 1: Preferred Product
- Policy information specific to preferred medications

Section 2: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 1: Preferred Product

EXCEPTIONS CRITERIA
FACTOR IX PRODUCTS

PREFERRED PRODUCTS: ALPROLIX, IDELVION, AND REBINYN

POLICY
This policy informs prescribers of preferred products and provides an exception process for targeted products through prior authorization.

I. PLAN DESIGN SUMMARY

This program applies to the Factor IX products specified in this policy. Coverage for targeted product is provided based on clinical circumstances that would exclude the use of the preferred products and may be based on previous use of a product. The coverage review process will ascertain situations where a clinical exception can be made. This program applies to all members requesting treatment with a targeted product.

Each referral is reviewed based on all utilization management (UM) programs implemented for the client.

Table. Factor IX Products

	Product(s)
Preferred*	• **Alprolix** (coagulation factor IX [recombinant], Fc fusion protein) • **Idelvion** (coagulation factor IX [recombinant], albumin fusion protein) • **Rebinyn** (coagulation factor IX [recombinant], glycoPEGylated)

Targeted	• **Benefix** (coagulation factor IX [recombinant]) • **Ixinity** (coagulation factor IX [recombinant]) • **Rixubis** (coagulation factor IX [recombinant])

*: Medications considered formulary or preferred on your plan may still require a clinical prior authorization review

II. EXCEPTION CRITERIA

This program applies to members requesting treatment for an indication that is FDA-approved for the preferred products.

Coverage for a targeted product is provided when the member has a documented inadequate response or intolerable adverse event with all of the preferred products.

Section 2: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

REBINYN (coagulation factor IX [recombinant], glycoPEGylated)

IDELVION (coagulation factor IX [recombinant], albumin fusion protein)

ALPROLIX (coagulation factor IX [recombinant], Fc fusion protein)

BENEFIX, IXINITY, RIXUBIS (coagulation factor IX [recombinant])

ALPHANINE SD (coagulation factor IX [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
Hemophilia B

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

II. PRESCRIBER SPECIALTIES

Must be prescribed by or in consultation with a hematologist.

III. CRITERIA FOR INITIAL APPROVAL

Hemophilia B

Authorization of 12 months may be granted for treatment of hemophilia B.

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 is experiencing benefit from therapy (e.g., reduced frequency or severity of bleeds).

REFERENCES:

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4. Ixinity [package insert]. Seattle, WA: Aptevo BioTherapeutics LLC; February 2021.
5. Rixubis [package insert]. Lexington, MA. Baxalta US Inc.; June 2020
6. Rebinyn [package insert]. DK-2880 Bagsvaerd, Denmark: Novo Nordisk A/S; August 2022.

SECTION 2

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9. 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 1, 2022.

Reference number(s)
1944-A

SPECIALTY GUIDELINE MANAGEMENT

REBINYN (coagulation factor IX [recombinant], glycoPEGylated)

IDELVION (coagulation factor IX [recombinant], albumin fusion protein)

ALPROLIX (coagulation factor IX [recombinant], Fc fusion protein)

BENEFIX, IXINITY, RIXUBIS (coagulation factor IX [recombinant])

ALPHANINE SD (coagulation factor IX [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
Hemophilia B

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

II. PRESCRIBER SPECIALTIES

Must be prescribed by or in consultation with a hematologist.

III. CRITERIA FOR INITIAL APPROVAL

Hemophilia B
Authorization of 12 months may be granted for treatment of hemophilia B.

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 is experiencing benefit from therapy (e.g., reduced frequency or severity of bleeds).

V. REFERENCES

1. Alprolix [package insert]. Waltham, MA: Bioverativ Therapeutics Inc.; October 2020.
2. BeneFIX [package insert]. Philadelphia, PA: Wyeth Pharmaceuticals Inc.; November 2022.
3. Ixinity [package insert]. Chicago, IL: Medexus Pharma, Inc.; May 2022.
4. Rixubis [package insert]. Lexington, MA: Baxalta US Inc.; June 2020.
5. AlphaNine SD [package insert]. Los Angeles, CA: Grifols Biologicals LLC; March 2021.
6. Idelvion [package insert]. Kankakee, IL: CSL Behring LLC; July 2021.
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Reference number(s)
1949-A

SPECIALTY GUIDELINE MANAGEMENT

PROFILNINE
(factor IX complex [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
Hemophilia B

B. Compendial Uses
1. Bleeding due to low levels of liver-dependent coagulation factors
2. Factor II deficiency

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

II. PRESCRIBER SPECIALTIES

Must be prescribed by or in consultation with a hematologist.

III. CRITERIA FOR INITIAL APPROVAL

A. Hemophilia B
Authorization of 12 months may be granted for treatment of hemophilia B.

B. Bleeding Due to Low Levels of Liver-dependent Coagulation Factors
Authorization of 12 months may be granted for treatment of bleeding due to low levels of liver-dependent coagulation factors.

C. Factor II Deficiency
Authorization of 12 months may be granted for treatment of factor II deficiency.

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 is experiencing benefit from therapy (e.g., reduced frequency or severity of bleeds).

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V. REFERENCES

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2. Micromedex Solutions [database online]. Ann Arbor, MI: Truven Health Analytics Inc. Updated periodically www.micromedexsolutions.com [available with subscription]. Accessed December 1, 2022.
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 1, 2022.

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SPECIALTY GUIDELINE MANAGEMENT

FACTOR VIII CONCENTRATES

POLICY

I. INDICATIONS

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

Table: Factor VIII Concentrates and Covered Uses

Brand	Generic	FDA-Approved Indication(s)	Compendial Indication(s)
Recombinant Factor VIII Concentrates			
Advate	antihemophilic factor [recombinant]	Hemophilia A	Acquired Hemophilia A
Afstyla	antihemophilic factor [recombinant], single chain	Hemophilia A	
Kogenate FS	antihemophilic factor [recombinant]	Hemophilia A	Acquired Hemophilia A
Kovaltry	antihemophilic factor [recombinant]	Hemophilia A	
Novoeight	antihemophilic factor [recombinant]	Hemophilia A	Acquired Hemophilia A
Nuwiq	antihemophilic factor [recombinant]	Hemophilia A	
Recombinate	antihemophilic factor [recombinant]	Hemophilia A	Acquired Hemophilia A
Xyntha	antihemophilic factor [recombinant]	Hemophilia A	Acquired Hemophilia A
Extended Half-life Recombinant Factor VIII Concentrates			
Adynovate	antihemophilic factor [recombinant], PEGylated	Hemophilia A	
Altuviiio	antihemophilic factor [recombinant], Fc-VWF-XTEN fusion protein-ehtl	Hemophilia A	
Eloctate	antihemophilic factor [recombinant], Fc fusion protein	Hemophilia A	
Jivi	antihemophilic factor [recombinant], PEGylated-aucl	Hemophilia A	
Esperoct	antihemophilic factor [recombinant], Glycopegylated-exei	Hemophilia A	
Human Plasma-Derived Factor VIII Concentrate			
Hemofil M	antihemophilic factor [human] monoclonal antibody purified	Hemophilia A	Acquired Hemophilia A
Human Plasma-Derived Factor VIII Concentrates That Contain Von Willebrand Factor			

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Alphanate **Humate-P**	antihemophilic factor/von Willebrand factor complex [human]	Hemophilia A, von Willebrand Disease	Acquired Hemophilia A, Acquired von Willebrand Syndrome
Koate	antihemophilic factor [human]	Hemophilia A	Acquired Hemophilia A, von Willebrand Disease

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

II. PRESCRIBER SPECIALTIES

Must be prescribed by or in consultation with a hematologist.

III. CRITERIA FOR INITIAL APPROVAL

A. Hemophilia A

Authorization of 12 months of Advate, Adynovate, Afstyla, Alphanate, Altuviiio, Eloctate, Esperoct, Hemofil M, Humate-P, Koate, Kogenate FS, Kovaltry, Novoeight, Nuwiq, Recombinate, or Xyntha may be granted for treatment of hemophilia A when either of the following criteria is met:

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).

Authorization of 12 months of Jivi may be granted for treatment of hemophilia A when BOTH of the following criteria are met:

1. Member has previously received treatment for hemophilia A with a factor VIII product.
2. Member is ≥ 12 years of age.

B. Von Willebrand Disease (VWD)

Authorization of 12 months of Alphanate, Humate-P, or Koate may be granted for treatment of VWD when any of the following criteria is met:

1. Member has type 1, 2A, 2M, or 2N VWD and has had an insufficient response to desmopressin or a documented clinical reason for not using desmopressin (see Appendix B).
2. Member has type 2B or type 3 VWD.

C. Acquired Hemophilia A

Authorization of 12 months of Advate, Alphanate, Hemofil M, Humate-P, Koate, Kogenate FS, Novoeight, Recombinate, or Xyntha may be granted for treatment of acquired hemophilia A.

D. Acquired von Willebrand Syndrome

Authorization of 12 months of Alphanate or Humate-P may be granted for treatment of acquired von Willebrand syndrome.

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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 is experiencing benefit from therapy (e.g., reduced frequency or severity of bleeds).

V. 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

*Factor assay levels are required to determine the diagnosis and are of value in monitoring treatment response.

Appendix B: Clinical Reasons For Not Utilizing Desmopressin in Patients with Hemophilia A and Type 1, 2A, 2M and 2N VWD

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. Severe type 1 von Willebrand disease
J. Stimate Nasal Spray is unavailable due to backorder/shortage issues (where applicable)

VI. REFERENCES

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2. Jivi [package insert]. Whippany, NJ: Bayer HealthCare LLC; August 2018.
3. Kogenate FS [package insert]. Whippany, NJ: Bayer HealthCare LLC; May 2016.
4. Kogenate FS with BIO-SET [package insert]. Whippany, NJ: Bayer HealthCare LLC; May 2016.
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POLICY Document for FACTOR VIII CONCENTRATES
ESPEROCT (Glycopegylated-exei)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, and overall, clinically appropriate use. This document provides specific information to both sections of the overall policy.

Section 1: Preferred Product
- Policy information specific to preferred medications

Section 2: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 1: Preferred Product

EXCEPTIONS CRITERIA
FACTOR VIII LONG-ACTING PRODUCTS

PREFERRED PRODUCTS: ADYNOVATE, ELOCTATE, AND JIVI

POLICY
This policy informs prescribers of preferred products and provides an exception process for targeted products through prior authorization.

I. PLAN DESIGN SUMMARY

This program applies to the Factor VIII long-acting products specified in this policy. Coverage for targeted products is provided based on clinical circumstances that would exclude the use of the preferred products and may be based on previous use of a product. The coverage review process will ascertain situations where a clinical exception can be made. This program applies to all members requesting treatment with a targeted product.

Each referral is reviewed based on all utilization management (UM) programs implemented for the client.

Table. Factor VIII Products

	Product(s)
Preferred*	• **Adynovate** (antihemophilic factor [recombinant], PEGylated) • **Eloctate** (antihemophilic factor [recombinant], Fc fusion protein) • **Jivi** (antihemophilic factor [recombinant], PEGylated-aucl)
Targeted	• **Esperoct** (antihemophilic factor [recombinant] glycopegylated-exei)

*: Medications considered formulary or preferred on your plan may still require a clinical prior authorization review

II. EXCEPTION CRITERIA

This program applies to members requesting treatment for an indication that is FDA-approved for the preferred products.

Coverage for a targeted product is provided when either of the following criteria are met:

A. Member has a documented inadequate response or intolerable adverse event with 3 of the preferred products.

B. Member is less than 12 years of age and has a documented inadequate response or intolerable adverse event with both Adynovate and Eloctate.

CVS/caremark

Section 2: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

FACTOR VIII CONCENTRATES

POLICY

I. INDICATIONS

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

Table: Factor VIII Concentrates and Covered Uses

Brand	Generic	FDA-Approved Indication(s)	Compendial Indication(s)
Recombinant Factor VIII Concentrates			
Advate	antihemophilic factor [recombinant]	Hemophilia A	Acquired Hemophilia A
Afstyla	antihemophilic factor [recombinant], single chain	Hemophilia A	
Kogenate FS	antihemophilic factor [recombinant]	Hemophilia A	Acquired Hemophilia A
Kovaltry	antihemophilic factor [recombinant]	Hemophilia A	
Novoeight	antihemophilic factor [recombinant]	Hemophilia A	Acquired Hemophilia A
Nuwiq	antihemophilic factor [recombinant]	Hemophilia A	
Recombinate	antihemophilic factor [recombinant]	Hemophilia A	Acquired Hemophilia A
Xyntha	antihemophilic factor [recombinant]	Hemophilia A	Acquired Hemophilia A
Extended Half-life Recombinant Factor VIII Concentrates			
Adynovate	antihemophilic factor [recombinant], PEGylated	Hemophilia A	
Altuviiio	antihemophilic factor [recombinant], Fc-VWF-XTEN fusion protein-ehtl	Hemophilia A	
Eloctate	antihemophilic factor [recombinant], Fc fusion protein	Hemophilia A	
Jivi	antihemophilic factor [recombinant], PEGylated-aucl	Hemophilia A	
Esperoct	antihemophilic factor [recombinant], Glycopegylated-exei	Hemophilia A	
Human Plasma-Derived Factor VIII Concentrate			
Hemofil M	antihemophilic factor [human] monoclonal antibody purified	Hemophilia A	Acquired Hemophilia A
Human Plasma-Derived Factor VIII Concentrates That Contain Von Willebrand Factor			
Alphanate **Humate-P**	antihemophilic factor/von Willebrand factor complex [human]	Hemophilia A, von Willebrand Disease	Acquired Hemophilia A, Acquired von Willebrand Syndrome
Koate	antihemophilic factor [human]	Hemophilia A	Acquired Hemophilia A, von Willebrand Disease

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

II. PRESCRIBER SPECIALTIES

Must be prescribed by or in consultation with a hematologist.

III. CRITERIA FOR INITIAL APPROVAL

A. Hemophilia A

Authorization of 12 months of Advate, Adynovate, Afstyla, Alphanate, Altuviiio, Eloctate, Esperoct, Hemofil-M, Humate-P, Koate, Kogenate FS, Kovaltry, Novoeight, Nuwiq, Recombinate, or Xyntha may be granted for treatment of hemophilia A when either of the following criteria is met:

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).

Authorization of 12 months of Jivi may be granted for treatment of hemophilia A when BOTH of the following criteria are met:

1. Member has previously received treatment for hemophilia A with a factor VIII product.
2. Member is ≥ 12 years of age.

B. Von Willebrand Disease (VWD)

Authorization of 12 months of Alphanate, Humate-P, or Koate may be granted for treatment of VWD when any of the following criteria is met:

1. Member has type 1, 2A, 2M, or 2N VWD and has had an insufficient response to desmopressin or a documented clinical reason for not using desmopressin (see Appendix B).
2. Member has type 2B or type 3 VWD.

C. Acquired Hemophilia A

Authorization of 12 months of Advate, Alphanate, Hemofil M, Humate-P, Koate, Kogenate FS, Novoeight, Recombinate, or Xyntha may be granted for treatment of acquired hemophilia A.

D. Acquired von Willebrand Syndrome

Authorization of 12 months of Alphanate or Humate-P may be granted for treatment of acquired von Willebrand syndrome.

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 is experiencing benefit from therapy (e.g., reduced frequency or severity of bleeds).

V. 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

*Factor assay levels are required to determine the diagnosis and are of value in monitoring treatment response.

Appendix B: Clinical Reasons For Not Utilizing Desmopressin in Patients with Hemophilia A and Type 1, 2A, 2M and 2N VWD

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. Severe type 1 von Willebrand disease
J. Stimate Nasal Spray is unavailable due to backorder/shortage issues (where applicable)

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POLICY Document for FACTOR VIII PRODUCTS
RECOMBINATE (recombinant)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, and overall, clinically appropriate use. This document provides specific information to both sections of the overall policy.

Section 1: Preferred Product
- Policy information specific to preferred medications

Section 2: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 1: Preferred Product

EXCEPTIONS CRITERIA
FACTOR VIII PRODUCTS

PREFERRED PRODUCTS: ADVATE, AFSTYLA, KOGENATE FS, KOVALTRY, NOVOEIGHT, NUWIQ, XYNTHA

POLICY
This policy informs prescribers of preferred products and provides an exception process for targeted products through prior authorization.

I. PLAN DESIGN SUMMARY

This program applies to the Factor VIII products specified in this policy. Coverage for targeted products is provided based on clinical circumstances that would exclude the use of the preferred products and may be based on previous use of a product. The coverage review process will ascertain situations where a clinical exception can be made. This program applies to all members requesting treatment with a targeted product.

Each referral is reviewed based on all utilization management (UM) programs implemented for the client.

Table. Factor VIII Products

	Product(s)
Preferred*	• **Advate** (antihemophilic factor [recombinant]) • **Afstyla** (antihemophilic factor [recombinant]) • **Kogenate FS** (antihemophilic factor [recombinant]) • **Kovaltry** (antihemophilic factor [recombinant]) • **Novoeight** (antihemophilic factor [recombinant]) • **Nuwiq** (antihemophilic factor [recombinant]) • **Xyntha** (antihemophilic factor [recombinant])
Targeted	• **Recombinate** (antihemophilic factor [recombinant])

*: Medications considered formulary or preferred on your plan may still require a clinical prior authorization review

II. EXCEPTION CRITERIA

This program applies to members requesting treatment for an indication that is FDA-approved for the preferred

products.

Coverage for a targeted product is provided when the member has a documented inadequate response or intolerable adverse event with at least three of the preferred products.

Section 2: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

FACTOR VIII CONCENTRATES

POLICY

I. INDICATIONS

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

Table: Factor VIII Concentrates and Covered Uses

Brand	Generic	FDA-Approved Indication(s)	Compendial Indication(s)
Recombinant Factor VIII Concentrates			
Advate	antihemophilic factor [recombinant]	Hemophilia A	Acquired Hemophilia A
Afstyla	antihemophilic factor [recombinant], single chain	Hemophilia A	
Kogenate FS	antihemophilic factor [recombinant]	Hemophilia A	Acquired Hemophilia A
Kovaltry	antihemophilic factor [recombinant]	Hemophilia A	
Novoeight	antihemophilic factor [recombinant]	Hemophilia A	Acquired Hemophilia A
Nuwiq	antihemophilic factor [recombinant]	Hemophilia A	
Recombinate	antihemophilic factor [recombinant]	Hemophilia A	Acquired Hemophilia A
Xyntha	antihemophilic factor [recombinant]	Hemophilia A	Acquired Hemophilia A
Extended Half-life Recombinant Factor VIII Concentrates			
Adynovate	antihemophilic factor [recombinant], PEGylated	Hemophilia A	
Altuviiio	antihemophilic factor [recombinant], Fc-VWF-XTEN fusion protein-ehtl	Hemophilia A	
Eloctate	antihemophilic factor [recombinant], Fc fusion protein	Hemophilia A	
Jivi	antihemophilic factor [recombinant], PEGylated-aucl	Hemophilia A	
Esperoct	antihemophilic factor [recombinant], Glycopegylated-exei	Hemophilia A	
Human Plasma-Derived Factor VIII Concentrate			
Hemofil M	antihemophilic factor [human] monoclonal antibody purified	Hemophilia A	Acquired Hemophilia A
Human Plasma-Derived Factor VIII Concentrates That Contain Von Willebrand Factor			

Alphanate **Humate-P**	antihemophilic factor/von Willebrand factor complex [human]	Hemophilia A, von Willebrand Disease	Acquired Hemophilia A, Acquired von Willebrand Syndrome
Koate	antihemophilic factor [human]	Hemophilia A	Acquired Hemophilia A, von Willebrand Disease

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

II. PRESCRIBER SPECIALTIES

Must be prescribed by or in consultation with a hematologist.

III. CRITERIA FOR INITIAL APPROVAL

A. Hemophilia A

Authorization of 12 months of Advate, Adynovate, Afstyla, Alphanate, Altuviiio, Eloctate, Esperoct, Hemofil-M, Humate-P, Koate, Kogenate FS, Kovaltry, Novoeight, Nuwiq, Recombinate, or Xyntha may be granted for treatment of hemophilia A when either of the following criteria is met:

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).

Authorization of 12 months of Jivi may be granted for treatment of hemophilia A when BOTH of the following criteria are met:

1. Member has previously received treatment for hemophilia A with a factor VIII product.
2. Member is ≥ 12 years of age.

B. Von Willebrand Disease (VWD)

Authorization of 12 months of Alphanate, Humate-P, or Koate may be granted for treatment of VWD when any of the following criteria is met:

1. Member has type 1, 2A, 2M, or 2N VWD and has had an insufficient response to desmopressin or a documented clinical reason for not using desmopressin (see Appendix B).
2. Member has type 2B or type 3 VWD.

C. Acquired Hemophilia A

Authorization of 12 months of Advate, Alphanate, Hemofil M, Humate-P, Koate, Kogenate FS, Novoeight, Recombinate, or Xyntha may be granted for treatment of acquired hemophilia A.

D. Acquired von Willebrand Syndrome

Authorization of 12 months of Alphanate or Humate-P may be granted for treatment of acquired von Willebrand syndrome.

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 is experiencing benefit from therapy (e.g., reduced frequency or severity of bleeds).

V. 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

*Factor assay levels are required to determine the diagnosis and are of value in monitoring treatment response.

Appendix B: Clinical Reasons For Not Utilizing Desmopressin in Patients with Hemophilia A and Type 1, 2A, 2M and 2N VWD

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. Severe type 1 von Willebrand disease
J. Stimate Nasal Spray is unavailable due to backorder/shortage issues (where applicable)

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POLICY Document for FASENRA (benralizumab)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, lower cost site of care and overall, clinically appropriate use. This document provides specific information to each of the three sections of the overall policy.

Section 1: Site of Care

- Policy information specific to site of care (outpatient, hospital outpatient, home infusion)

Section 2: Clinical Criteria

- Policy information specific to the clinical appropriateness for the medication

Section 1: Site of Care

CareFirst Site of Care Criteria
Administration of Subcutaneous Fasenra

POLICY

I. CRITERIA FOR APPROVAL FOR ADMINISTRATION IN OUTPATIENT HOSPITAL SETTING

This policy provides coverage for provider administered Fasenra* in an outpatient hospital setting for up to 45 days when a member is new to therapy or is reinitiating therapy after not being on therapy for at least 6 months.

This policy provides coverage for administration of Fasenra in an outpatient hospital setting for a longer course of treatment when ANY of the following criteria are met:

A. The member has experienced an adverse reaction to the drug that did not respond to conventional interventions (eg, acetaminophen, steroids, diphenhydramine, fluids or other pre-medications) or a severe adverse event (anaphylaxis, anaphylactoid reactions, myocardial infarction, thromboembolism, or seizures) during or immediately after administration.
B. The member is medically unstable (eg respiratory, cardiovascular, or renal conditions).
C. The member has significant behavioral issues and/or physical or cognitive impairment that would impact the safety of drug administration AND the patient does not have access to a caregiver.
D. The member is less than 14 years of age.

For situations where administration of Fasenra does not meet the criteria for outpatient hospital administration, coverage for Fasenra is provided when administered in alternative sites such as; physician office, home infusion or ambulatory care.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the site of care prior authorization review (where applicable):

A. Medical records supporting the member has experienced an adverse reaction that did not respond to conventional interventions or a severe adverse event during or immediately after administration
B. Medical records supporting the member is medically unstable
C. Medical records supporting the member has behavioral issues and/or physical or cognitive impairment and no access to a caregiver

CVS/caremark

Section 2: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

FASENRA (benralizumab)

POLICY

III. INDICATIONS

The indications below including FDA-approved indications and compendial 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.

IV. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
A. For initial requests:
   1. Member's chart 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.

V. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with an allergist/immunologist or pulmonologist.

VI. CRITERIA FOR INITIAL APPROVAL

Authorization of 6 months may be granted for treatment of asthma when all of the following criteria are met:
A. Member is 12 years of age or older.
B. Member meets either of the following criteria:
   1. Member has a baseline blood eosinophil count of at least 150 cells per microliter; or
   2. Member is dependent on systemic corticosteroids
C. Member has uncontrolled asthma as demonstrated by experiencing at least one of the following within the past year:

1. Two or more asthma exacerbations requiring oral or injectable corticosteroid treatment.
2. One or more asthma exacerbation resulting in hospitalization or emergency medical care visit.
3. Poor symptom control (frequent symptoms or reliever use, activity limited by asthma, night waking due to asthma).

D. Member has inadequate asthma control despite current treatment with both of the following medications at optimized doses:
   1. High dose inhaled corticosteroid
   2. Additional controller (i.e., long acting beta$_2$-agonist, long acting muscarinic antagonist, leukotriene modifier, or sustained-release theophylline)

E. Member will continue to use maintenance asthma treatments (e.g., inhaled corticosteroid, additional controller) in combination with Fasenra.

F. Member will not use Fasenra concomitantly with other biologics indicated for asthma (e.g., Cinqair, Dupixent, Nucala, Tezspire, Xolair).

VII. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for treatment of asthma when all of the following criteria are met:

A. Member is 12 years of age or older.

B. Asthma control has improved on Fasenra treatment 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 Fasenra.

D. Member will not use Fasenra concomitantly with other biologics indicated for asthma (e.g., Cinqair, Dupixent, Nucala, Tezspire, Xolair).

VIII. OTHER

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.

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SECTION 2

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Reference number(s)
1943-A

SPECIALTY GUIDELINE MANAGEMENT

FEIBA (anti-inhibitor coagulant complex [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
Hemophilia A and hemophilia B with inhibitors

B. Compendial Use
Acquired hemophilia A

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

II. PRESCRIBER SPECIALTIES

Must be prescribed by or in consultation with a hematologist.

III. CRITERIA FOR INITIAL APPROVAL

A. Hemophilia A with Inhibitors
Authorization of 12 months may be granted for treatment of hemophilia A with inhibitors (see Appendix) when the inhibitor titer is ≥ 5 Bethesda units per milliliter (BU/mL) or if the patient has a history of an inhibitor titer ≥ 5 BU.

B. Hemophilia B with Inhibitors
Authorization of 12 months may be granted for treatment of hemophilia B with inhibitors (see Appendix) when the inhibitor titer is ≥ 5 Bethesda units per milliliter (BU/mL) or if the patient has a history of an inhibitor titer ≥ 5 BU.

C. Acquired Hemophilia A
Authorization of 12 months may be granted for treatment of acquired hemophilia 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 the member is experiencing benefit from therapy (e.g., reduced frequency or severity of bleeds).

V. APPENDIX

Appendix: Inhibitors - Bethesda Units (BU)
The presence of inhibitors is confirmed by a specific blood test called the Bethesda inhibitor assay.

- High-titer inhibitors:
  - ≥ 5 BU/mL
  - Inhibitors act strongly and quickly neutralize factor
- Low-titer inhibitors:
  - < 5 BU/mL
  - Inhibitors act weakly and slowly neutralize factor

VI. REFERENCES

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Reference number(s)
3864-A

SPECIALTY GUIDELINE MANAGEMENT

FENSOLVI (leuprolide 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
Fensolvi is indicated for the treatment of pediatric patients 2 years of age and older with central precocious puberty (CPP).

B. Compendial Use
Gender dysphoria (also known as gender non-conforming or transgender persons)

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. PRESCRIBER SPECIALTIES

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 patients less than 18 years of age.

IV. 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. Gender dysphoria

1. Authorization of 12 months may be granted for pubertal hormonal suppression in an adolescent member when all of the following criteria are met:
   i. The member has a diagnosis of gender dysphoria.
   ii. The member has reached Tanner stage 2 of puberty or greater.
   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 transition when all of the following criteria are met:
   i. The member has a diagnosis of gender dysphoria.
   ii. The member will receive Fensolvi concomitantly with gender-affirming hormones.
   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.

V. CONTINUATION OF THERAPY

A. Central precocious puberty (CPP)

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. Gender dysphoria

1. Authorization of 12 months may be granted for continued treatment for pubertal hormonal suppression 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 has previously reached Tanner stage 2 of puberty or greater.
   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 transition in members requesting reauthorization when all of the following criteria are met:
   i. The member has a diagnosis of gender dysphoria.
   ii. The member will receive Fensolvi concomitantly with gender-affirming hormones.
   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.

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Reference number(s)
2989-A

SPECIALTY GUIDELINE MANAGEMENT

FIBRYGA (fibrinogen [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
Fibryga is indicated for the treatment of acute bleeding episodes in adults and children with congenital fibrinogen deficiency, including afibrinogenemia and hypofibrinogenemia.

Fibryga is not indicated for dysfibrinogenemia.

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

II. CRITERIA FOR INITIAL APPROVAL

Congenital Fibrinogen Deficiency
Authorization of 1 month may be granted for treatment of acute bleeding episodes in members with a diagnosis of congenital fibrinogen deficiency, including afibrinogenemia and hypofibrinogenemia.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

1. Fibryga [package insert]. Paramus, NJ: Octapharma USA, Inc.; December 2020.
2. National Hemophilia Foundation. MASAC recommendations concerning products licensed for the treatment of hemophilia and other bleeding disorders. Revised April 2022. MASAC Document #272. https://www.hemophilia.org/sites/default/files/document/files/272_Treatment.pdf. Accessed September 22, 2022.

2. Authorization of 12 months may be granted for continued treatment for gender transition in members requesting reauthorization when all of the following criteria are met:
   i. The member has a diagnosis of gender dysphoria.
   ii. The member will receive Fensolvi concomitantly with gender-affirming hormones.
   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.

VI. REFERENCES

1. Fensolvi [package insert]. Fort Collins, CO: Tolmar, Inc.; May 2020.
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POLICY Document for FIRMAGON (degarelix)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, and overall, clinically appropriate use. This document provides specific information to both sections of the overall policy.

Section 1: Preferred Product
- Policy information specific to preferred medications

Section 2: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 3: Oncology Clinical Policy
- Policy information specific to regimen review per NCCN Guidelines.

Section 1: Preferred Product

EXCEPTIONS CRITERIA
GONADOTROPIN RELEASING HORMONE AGONISTS

PREFERRED PRODUCT: ELIGARD

POLICY
This policy informs prescribers of preferred products and provides an exception process for targeted products through prior authorization.

I. PLAN DESIGN SUMMARY

This program applies to the gonadotropin releasing hormone agonist products specified in this policy. Coverage for targeted products is provided based on clinical circumstances that would exclude the use of the preferred product and may be based on previous use of a product. The coverage review process will ascertain situations where a clinical exception can be made. This program applies to all members requesting treatment with Camcevi and Lupron Depot. This program also applies to members who are new to treatment with Firmagon, Trelstar, or Zoladex for the first time.

Each referral is reviewed based on all utilization management (UM) programs implemented for the client.

Table. Gonadotropin releasing hormone agonists

	Product(s)
Preferred*	• **Eligard** (leuprolide acetate)
Targeted	• **Camcevi** (leuprolide mesylate) • **Firmagon** (degarelix) • **Lupron Depot** (leuprolide acetate for depot suspension) • **Trelstar** (triptorelin) • **Zoladex** (goserelin acetate)

*: Medications considered formulary or preferred on your plan may still require a clinical prior authorization review.

II. EXCEPTION CRITERIA

This program applies to members requesting treatment for prostate cancer.

A. Firmagon, Trelstar, and Zoladex

Coverage for the Firmagon, Trelstar, and Zoladex is provided when any of the following criteria is met:

1. Member is currently receiving treatment with the requested targeted product, excluding when the requested targeted product is obtained as samples or via manufacturer's patient assistance programs.
2. Member has a documented hypersensitivity to the preferred product.

B. Camcevi and Lupron Depot

Coverage for Camcevi and Lupron Depot is provided when the member has a documented hypersensitivity to the preferred product.

Section 2: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

FIRMAGON (degarelix)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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

Firmagon is indicated for the treatment of advanced prostate cancer.

B. Compendial Uses

Prostate cancer

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

II. CRITERIA FOR INITIAL APPROVAL

Authorization of 12 months may be granted for treatment of prostate cancer.

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., serum testosterone less than 50 ng/dL) and who have not experienced an unacceptable toxicity.

Section 3: Oncology Clinical Policy

Oncology Clinical Policy

Program Description

The National Comprehensive Care Network® (NCCN®) is an alliance of leading cancer centers devoted to patient care, research and education dedicated to improving the quality, effectiveness and efficiency of cancer care so patients can live better lives.[1] It is comprised of oncology experts who convene regularly to establish the best treatments for patients. NCCN develops various resources for use by stakeholders in the health care delivery system. These resources include, but are not limited to, the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®), the NCCN Drugs & Biologics Compendium (NCCN Compendium®) and the NCCN Chemotherapy Order Templates (NCCN Templates®).

NCCN templates are based on NCCN Clinical Practice Guidelines and NCCN Compendium. The NCCN Compendium lists the appropriate drugs and biologics for specific cancers using U.S. Food and Drug Administration (FDA)-approved disease indications and specific NCCN panel recommendations. Each recommendation is supported by a level of evidence category.

NCCN Categories of Evidence and Consensus[2]
Category 1: Based on high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2A: Based on lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2B: Based on lower-level evidence, there is NCCN consensus that the intervention is appropriate.
Category 3: Based any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

Policy for Regimen Prior Authorization

A regimen prior authorization allows submission of a single prior authorization request for all oncology drugs or biologics within an NCCN template that require prior authorization.

This policy provides coverage of a regimen review when *all* the following criteria are met:

a. Regimen prior authorization reviews, based on NCCN templates, are initiated through the provider portal: https://provider.carefirst.com/providers/home.page
b. If the prior authorization request is submitted via phone or fax, each drug or biologic will need to be submitted and reviewed as a separate prior authorization request for review with drug-specific criteria.
c. The prior authorization review is requested for an oncology drug or biologic that requires prior authorization on the medical benefit.
d. The indication is for a cancer that is eligible for regimen review. Currently, the cancer types in scope for regimen review include breast, lung, colon and rectal cancer.
e. The member is eligible for regimen review.

In addition, the following criteria must be met for approval:

a. The requested regimen for the drug(s) or biologic(s) and indication is consistent with an NCCN recommendation with a level of evidence category of 1 or 2A.
b. The NCCN template must be accepted by the provider without modification.

Authorizations may be granted for 12 months.
Further review may be indicated where the above criteria are not met.

Continuation of Therapy

To submit a request for continuation of therapy, a new regimen prior authorization review must be requested. Upon template selection, the template must be modified to include the appropriate therapies being used for maintenance treatment. The regimen request will be submitted for further review.

Dosage and Administration

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

CVS/caremark

REFERENCES:

SECTION 1

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2. Camcevi [package insert]. Durham, NC: Accord BioPharma Inc.; May 2021.
3. Firmagon [package insert]. Parsippany, NJ: Ferring Pharmaceuticals, Inc.; February 2020.
4. Lupron Depot [package insert]. North Chicago, IL: AbbVie Inc.; April 2022.
5. Trelstar [package insert]. Ewing, NJ: Verity Pharmaceuticals Inc.; December 2021.
6. Zoladex [package insert]. Deerfield, IL: TerSera Therapeutics LLC; December 2020.

SECTION 2

1. Firmagon [package insert]. Parsippany, NJ: Ferring Pharmaceuticals Inc.; February 2020.
2. The NCCN Drugs & Biologics Compendium® © 2022 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed February 1, 2022.

SECTION 3

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3. National Comprehensive Cancer Network. NCCN Guidelines website. http://www.nccn.org/professionals/physician_gls/f_guidelines.asp, accessed September 16, 2019. *(Note: An account may be required.)*
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5. National Comprehensive Cancer Network. NCCN Chemotherapy Order Templates (NCCN Templates) website. https://www.nccn.org/professionals/OrderTemplates/Default.aspx, accessed September 16, 2019. *(Note: A subscription may be required.)*

Reference number(s)
1702-A

SPECIALTY GUIDELINE MANAGEMENT

FOLOTYN (pralatrexate)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Treatment of patients with relapsed or refractory peripheral T-cell lymphoma (PTCL)

B. Compendial Uses
1. Adult T-cell leukemia/lymphoma (ATLL)
2. Mycosis fungoides/Sezary syndrome (MF/SS)
3. Cutaneous anaplastic large cell lymphoma (ALCL)
4. Extranodal NK/T-cell lymphoma
5. Hepatosplenic T-cell lymphoma
6. Anaplastic large cell lymphoma
7. Peripheral T-cell lymphoma not otherwise specified
8. Angioimmunoblastic T-cell lymphoma
9. Enteropathy associated T-cell lymphoma
10. Monomorphic epitheliotropic intestinal T-cell lymphoma
11. Nodal peripheral T-cell lymphoma with TFH phenotype
12. Follicular T-cell lymphoma
13. Breast implant associated anaplastic large cell lymphoma (ALCL)

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

II. CRITERIA FOR INITIAL APPROVAL

A. Peripheral T-cell lymphoma (PTCL)
Authorization of 12 months may be granted for treatment of PTCL (including the following subtypes: anaplastic large cell lymphoma, peripheral T-cell lymphoma not otherwise specified, angioimmunoblastic T-cell lymphoma, enteropathy associated T-cell lymphoma, monomorphic epitheliotropic intestinal T-cell lymphoma, nodal peripheral T-cell lymphoma with TFH phenotype, or follicular T-cell lymphoma) when both of the following criteria are met:
1. The requested medication will be used as a single agent.
2. The requested medication will be used to treat relapsed or refractory disease or for initial palliative therapy.

B. Adult T-cell leukemia/lymphoma (ATLL)
Authorization of 12 months may be granted for treatment of ATLL when both of the following criteria are met:
1. The requested medication is used as a single agent.

2. The requested medication is used as subsequent therapy.

C. Mycosis fungoides/Sezary syndrome (MF/SS)
Authorization of 12 months may be granted for treatment of MF or SS.

D. Cutaneous anaplastic large cell lymphoma
Authorization of 12 months may be granted for treatment of cutaneous anaplastic large cell lymphoma (ALCL) when the requested medication is used as a single agent.

E. Extranodal NK/T-cell lymphoma
Authorization of 12 months may be granted for treatment of extranodal NK/T-cell lymphoma when all of the following criteria are met:
1. The requested medication will be used as a single agent.
2. The member has relapsed or refractory disease.
3. The member has had an inadequate response or contraindication to asparaginase-based therapy (e.g., pegaspargase).

F. Hepatosplenic T-cell lymphoma
Authorization of 12 months may be granted for treatment of hepatosplenic T-cell lymphoma when both of the following criteria are met:
1. The requested medication will be used as a single agent.
2. The member has had two or more previous lines of chemotherapy.

G. Breast implant-associated anaplastic large cell lymphoma (ALCL)
Authorization of 12 months may be granted for treatment of breast implant associated ALCL when both of the following criteria are met:
1. The requested medication will be used as a single agent.
2. The requested medication will be 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. Folotyn [package insert]. East Windsor, NJ: Acrotech Biopharma LLC; September 2020.
2. The NCCN Drugs & Biologics Compendium® © 2022 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed April 5, 2022.

POLICY Document for FASLODEX (fulvestrant) fulvestrant

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, and overall, clinically appropriate use. This document provides specific information to both sections of the overall policy.

Section 1: Clinical Criteria

- Policy information specific to the clinical appropriateness for the medication

Section 2: Oncology Clinical Policy

- Policy information specific to regimen review per NCCN Guidelines.

Section 1: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

FASLODEX (fulvestrant)
fulvestrant

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Faslodex is indicated for the treatment of:
1. Hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced breast cancer in postmenopausal women not previously treated with endocrine therapy.
2. HR-positive advanced breast cancer in postmenopausal women with disease progression following endocrine therapy.
3. HR-positive, HER2-negative advanced or metastatic breast cancer in postmenopausal women in combination with ribociclib, as initial endocrine based therapy or following disease progression on endocrine therapy.
4. HR-positive, HER2-negative advanced or metastatic breast cancer in combination with palbociclib or abemaciclib in women with disease progression after endocrine therapy

B. Compendial Uses
1. Breast cancer
2. Low grade serous ovarian carcinoma
3. Endometrial carcinoma
4. Uterine sarcoma

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

II. DOCUMENTATION

Submission of hormone receptor (HR) 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 recurrent, advanced, or metastatic HR-positive breast cancer.

B. Low Grade Serous Ovarian Carcinoma
Authorization of 12 months may be granted for treatment of recurrence of low-grade serous ovarian carcinoma as a single agent for members who previously received an aromatase inhibitor (e.g., letrozole, anastrozole, exemestane).

C. Endometrial carcinoma
Authorization of 12 months may be granted for treatment of endometrial carcinoma as a single agent.

D. Uterine sarcoma
Authorization of 12 months may be granted for treatment of low-grade endometrial stromal sarcoma (ESS), adenosarcoma without sarcomatous overgrowth, or estrogen receptor/ progesterone receptor positive (ER/PR+) uterine sarcomas 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.

Section 2: Oncology Clinical Policy

PROGRAM DESCRIPTION

The National Comprehensive Care Network® (NCCN®) is an alliance of leading cancer centers devoted to patient care, research and education dedicated to improving the quality, effectiveness, and efficiency of cancer care so patients can live better lives.[1] It is comprised of oncology experts who convene regularly to establish the best treatments for patients. NCCN develops various resources for use by stakeholders in the health care delivery system. These resources include, but are not limited to, the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®), the NCCN Drugs & Biologics Compendium (NCCN Compendium®) and the NCCN Chemotherapy Order Templates (NCCN Templates®).

NCCN Templates® are based on NCCN Guidelines® and NCCN Compendium®. The NCCN Compendium lists the appropriate drugs and biologics as treatment options for specific cancers using U.S. Food and Drug Administration (FDA)-approved disease indications and specific NCCN panel recommendations. Each recommendation is supported by a level of evidence category.

NCCN Categories of Evidence and Consensus[2]

- Category 1: Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
- Category 2A: Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.

• Category 2B: Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.
• Category 3: Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

POLICY

Policy for Regimen Prior Authorization
A regimen prior authorization allows submission of a single prior authorization request for all oncology drugs or biologics within an NCCN template that require prior authorization.

PROCEDURE

This policy provides coverage of a regimen review when all of the following criteria are met:
1. Regimen prior authorization reviews, based on NCCN templates, are initiated through the provider portal.
    - If the prior authorization request is submitted via phone or fax, each drug or biologic will need to be submitted and reviewed as a separate prior authorization request for review with drug-specific criteria.
2. The prior authorization review is requested for an oncology drug or biologic.
3. The member is eligible for regimen review.
4. The indication is for a cancer that is eligible for regimen review. Currently, the cancer types in scope for regimen review include the following:
    - Ampullary Adenocarcinoma
    - Anal Carcinoma
    - B-Cell Lymphomas
    - Basal Cell Skin Cancer
    - Biliary Tract Cancers
    - Bone Cancer
    - Breast Cancer
    - Bladder Cancer
    - Central Nervous System Cancers
    - Cervical Cancer
    - Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma
    - Chronic Myeloid leukemia
    - Colon Cancer
    - Dermatofibrosarcoma Protuberans
    - Esophageal Cancer
    - Gastric Cancer
    - Gastrointestinal Stromal Tumors
    - Gestational Trophoblastic Neoplasms
    - Hairy Cell Leukemia
    - Head and Neck Cancers
    - Hodgkin Lymphoma
    - Hepatocellular Carcinoma
    - Kaposi Sarcoma
    - Kidney Cancer
    - Melanoma: Cutaneous
    - Melanoma: Uveal
    - Merkel Cell Carcinoma
    - Mesothelioma: Peritoneal
    - Mesothelioma: Pleural
    - Myelodysplastic Syndromes
    - Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Gene Fusions
    - Myeloproliferative Neoplasms
    - Neuroendocrine and Adrenal Tumors

- Non-Small Cell Lung Cancer
- Occult Primary
- Ovarian Cancer
- Pancreatic Cancer
- Penile Cancer
- Prostate Cancer
- Rectal Cancer
- Small Bowl Adenocarcinoma
- Small Cell Lung Cancer
- Soft Tissue Sarcoma
- Squamous Cell Skin Cancer
- Systemic Mastocytosis
- Systemic Light Chain Amyloidosis
- Testicular Cancer
- Thymomas and Thymic Carcinomas
- Thyroid Carcinoma
- Uterine Neoplasms
- Vulvar Cancer
- Waldenström Macroglobulinemia / Lymphoplasmacytic Lymphoma

In addition, the following criteria must be met for approval:

1. The requested regimen for the drug(s) or biologic(s) and indication is consistent with an NCCN recommendation with a level of evidence category of 1 or 2A.
2. The NCCN template must be accepted by the provider without modification.

Further review may be indicated when the above criteria are not met.

Authorizations may be granted for 12 months or as medically required, based on the member's condition and provider's assessment.

Supportive Care: Myeloid Growth Factor Therapy
Granulocyte colony stimulating factors are recommended for primary prophylaxis based on the febrile neutropenia risk of the chemotherapy regimen. Febrile neutropenia risk levels vary by NCCN Chemotherapy Order template and are listed at the top of the template. Regimens associated with a high or intermediate risk of febrile neutropenia may include a granulocyte colony stimulating factor as part of the prior authorization.

Continuation of Therapy
To submit a request for continuation of therapy, a new regimen prior authorization review must be requested. Upon template selection, the template must be modified to include the appropriate therapies being used for maintenance treatment. The regimen request will be submitted for further review.

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

REFERENCES:

SECTION 1

1. Faslodex [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; September 2020.
2. Fulvestrant [package insert]. Princeton, NJ: Sandoz Inc.; June 2021.
3. The NCCN Drugs & Biologics Compendium® © 2022 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed November 7, 2022.

SECTION 2

1. National Comprehensive Cancer Network. About NCCN website. https://www.nccn.org/home/about, accessed June 6, 2023.
2. National Comprehensive Cancer Network. NCCN Categories of Evidence and Consensus website, https://www.nccn.org/guidelines/guidelines-process/development-and-update-of-guidelines, accessed June 6, 2023.
3. National Comprehensive Cancer Network. NCCN Guidelines website. https://www.nccn.org/guidelines/category_1, accessed June 6, 2023. (Note: An account may be required.)
4. National Comprehensive Cancer Network. NCCN Drugs and Biologics Compendium website https://www.nccn.org/compendia-templates/compendia/drugs-and-biologics-compendia, accessed June 6, 2023. (Note: A subscription may be required.)
5. National Comprehensive Cancer Network. NCCN Chemotherapy Order Templates (NCCN Templates) website. https://www.nccn.org/compendia-templates/nccn-templates-main/browse-by-cancer-type, accessed June 6, 2023. (Note: A subscription may be required.)

Reference number(s)
5080-A

SPECIALTY GUIDELINE MANAGEMENT

FYARRO (sirolimus protein-bound particles for injectable suspension) (albumin-bound)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Fyarro is indicated for the treatment of adult patients with locally advanced unresectable or metastatic malignant perivascular epithelioid cell tumor (PEComa).

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

II. CRITERIA FOR INITIAL APPROVAL

Perivascular Epithelioid Cell Tumor (PEComa)
Authorization of 12 months may be granted for the treatment of locally advanced unresectable or metastatic malignant PEComa when 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. Fyarro [package insert]. Pacific Palisades, CA: Aadi Bioscience, Inc; December 2021.
2. The NCCN Drugs & Biologics Compendium® © 2022 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed November 6, 2022.

Reference number(s)
2067-A

SPECIALTY GUIDELINE MANAGEMENT

Intramuscular Immune Globulin:
GamaSTAN® (Immune Globulin [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 Indications
GamaSTAN is a human immune globulin indicated for:

A. Hepatitis A
GamaSTAN is indicated for prophylaxis following exposure to hepatitis A. The prophylactic value of GamaSTAN is greatest when given before or soon after exposure to hepatitis A. GamaSTAN is not indicated in persons with clinical manifestations of hepatitis A or in those exposed more than 2 weeks previously.

B. Measles (Rubeola)
GamaSTAN is indicated to prevent or modify measles in a susceptible person exposed fewer than 6 days previously. A susceptible person is one who has not been vaccinated and has not had measles previously.
• GamaSTAN may be especially indicated for susceptible household contacts of measles patients, particularly contacts under 1 year of age, for whom the risk of complications is highest.
• GamaSTAN is also indicated for pregnant women without evidence of immunity.
• Do not give GamaSTAN and measles vaccine at the same time. If a child is older than 12 months and has received GamaSTAN, give measles vaccine about five months later when the measles antibody titer will have disappeared.
If a susceptible child exposed to measles is immunocompromised, give GamaSTAN immediately.

C. Varicella
GamaSTAN is indicated to modify varicella.
• Passive immunization against varicella in immunosuppressed patients is best accomplished by use of Varicella Zoster Immune Globulin (Human). If unavailable, GamaSTAN, promptly given, may also modify varicella.

D. Rubella
GamaSTAN is indicated to modify rubella in exposed women who will not consider a therapeutic abortion.
• Some studies suggest that the use of GamaSTAN in exposed, susceptible women can lessen the likelihood of infection and fetal damage; therefore, GamaSTAN may benefit those women who will not consider a therapeutic abortion.
• Do not give GamaSTAN for routine prophylaxis of rubella in early pregnancy to an unexposed woman.

Limitations of Use
• GamaSTAN is not standardized with respect to antibody titers against hepatitis B surface antigen (HBsAg) and must not be used for prophylaxis of viral hepatitis type B. Prophylactic treatment to prevent

hepatitis B can best be accomplished with use of Hepatitis B Immune Globulin (Human), often in combination with Hepatitis B Vaccine.
• GamaSTAN is not indicated for routine prophylaxis or treatment of rubella, poliomyelitis, mumps, or varicella.

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

II. CRITERIA FOR INITIAL APPROVAL

A. Prophylaxis of hepatitis A

Authorization of 1 month may be granted for prophylaxis of hepatitis A when one of the following criteria is met:

1. Member was exposed to hepatitis A virus within the past 2 weeks (e.g., household contact, sexual contact, and childcare center or classroom contact with an infected person), and is NOT exhibiting clinical manifestation of disease OR
2. Member is at high risk for hepatitis A exposure (examples of populations at high risk for hepatitis A are travelers to and workers in countries of high endemicity of infection and illicit drug users).

B. Prophylaxis of measles (rubeola)

1. Authorization of 1 month may be granted for prophylaxis of measles in unvaccinated members who have not had measles previously and were exposed to measles within the past 6 days.

C. Prophylaxis of varicella

Authorization of 1 month may be granted for prophylaxis of varicella when all of the following criteria are met:

1. Member was exposed to varicella within the past 10 days
2. Member is at high risk for severe varicella (e.g., immunocompromised persons, newborns/infants, pregnant women)
3. Varicella zoster immune globulin (e.g., Varizig®) is not available

D. Prophylaxis of rubella

Authorization of 1 month may be granted for prophylaxis of rubella when both of the following criteria are met:

1. Member was recently exposed to rubella
2. Member is currently pregnant

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

1. GamaSTAN [package insert]. Research Triangle Park, NC: Grifols Therapeutics, Inc.; February 2018.
2. Nelson NP, Link-Gelles R, Hofmeister MG, et al. Update: Recommendations of the Advisory Committee on Immunization Practices for Use of Hepatitis A Vaccine for Postexposure Prophylaxis and for Preexposure Prophylaxis for International Travel. MMWR Morb Mortal Wkly Rep 2018;67:1216–1220.

3. Centers for Disease Control and Prevention. Prevention of Measles, Rubella, Congenital Rubella Syndrome, and Mumps, 2013. Summary Recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR.* 2013;62(4).
4. Centers for Disease Control and Prevention Health Information for International Travel (Yellow Book). Varicella (Chickenpox). https://wwwnc.cdc.gov/travel/yellowbook/2018/infectious-diseases-related-to-travel/varicella-chickenpox . Accessed June 8, 2022.

POLICY Document for FIRMAGON (degarelix)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, and overall, clinically appropriate use. This document provides specific information to both sections of the overall policy.

Section 1: Preferred Product
- Policy information specific to preferred medications

Section 2: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 3: Oncology Clinical Policy
- Policy information specific to regimen review per NCCN Guidelines.

Section 1: Preferred Product

EXCEPTIONS CRITERIA
GONADOTROPIN RELEASING HORMONE AGONISTS

PREFERRED PRODUCT: ELIGARD

POLICY
This policy informs prescribers of preferred products and provides an exception process for targeted products through prior authorization.

I. PLAN DESIGN SUMMARY

This program applies to the gonadotropin releasing hormone agonist products specified in this policy. Coverage for targeted products is provided based on clinical circumstances that would exclude the use of the preferred product and may be based on previous use of a product. The coverage review process will ascertain situations where a clinical exception can be made. This program applies to all members requesting treatment with Camcevi and Lupron Depot. This program also applies to members who are new to treatment with Firmagon, Trelstar, or Zoladex for the first time.

Each referral is reviewed based on all utilization management (UM) programs implemented for the client.

Table. Gonadotropin releasing hormone agonists

	Product(s)
Preferred*	• **Eligard** (leuprolide acetate)
Targeted	• **Camcevi** (leuprolide mesylate) • **Firmagon** (degarelix) • **Lupron Depot** (leuprolide acetate for depot suspension) • **Trelstar** (triptorelin) • **Zoladex** (goserelin acetate)

*: Medications considered formulary or preferred on your plan may still require a clinical prior authorization review.

II. EXCEPTION CRITERIA

This program applies to members requesting treatment for prostate cancer.

A. Firmagon, Trelstar, and Zoladex

Coverage for the Firmagon, Trelstar, and Zoladex is provided when any of the following criteria is met:

1. Member is currently receiving treatment with the requested targeted product, excluding when the requested targeted product is obtained as samples or via manufacturer's patient assistance programs.
2. Member has a documented hypersensitivity to the preferred product.

B. Camcevi and Lupron Depot

Coverage for Camcevi and Lupron Depot is provided when the member has a documented hypersensitivity to the preferred product.

Section 2: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

FIRMAGON (degarelix)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Firmagon is indicated for the treatment of 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.

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., serum testosterone less than 50 ng/dL) and who have not experienced an unacceptable toxicity.

Section 3: Oncology Clinical Policy

PROGRAM DESCRIPTION

The National Comprehensive Care Network® (NCCN®) is an alliance of leading cancer centers devoted to patient care, research and education dedicated to improving the quality, effectiveness, and efficiency of cancer care so patients can

live better lives.[1] It is comprised of oncology experts who convene regularly to establish the best treatments for patients. NCCN develops various resources for use by stakeholders in the health care delivery system. These resources include, but are not limited to, the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®), the NCCN Drugs & Biologics Compendium (NCCN Compendium®) and the NCCN Chemotherapy Order Templates (NCCN Templates®).

NCCN Templates® are based on NCCN Guidelines® and NCCN Compendium®. The NCCN Compendium lists the appropriate drugs and biologics as treatment options for specific cancers using U.S. Food and Drug Administration (FDA)-approved disease indications and specific NCCN panel recommendations. Each recommendation is supported by a level of evidence category.

NCCN Categories of Evidence and Consensus[2]

- Category 1: Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
- Category 2A: Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
- Category 2B: Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.
- Category 3: Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

POLICY

Policy for Regimen Prior Authorization

A regimen prior authorization allows submission of a single prior authorization request for all oncology drugs or biologics within an NCCN template that require prior authorization.

PROCEDURE

This policy provides coverage of a regimen review when all of the following criteria are met:

1. Regimen prior authorization reviews, based on NCCN templates, are initiated through the provider portal.
   - If the prior authorization request is submitted via phone or fax, each drug or biologic will need to be submitted and reviewed as a separate prior authorization request for review with drug-specific criteria.
2. The prior authorization review is requested for an oncology drug or biologic.
3. The member is eligible for regimen review.
4. The indication is for a cancer that is eligible for regimen review. Currently, the cancer types in scope for regimen review include the following:
   - Ampullary Adenocarcinoma
   - Anal Carcinoma
   - B-Cell Lymphomas
   - Basal Cell Skin Cancer
   - Biliary Tract Cancers
   - Bone Cancer
   - Breast Cancer
   - Bladder Cancer
   - Central Nervous System Cancers
   - Cervical Cancer
   - Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma
   - Chronic Myeloid leukemia
   - Colon Cancer
   - Dermatofibrosarcoma Protuberans
   - Esophageal Cancer
   - Gastric Cancer

- Gastrointestinal Stromal Tumors
- Gestational Trophoblastic Neoplasms
- Hairy Cell Leukemia
- Head and Neck Cancers
- Hodgkin Lymphoma
- Hepatocellular Carcinoma
- Kaposi Sarcoma
- Kidney Cancer
- Melanoma: Cutaneous
- Melanoma: Uveal
- Merkel Cell Carcinoma
- Mesothelioma: Peritoneal
- Mesothelioma: Pleural
- Myelodysplastic Syndromes
- Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Gene Fusions
- Myeloproliferative Neoplasms
- Neuroendocrine and Adrenal Tumors
- Non-Small Cell Lung Cancer
- Occult Primary
- Ovarian Cancer
- Pancreatic Cancer
- Penile Cancer
- Prostate Cancer
- Rectal Cancer
- Small Bowl Adenocarcinoma
- Small Cell Lung Cancer
- Soft Tissue Sarcoma
- Squamous Cell Skin Cancer
- Systemic Mastocytosis
- Systemic Light Chain Amyloidosis
- Testicular Cancer
- Thymomas and Thymic Carcinomas
- Thyroid Carcinoma
- Uterine Neoplasms
- Vulvar Cancer
- Waldenström Macroglobulinemia / Lymphoplasmacytic Lymphoma

In addition, the following criteria must be met for approval:

1. The requested regimen for the drug(s) or biologic(s) and indication is consistent with an NCCN recommendation with a level of evidence category of 1 or 2A.
2. The NCCN template must be accepted by the provider without modification.

Further review may be indicated when the above criteria are not met.

Authorizations may be granted for 12 months or as medically required, based on the member's condition and provider's assessment.

Supportive Care: Myeloid Growth Factor Therapy

Granulocyte colony stimulating factors are recommended for primary prophylaxis based on the febrile neutropenia risk of the chemotherapy regimen. Febrile neutropenia risk levels vary by NCCN Chemotherapy Order template and are listed at the top of the template. Regimens associated with a high or intermediate risk of febrile neutropenia may include a granulocyte colony stimulating factor as part of the prior authorization.

Continuation of Therapy

To submit a request for continuation of therapy, a new regimen prior authorization review must be requested. Upon

template selection, the template must be modified to include the appropriate therapies being used for maintenance treatment. The regimen request will be submitted for further review.

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

REFERENCES:

SECTION 1

1. Eligard [package insert]. Fort Collins, CO: Tolmar Pharmaceuticals, Inc.; April 2019.
2. Camcevi [package insert]. Durham, NC: Accord BioPharma Inc.; May 2021.
3. Firmagon [package insert]. Parsippany, NJ: Ferring Pharmaceuticals, Inc.; February 2020.
4. Lupron Depot [package insert]. North Chicago, IL: AbbVie Inc.; April 2022.
5. Trelstar [package insert]. Ewing, NJ: Verity Pharmaceuticals Inc.; December 2021.
6. Zoladex [package insert]. Deerfield, IL: TerSera Therapeutics LLC; December 2020.

SECTION 2

1. Firmagon [package insert]. Parsippany, NJ: Ferring Pharmaceuticals Inc.; February 2020.
2. The NCCN Drugs & Biologics Compendium® © 2023 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed February 1, 2023.

SECTION 3

1. National Comprehensive Cancer Network. About NCCN website. https://www.nccn.org/home/about, accessed June 6, 2023.
2. National Comprehensive Cancer Network. NCCN Categories of Evidence and Consensus website, https://www.nccn.org/guidelines/guidelines-process/development-and-update-of-guidelines, accessed June 6, 2023.
3. National Comprehensive Cancer Network. NCCN Guidelines website. https://www.nccn.org/guidelines/category_1, accessed June 6, 2023. (Note: An account may be required.)
4. National Comprehensive Cancer Network. NCCN Drugs and Biologics Compendium website https://www.nccn.org/compendia-templates/compendia/drugs-and-biologics-compendia, accessed June 6, 2023. (Note: A subscription may be required.)
5. National Comprehensive Cancer Network. NCCN Chemotherapy Order Templates (NCCN Templates) website. https://www.nccn.org/compendia-templates/nccn-templates-main/browse-by-cancer-type, accessed June 6, 2023. (Note: A subscription may be required.)

Reference number(s)
2796-A

SPECIALTY GUIDELINE MANAGEMENT

GAMIFANT (emapalumab-lzsg)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Gamifant is indicated for the treatment of adult and pediatric (newborn and older) patients with primary hemophagocytic lymphohistiocytosis (HLH) with refractory, recurrent or progressive disease or intolerance with conventional HLH therapy.

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: medical record documentation (i.e., chart notes or laboratory report) confirming the diagnosis of HLH with the presence of one of the following: A) a mutation in one of the following genes: PRF1, UNC13D, STX11 and STXBP2, or B) presence of at least 5 clinical signs and symptoms of disease. (See Appendix A)

III. CRITERIA FOR INITIAL APPROVAL

Primary HLH
Authorization of 6 months may be granted for treatment of primary HLH when all of the following criteria are met:

A. Member has refractory, recurrent or progressive disease or intolerance with conventional HLH therapy.
B. Member's diagnosis of primary HLH was confirmed by either of the following:
    1. Mutation in one of the following genes: PRF1, UNC13D, STX11 and STXBP2
    2. Presence of at least 5 clinical signs and symptoms of HLH (See Appendix A)
C. Possible causes of secondary or acquired forms of HLH (e.g., autoimmune disease, persistent infection, malignancy, or loss of inhibitory immune mechanisms) have been ruled out.
D. Member has been evaluated for tuberculosis (TB) risk factors and has undergone pretreatment screening for latent TB with the purified protein derivative (PPD) skin test or interferon gamma release assay.
E. If member has a positive test result or is at risk for TB, prophylactic treatment for TB must be initiated before starting therapy.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for primary HLH who have achieved or maintained positive clinical response.

V. APPENDIX

CLINICAL SIGNS AND SYMPTOMS OF HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS (HLH)

1. Fever
2. Splenomegaly
3. Cytopenias (affecting at least 2 of 3 lineages in the peripheral blood: hemoglobin less than 9 g/dL [hemoglobin less than 10 g/dL in infants younger than 4 weeks], platelets less than 100,000/microliter, neutrophils less than 1,000/microliter)
4. Hypertriglyceridemia (fasting triglyceride greater than or equal to 265 mg/dL) or hypofibrinogenemia (less than or equal to 150 mg/dL)
5. Hemophagocytosis in bone marrow or spleen or lymph nodes or liver with no evidence of malignancy
6. Low or absent natural killer (NK) cell activity
7. Ferritin greater than or equal to 500 ng/mL
8. Soluble CD25 (soluble IL-2 receptor alpha) level greater than or equal to 2400 U/mL, or above age-adjusted, laboratory-specific normal levels (defined as 2 standard deviation from the mean)

VI. REFERENCES

1. Gamifant [package insert]. Waltham, MA: Sobi, Inc.; June 2020.
2. Henter JI, Horne A, Arico M et al. HLH-2004: diagnostic and therapeutic guidelines for hemophagocytic lymphohistiocytosis. Pediatr Blood Cancer. 2007;48:124-131.
3. Allen CE and McClain KL. Hematology Am Soc Hematol Educ Program. 2015;2015:177-82.
4. Janka, G.E. and E.M. Schneider, Modern management of children with haemophagocytic lymphohistiocytosis. Br J Haematol, 2004. 124(1): p. 4-14.

POLICY Document for GEMZAR (gemcitabine) INFUGEM (gemcitabine) gemcitabine

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, and overall, clinically appropriate use. This document provides specific information to both sections of the overall policy.

Section 1: Clinical Criteria

- Policy information specific to the clinical appropriateness for the medication

Section 2: Oncology Clinical Policy

- Policy information specific to regimen review per NCCN Guidelines.

Section 1: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

GEMZAR (gemcitabine)
INFUGEM (gemcitabine)
gemcitabine

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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
   In combination with carboplatin for the treatment of patients with advanced ovarian cancer that has relapsed at least 6 months after completion of platinum-based therapy
2. Breast cancer
   In combination with paclitaxel for the first-line treatment of patients with metastatic breast cancer after failure of prior anthracycline-containing adjuvant chemotherapy, unless anthracyclines were clinically contraindicated
3. Non-small cell lung cancer
   In combination with cisplatin for the first-line treatment of patients with inoperable, locally advanced (Stage IIIA or IIIB), or metastatic (Stage IV) non-small cell lung cancer (NSCLC)
4. Pancreatic cancer
   As first-line treatment for patients with locally advanced (nonresectable Stage II or Stage III) or metastatic (Stage IV) adenocarcinoma of the pancreas. Gemzar, Infugem or gemcitabine is indicated for patients previously treated with fluorouracil.

B. Compendial Uses

1. Ampullary adenocarcinoma

2. Bladder cancer, primary carcinoma of the urethra, upper genitourinary tract tumors, transitional cell carcinoma of the urinary tract, urothelial carcinoma of the prostate, non-urothelial and urothelial cancer with variant histology
3. Bone cancer
   a. Ewing's sarcoma
   b. Osteosarcoma
4. Breast cancer
5. Cervical cancer
6. Head and neck cancers (including very advanced head and neck cancer, cancer of the nasopharynx, and salivary gland tumors)
7. Hepatobiliary and biliary tract cancer
   a. Extrahepatic cholangiocarcinoma
   b. Intrahepatic cholangiocarcinoma
   c. Gallbladder cancer
8. Hodgkin lymphoma
   a. Classic Hodgkin lymphoma
   b. Nodular lymphocyte-predominant Hodgkin lymphoma
9. Kidney cancer
10. Malignant pleural or peritoneal mesothelioma
11. Non-small cell lung cancer (NSCLC)
12. Occult primary tumors (cancer of unknown primary)
13. Ovarian cancer, fallopian tube cancer, and primary peritoneal cancer: epithelial ovarian cancer, fallopian tube cancer, and primary peritoneal cancer
14. Pancreatic adenocarcinoma
15. Small cell lung cancer (SCLC)
16. Soft tissue sarcoma
    a. Angiosarcoma
    b. Extremity/Body wall, head/neck
    c. Retroperitoneal/intra-abdominal
    d. Rhabdomyosarcoma
    e. Solitary fibrous tumor
    f. Dermatofibrosarcoma protuberans (DFSP) with fibrosarcomatous transformation
17. Testicular cancer
18. Thymomas and thymic carcinomas
19. Uterine neoplasms (including uterine sarcoma and uterine leiomyosarcoma)
20. Kaposi Sarcoma
21. Primary cutaneous lymphomas
    a. Mycosis fungoides/Sezary syndrome
    b. Primary cutaneous CD30+ T-Cell lymphoproliferative disorders
22. T-Cell lymphomas
    a. Peripheral T-Cell lymphomas
    b. Adult T-Cell leukemia/lymphoma
    c. Breast implant-associated anaplastic large cell lymphoma
    d. Extranodal natural killer (NK)/T-Cell lymphoma
    e. Hepatosplenic T-Cell lymphoma
23. Gestational trophoblastic neoplasia
24. B-Cell lymphomas
    a. Follicular lymphoma (grade 1-2)
    b. Histologic transformation of indolent lymphomas to diffuse large B-Cell lymphoma
    c. Mantle cell lymphoma
    d. Diffuse large B-Cell lymphoma
    e. High-Grade B-Cell lymphomas
    f. Burkitt lymphoma
    g. AIDS-Related B-Cell lymphomas
    h. Post-Transplant lymphoproliferative disorders

25. Small bowel adenocarcinoma
26. Malignant germ cell tumor

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

II. CRITERIA FOR INITIAL APPROVAL

A. Pancreatic Adenocarcinoma
Authorization of 6 months may be granted for treatment of pancreatic adenocarcinoma.

B. Breast Cancer
Authorization of 6 months may be granted for treatment of members with no response to preoperative systemic therapy, recurrent, or metastatic breast cancer.

C. Hepatobiliary and Biliary Tract Cancer
Authorization of 6 months may be granted for treatment of hepatobiliary and biliary tract cancer (including intrahepatic and extrahepatic cholangiocarcinoma, and gallbladder cancer).

D. Ampullary Adenocarcinoma
Authorization of 6 months may be granted for treatment of ampullary adenocarcinoma.

E. Ovarian Cancer, Fallopian Tube Cancer, and Primary Peritoneal Cancer
Authorization of 6 months may be granted for treatment of advanced, 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 carcinoma/ovarian borderline epithelial tumors (low malignant potential), mucinous carcinoma of the ovary, or malignant germ cell tumor residual disease.

F. Non-Small Cell Lung Cancer (NSCLC)
Authorization of 6 months may be granted for treatment of NSCLC.

G. Cervical Cancer
Authorization of 6 months may be granted for treatment of cervical cancer.

H. Bladder Cancer, Primary Carcinoma of the Urethra, Upper Genitourinary Tract Tumors, Transitional Cell Carcinoma of the Urinary Tract, Urothelial Carcinoma of the Prostate, and Non-Urothelial and Urothelial Cancer with Variant Histology
Authorization of 6 months may be granted for treatment of bladder cancer, primary carcinoma of the urethra, upper genitourinary tract tumors, transitional cell carcinoma of the urinary tract, urothelial carcinoma of the prostate, and non-urothelial and urothelial cancer with variant histology.

I. Small Cell Lung Cancer (SCLC)
Authorization of 6 months may be granted for treatment of SCLC.

J. Soft Tissue Sarcoma
Authorization of 6 months may be granted for treatment of soft tissue sarcoma (including angiosarcoma, extremity/body wall, head/neck, retroperitoneal/intra-abdominal, rhabdomyosarcoma, solitary fibrous tumor, dermatofibrosarcoma protuberans (DFSP) with fibrosarcomatous transformation).

K. Bone Cancer

1. Ewing's Sarcoma
Authorization of 6 months may be granted for treatment of relapsed, progressive, or metastatic Ewing's sarcoma.

2. **Osteosarcoma**
   Authorization of 6 months may be granted for treatment of relapsed/refractory or metastatic osteosarcoma.

L. Head and Neck Cancer
Authorization of 6 months may be granted for treatment of head and neck cancer (including very advanced head and neck cancer, cancer of the nasopharynx, and salivary gland tumors).

M. Hodgkin Lymphoma

1. **Hodgkin Lymphoma**
   Authorization of 6 months may be granted for treatment of Hodgkin lymphoma including classic Hodgkin lymphoma and pediatric Hodgkin lymphoma.

2. **Nodular Lymphocyte-Predominant Hodgkin Lymphoma**
   Authorization of 6 months may be granted for treatment of progressive, relapsed, or refractory nodular lymphocyte-predominant Hodgkin lymphoma.

N. Kidney Cancer
Authorization of 6 months may be granted for treatment of relapsed or metastatic kidney cancer.

O. Malignant Pleural or Peritoneal Mesothelioma
Authorization of 6 months may be granted for treatment of malignant pleural or peritoneal mesothelioma, including pericardial mesothelioma and tunica vaginalis testis mesothelioma.

P. Occult Primary Tumors (cancer of unknown primary)
Authorization of 6 months may be granted for treatment of occult primary tumors.

Q. Testicular Cancer
Authorization of 6 months may be granted for treatment of testicular cancer.

R. Thymomas and Thymic Carcinomas
Authorization of 6 months may be granted for treatment of thymomas and thymic carcinomas.

S. Uterine Neoplasms
Authorization of 6 months may be granted for treatment of uterine neoplasms (including uterine sarcoma and uterine leiomyosarcoma).

T. Kaposi Sarcoma
Authorization of 6 months may be granted for treatment of Kaposi Sarcoma.

U. Primary Cutaneous Lymphomas
Authorization of 6 months may be granted for treatment of primary cutaneous lymphomas (including mycosis fungoides/Sezary syndrome and primary cutaneous CD30+ T-Cell lymphoproliferative disorders).

V. T-Cell Lymphomas
Authorization of 6 months may be granted for treatment of T-Cell lymphomas (including peripheral T-Cell lymphomas, adult T-Cell leukemia/lymphoma, hepatosplenic T-Cell lymphoma, breast implant-associated anaplastic large cell lymphoma, and extranodal NK/T-Cell lymphoma).

W. Gestational Trophoblastic Neoplasia
Authorization of 6 months may be granted for treatment of gestational trophoblastic neoplasia.

X. B-Cell Lymphomas

Authorization of 6 months may be granted for treatment of B-Cell lymphomas (including follicular lymphoma [grade 1-2], histologic transformation of indolent lymphomas to diffuse large B-Cell lymphoma, mantle cell lymphoma, diffuse large B-Cell lymphoma, high-grade B-Cell lymphomas, Burkitt lymphoma, AIDS-Related B-Cell lymphomas, and post-transplant lymphoproliferative disorders).

Y. Small Bowel Adenocarcinoma
Authorization of 6 months may be granted for treatment of small bowel adenocarcinoma.

Z. Malignant Germ Cell Tumor
Authorization of 6 months may be granted for treatment of malignant germ cell tumor.

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 there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

Section 2: Oncology Clinical Policy

PROGRAM DESCRIPTION

The National Comprehensive Care Network® (NCCN®) is an alliance of leading cancer centers devoted to patient care, research and education dedicated to improving the quality, effectiveness, and efficiency of cancer care so patients can live better lives.[1] It is comprised of oncology experts who convene regularly to establish the best treatments for patients. NCCN develops various resources for use by stakeholders in the health care delivery system. These resources include, but are not limited to, the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®), the NCCN Drugs & Biologics Compendium (NCCN Compendium®) and the NCCN Chemotherapy Order Templates (NCCN Templates®).

NCCN Templates® are based on NCCN Guidelines® and NCCN Compendium®. The NCCN Compendium lists the appropriate drugs and biologics as treatment options for specific cancers using U.S. Food and Drug Administration (FDA)-approved disease indications and specific NCCN panel recommendations. Each recommendation is supported by a level of evidence category.

NCCN Categories of Evidence and Consensus[2]

- Category 1: Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
- Category 2A: Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
- Category 2B: Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.
- Category 3: Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

POLICY

Policy for Regimen Prior Authorization
A regimen prior authorization allows submission of a single prior authorization request for all oncology drugs or biologics within an NCCN template that require prior authorization.

PROCEDURE

This policy provides coverage of a regimen review when all of the following criteria are met:
1. Regimen prior authorization reviews, based on NCCN templates, are initiated through the provider portal.
    - If the prior authorization request is submitted via phone or fax, each drug or biologic will need to be submitted and reviewed as a separate prior authorization request for review with drug-specific criteria.
2. The prior authorization review is requested for an oncology drug or biologic.
3. The member is eligible for regimen review.
4. The indication is for a cancer that is eligible for regimen review. Currently, the cancer types in scope for regimen review include the following:
    - Ampullary Adenocarcinoma
    - Anal Carcinoma
    - B-Cell Lymphomas
    - Basal Cell Skin Cancer
    - Biliary Tract Cancers
    - Bone Cancer
    - Breast Cancer
    - Bladder Cancer
    - Central Nervous System Cancers
    - Cervical Cancer
    - Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma
    - Chronic Myeloid leukemia
    - Colon Cancer
    - Dermatofibrosarcoma Protuberans
    - Esophageal Cancer
    - Gastric Cancer
    - Gastrointestinal Stromal Tumors
    - Gestational Trophoblastic Neoplasms
    - Hairy Cell Leukemia
    - Head and Neck Cancers
    - Hodgkin Lymphoma
    - Hepatocellular Carcinoma
    - Kaposi Sarcoma
    - Kidney Cancer
    - Melanoma: Cutaneous
    - Melanoma: Uveal
    - Merkel Cell Carcinoma
    - Mesothelioma: Peritoneal
    - Mesothelioma: Pleural
    - Myelodysplastic Syndromes
    - Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Gene Fusions
    - Myeloproliferative Neoplasms
    - Neuroendocrine and Adrenal Tumors
    - Non-Small Cell Lung Cancer
    - Occult Primary
    - Ovarian Cancer
    - Pancreatic Cancer
    - Penile Cancer
    - Prostate Cancer
    - Rectal Cancer
    - Small Bowl Adenocarcinoma
    - Small Cell Lung Cancer
    - Soft Tissue Sarcoma
    - Squamous Cell Skin Cancer
    - Systemic Mastocytosis
    - Systemic Light Chain Amyloidosis

- o Testicular Cancer
- o Thymomas and Thymic Carcinomas
- o Thyroid Carcinoma
- o Uterine Neoplasms
- o Vulvar Cancer
- o Waldenström Macroglobulinemia / Lymphoplasmacytic Lymphoma

In addition, the following criteria must be met for approval:

1. The requested regimen for the drug(s) or biologic(s) and indication is consistent with an NCCN recommendation with a level of evidence category of 1 or 2A.
2. The NCCN template must be accepted by the provider without modification.

Further review may be indicated when the above criteria are not met.

Authorizations may be granted for 12 months or as medically required, based on the member's condition and provider's assessment.

Supportive Care: Myeloid Growth Factor Therapy
Granulocyte colony stimulating factors are recommended for primary prophylaxis based on the febrile neutropenia risk of the chemotherapy regimen. Febrile neutropenia risk levels vary by NCCN Chemotherapy Order template and are listed at the top of the template. Regimens associated with a high or intermediate risk of febrile neutropenia may include a granulocyte colony stimulating factor as part of the prior authorization.

Continuation of Therapy
To submit a request for continuation of therapy, a new regimen prior authorization review must be requested. Upon template selection, the template must be modified to include the appropriate therapies being used for maintenance treatment. The regimen request will be submitted for further review.

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

REFERENCES:

SECTION 1

1. Gemzar [package insert]. Indianapolis, IN: Lilly USA, LLC; May 2019.
2. Infugem [package insert]. Cranbury, NJ: Sun Pharmaceutical Industries, Inc.; January 2020.
3. Gemcitabine [package insert]. Chicago, IL: Meitheal Pharmaceuticals; August 2019.
4. The NCCN Drugs & Biologics Compendium® © 2022 National Comprehensive Cancer Network, Inc. Available at: https://www.nccn.org. Accessed July 20, 2022.
5. Lexicomp [database online]. Hudson, OH: Lexi-Comp, Inc.; https://online.lexi.com/lco/action/index/dataset/complete_ashp [available with subscription]. Accessed July 20, 2022.
6. Clinical Pharmacology [database online]. Tampa, FL: Elsevier; https://www.clinicalkey.com/pharmacology [available with subscription]. Accessed July 20, 2022.
7. Micromedex Solutions [database online]. Ann Arbor, MI: Truven Health Analytics Inc. Updated periodically. www.micromedexsolutions.com [available with subscription]. Accessed July 20, 2022.

SECTION 2

1. National Comprehensive Cancer Network. About NCCN website. https://www.nccn.org/home/about, accessed June 6, 2023.

2. National Comprehensive Cancer Network. NCCN Categories of Evidence and Consensus website, https://www.nccn.org/guidelines/guidelines-process/development-and-update-of-guidelines, accessed June 6, 2023.
3. National Comprehensive Cancer Network. NCCN Guidelines website. https://www.nccn.org/guidelines/category_1, accessed June 6, 2023. (Note: An account may be required.)
4. National Comprehensive Cancer Network. NCCN Drugs and Biologics Compendium website https://www.nccn.org/compendia-templates/compendia/drugs-and-biologics-compendia, accessed June 6, 2023. (Note: A subscription may be required.)
5. National Comprehensive Cancer Network. NCCN Chemotherapy Order Templates (NCCN Templates) website. https://www.nccn.org/compendia-templates/nccn-templates-main/browse-by-cancer-type, accessed June 6, 2023. (Note: A subscription may be required.)

Reference number
2075-A

SPECIALTY GUIDELINE MANAGEMENT

GAZYVA (obinutuzumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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 Lymphocytic Leukemia (CLL)
   Gazyva, in combination with chlorambucil, is indicated for the treatment of patients with previously untreated CLL.
2. Follicular Lymphoma
   a. Gazyva, in combination with bendamustine followed by Gazyva monotherapy, is indicated for the treatment of patients with follicular lymphoma who relapsed after, or are refractory to, a rituximab-containing regimen.
   b. Gazyva, in combination with chemotherapy followed by Gazyva monotherapy in patients achieving at least a partial remission, is indicated for the treatment of adult patients with previously untreated stage II bulky, III or IV follicular lymphoma.

B. Compendial Uses
1. Chronic lymphocytic leukemia/ small lymphocytic lymphoma (CLL/ SLL)
2. Follicular lymphoma
3. Marginal zone lymphomas
   a. Extranodal (gastric and non-gastric MALT lymphoma) marginal zone lymphoma
   b. Nodal marginal zone lymphoma
   c. Splenic marginal zone lymphoma
4. Histologic transformation of indolent lymphomas to diffuse large B-cell lymphoma
5. Mantle cell lymphoma
6. Diffuse large B-cell lymphoma
7. High-grade B-cell lymphomas (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. Burkitt lymphoma
9. HIV-related B-cell lymphomas
10. Post-transplant lymphoproliferative disorders
11. Castleman's disease
12. Hairy Cell Leukemia

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

II. CRITERIA FOR INITAL APPROVAL

A. Chronic Lymphocytic Leukemia (CLL) and Small Lymphocytic Lymphoma (SLL)
Authorization of 6 months may be granted for the treatment of CLL/SLL as a single agent or in combination with acalabrutinib, venetoclax, bendamustine, or chlorambucil.

B. Follicular Lymphoma (FL)

Authorization of 6 months, up to 30 months total, may be granted for the treatment of follicular lymphoma when any of the following criteria are met:

1. The requested medication will be used in combination with CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) regimen, CVP (cyclophosphamide, vincristine and prednisone) regimen, or bendamustine as first line therapy.
2. The requested medication will be used as a single agent or in combination with lenalidomide, bendamustine, CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) or CVP (cyclophosphamide, vincristine, and prednisone) for subsequent therapy.
3. The requested medication will be used as maintenance therapy as a single agent.
4. The requested medication will be used as a substitute for rituximab in members experiencing intolerance or rare complications from rituximab such as mucocutaneous reactions including paraneoplastic pemphigus, Stevens-Johnson syndrome, lichenoid dermatitis, vesiculobullous dermatitis, and toxic epidermal necrolysis.

C. Extranodal Marginal Zone Lymphoma and Splenic Marginal Zone Lymphoma

Authorization of 6 months may be granted for the treatment of extranodal marginal zone lymphoma (gastric and non-gastric MALT lymphoma) or splenic marginal zone lymphoma when any of the following criteria are met:

1. The requested medication will be used as subsequent therapy in combination with bendamustine or lenalidomide.
2. The requested medication be used as maintenance therapy when the member has been previously treated with the requested medication and bendamustine.
3. The requested medication is used as a substitute for rituximab in members experiencing intolerance or rare complications from rituximab such as mucocutaneous reactions including paraneoplastic pemphigus, Stevens-Johnson syndrome, lichenoid dermatitis, vesiculobullous dermatitis, and toxic epidermal necrolysis.

D. Nodal Marginal Zone Lymphoma

Authorization of 6 months may be granted for the treatment of nodal marginal zone lymphoma when any of the following criteria are met:

1. The requested medication will be used as first-line therapy in combination with CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) regimen, CVP (cyclophosphamide, vincristine and prednisone) regimen, or bendamustine.
2. The requested medication will be used as subsequent therapy in combination with bendamustine or lenalidomide.
3. The requested medication be used as maintenance therapy when the member has been previously treated with the requested medication and bendamustine.
4. The requested medication is used as a substitute for rituximab in members experiencing intolerance or rare complications from rituximab such as mucocutaneous reactions including paraneoplastic pemphigus, Stevens-Johnson syndrome, lichenoid dermatitis, vesiculobullous dermatitis, and toxic epidermal necrolysis.

E. Hairy Cell Leukemia

Authorization of 6 months may be granted in combination with vemurafenib as initial therapy for treatment of hairy cell leukemia in members who are unable to tolerate purine analogs.

F. Diffuse Large B-Cell Lymphoma when used as pre- treatment with glofitamab (Columvi)

Authorization of 1 month may be granted for treatment of diffuse large B-cell lymphoma when used as pre-treatment for up to 1 dose in cycle 1 of glofitamab therapy.

G. Histologic Transformation of Indolent Lymphomas to Diffuse Large B-Cell Lymphoma, Mantle Cell Lymphoma, Diffuse Large B-Cell Lymphoma, High-Grade B-Cell Lymphomas(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), Burkitt Lymphoma, HIV-Related B-Cell Lymphomas, Post-Transplant Lymphoproliferative Disorders, and Castleman's Disease
Authorization of 6 months may be granted for the treatment of histologic transformation of indolent lymphomas to diffuse large B-cell lymphoma, mantle cell lymphoma, diffuse large B-cell lymphoma, high-grade B-cell lymphomas (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), Burkitt lymphoma, HIV-related B-cell lymphomas, post-transplant lymphoproliferative disorders, or Castleman's disease when the requested medication is used as a substitute for rituximab in members experiencing intolerance or rare complications from rituximab such as mucocutaneous reactions including paraneoplastic pemphigus, Stevens-Johnson syndrome, lichenoid dermatitis, vesiculobullous dermatitis, and toxic epidermal necrolysis.

III. CONTINUATION OF THERAPY

A. Follicular Lymphoma (FL)
Authorization of 12 months, up to 30 months total, may be granted for continued treatment in members requesting reauthorization for follicular lymphoma when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

B. Diffuse Large B-Cell Lymphoma when used as pre- treatment with glofitamab (Columvi)
All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

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 when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

IV. APPENDIX

Re-challenge with the same anti-CD20 monoclonal antibody is not recommended and it is unclear if the use of an alternative anti-CD20 monoclonal antibody poses the same risk of recurrence.

V. REFERENCES

1. Gazyva [package insert]. South San Francisco, CA: Genentech, Inc.; July 2022.
2. Columvi [package insert]. South San Francisco, CA: Genentech, Inc.; June 2023.
3. The NCCN Drugs & Biologics Compendium® © 2023 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed June 2, 2023.

Reference number(s)
2040-A

SPECIALTY GUIDELINE MANAGEMENT

GEMZAR (gemcitabine)
INFUGEM (gemcitabine)
gemcitabine

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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
   In combination with carboplatin for the treatment of patients with advanced ovarian cancer that has relapsed at least 6 months after completion of platinum-based therapy
2. Breast cancer
   In combination with paclitaxel for the first-line treatment of patients with metastatic breast cancer after failure of prior anthracycline-containing adjuvant chemotherapy, unless anthracyclines were clinically contraindicated
3. Non-small cell lung cancer
   In combination with cisplatin for the first-line treatment of patients with inoperable, locally advanced (Stage IIIA or IIIB), or metastatic (Stage IV) non-small cell lung cancer (NSCLC)
4. Pancreatic cancer
   As first-line treatment for patients with locally advanced (nonresectable Stage II or Stage III) or metastatic (Stage IV) adenocarcinoma of the pancreas. Gemzar, Infugem or gemcitabine is indicated for patients previously treated with fluorouracil.

B. Compendial Uses
1. Ampullary adenocarcinoma
2. Bladder cancer, primary carcinoma of the urethra, upper genitourinary tract tumors, transitional cell carcinoma of the urinary tract, urothelial carcinoma of the prostate, non-urothelial and urothelial cancer with variant histology
3. Bone cancer
   a. Ewing's sarcoma
   b. Osteosarcoma
4. Breast cancer
5. Cervical cancer
6. Head and neck cancers (including very advanced head and neck cancer, cancer of the nasopharynx, and salivary gland tumors)
7. Biliary tract cancer
   a. Extrahepatic cholangiocarcinoma
   b. Intrahepatic cholangiocarcinoma
   c. Gallbladder cancer
8. Hodgkin lymphoma
   a. Classic Hodgkin lymphoma
   b. Nodular lymphocyte-predominant Hodgkin lymphoma

9. Kidney cancer
10. Pleural or peritoneal mesothelioma
11. Non-small cell lung cancer (NSCLC)
12. Occult primary tumors (cancer of unknown primary)
13. Ovarian cancer, fallopian tube cancer, and primary peritoneal cancer: epithelial ovarian cancer, fallopian tube cancer, and primary peritoneal cancer
14. Pancreatic adenocarcinoma
15. Small cell lung cancer (SCLC)
16. Soft tissue sarcoma
    a. Angiosarcoma
    b. Extremity/Body wall, head/neck
    c. Retroperitoneal/intra-abdominal
    d. Rhabdomyosarcoma
    e. Solitary fibrous tumor
    f. Dedifferentiated chordoma
    g. Dermatofibrosarcoma protuberans (DFSP) with fibrosarcomatous transformation
17. Testicular cancer
18. Thymomas and thymic carcinomas
19. Uterine neoplasms (including uterine sarcoma and uterine leiomyosarcoma)
20. Kaposi Sarcoma
21. Primary cutaneous lymphomas
    a. Mycosis fungoides/Sezary syndrome
    b. Primary cutaneous CD30+ T-Cell lymphoproliferative disorders
22. T-Cell lymphomas
    a. Peripheral T-Cell lymphomas
    b. Adult T-Cell leukemia/lymphoma
    c. Breast implant-associated anaplastic large cell lymphoma
    d. Extranodal natural killer (NK)/T-Cell lymphoma
    e. Hepatosplenic T-Cell lymphoma
23. Gestational trophoblastic neoplasia
24. B-Cell lymphomas
    a. Follicular lymphoma (grade 1-2)
    b. Histologic transformation of indolent lymphomas to diffuse large B-Cell lymphoma
    c. Mantle cell lymphoma
    d. Diffuse large B-Cell lymphoma
    e. High-Grade B-Cell lymphomas
    f. Burkitt lymphoma
    g. Human immunodeficiency virus (HIV)-Related B-Cell lymphomas
    h. Post-Transplant lymphoproliferative disorders
25. Small bowel adenocarcinoma
26. Malignant germ cell tumor
27. Vulvar cancer

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

II. CRITERIA FOR INITIAL APPROVAL

A. Pancreatic Adenocarcinoma

Authorization of 6 months may be granted for treatment of pancreatic adenocarcinoma.

B. Breast Cancer

Authorization of 6 months may be granted for treatment of members with no response to preoperative systemic therapy, recurrent, or metastatic breast cancer.

C. Biliary Tract Cancer
Authorization of 6 months may be granted for treatment of biliary tract cancer (including intrahepatic and extrahepatic cholangiocarcinoma, and gallbladder cancer).

D. Ampullary Adenocarcinoma
Authorization of 6 months may be granted for treatment of ampullary adenocarcinoma.

E. Ovarian Cancer, Fallopian Tube Cancer, and Primary Peritoneal Cancer
Authorization of 6 months may be granted for treatment of advanced, 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 carcinoma/ovarian borderline epithelial tumors (low malignant potential), mucinous carcinoma of the ovary, or malignant germ cell tumor residual disease.

F. Non-Small Cell Lung Cancer (NSCLC)
Authorization of 6 months may be granted for treatment of NSCLC.

G. Cervical Cancer
Authorization of 6 months may be granted for treatment of cervical cancer.

H. Bladder Cancer, Primary Carcinoma of the Urethra, Upper Genitourinary Tract Tumors, Transitional Cell Carcinoma of the Urinary Tract, Urothelial Carcinoma of the Prostate, and Non-Urothelial and Urothelial Cancer with Variant Histology
Authorization of 6 months may be granted for treatment of bladder cancer, primary carcinoma of the urethra, upper genitourinary tract tumors, transitional cell carcinoma of the urinary tract, urothelial carcinoma of the prostate, and non-urothelial and urothelial cancer with variant histology.

I. Small Cell Lung Cancer (SCLC)
Authorization of 6 months may be granted for treatment of SCLC.

J. Soft Tissue Sarcoma
Authorization of 6 months may be granted for treatment of soft tissue sarcoma (including angiosarcoma, extremity/body wall, head/neck, retroperitoneal/intra-abdominal, rhabdomyosarcoma, solitary fibrous tumor, dedifferentiated chordoma, and dermatofibrosarcoma protuberans (DFSP) with fibrosarcomatous transformation).

K. Bone Cancer

1. Ewing's Sarcoma
Authorization of 6 months may be granted for treatment of relapsed, progressive, or metastatic Ewing's sarcoma.

2. Osteosarcoma
Authorization of 6 months may be granted for treatment of relapsed/refractory or metastatic osteosarcoma.

L. Head and Neck Cancer
Authorization of 6 months may be granted for treatment of head and neck cancer (including very advanced head and neck cancer, cancer of the nasopharynx, and salivary gland tumors).

M. Hodgkin Lymphoma

1. Hodgkin Lymphoma
Authorization of 6 months may be granted for treatment of Hodgkin lymphoma including classic Hodgkin lymphoma and pediatric Hodgkin lymphoma.

2. Nodular Lymphocyte-Predominant Hodgkin Lymphoma
Authorization of 6 months may be granted for treatment of progressive, relapsed, or refractory nodular lymphocyte-predominant Hodgkin lymphoma.

N. Kidney Cancer
Authorization of 6 months may be granted for treatment of relapsed or metastatic kidney cancer.

O. Pleural or Peritoneal Mesothelioma
Authorization of 6 months may be granted for treatment of pleural or peritoneal mesothelioma, including pericardial mesothelioma and tunica vaginalis testis mesothelioma.

P. Occult Primary Tumors (cancer of unknown primary)
Authorization of 6 months may be granted for treatment of occult primary tumors.

Q. Testicular Cancer
Authorization of 6 months may be granted for treatment of testicular cancer.

R. Thymomas and Thymic Carcinomas
Authorization of 6 months may be granted for treatment of thymomas and thymic carcinomas.

S. Uterine Neoplasms
Authorization of 6 months may be granted for treatment of uterine neoplasms (including uterine sarcoma and uterine leiomyosarcoma).

T. Kaposi Sarcoma
Authorization of 6 months may be granted for treatment of Kaposi Sarcoma.

U. Primary Cutaneous Lymphomas
Authorization of 6 months may be granted for treatment of primary cutaneous lymphomas (including mycosis fungoides/Sezary syndrome and primary cutaneous CD30+ T-Cell lymphoproliferative disorders).

V. T-Cell Lymphomas
Authorization of 6 months may be granted for treatment of T-Cell lymphomas (including peripheral T-Cell lymphomas, adult T-Cell leukemia/lymphoma, hepatosplenic T-Cell lymphoma, breast implant-associated anaplastic large cell lymphoma, and extranodal NK/T-Cell lymphoma).

W. Gestational Trophoblastic Neoplasia
Authorization of 6 months may be granted for treatment of gestational trophoblastic neoplasia.

X. B-Cell Lymphomas
Authorization of 6 months may be granted for treatment of B-Cell lymphomas (including follicular lymphoma [grade 1-2], histologic transformation of indolent lymphomas to diffuse large B-Cell lymphoma, mantle cell lymphoma, diffuse large B-Cell lymphoma, high-grade B-Cell lymphomas, Burkitt lymphoma, HIV-Related B-Cell lymphomas, and post-transplant lymphoproliferative disorders).

Y. Small Bowel Adenocarcinoma
Authorization of 6 months may be granted for treatment of small bowel adenocarcinoma.

Z. Malignant Germ Cell Tumor
Authorization of 6 months may be granted for treatment of malignant germ cell tumor.

AA. Vulvar Cancer
Authorization of 6 months may be granted for treatment of vulvar cancer as concurrent chemoradiation as a single agent if cisplatin is unavailable.

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 there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

IV. REFERENCES

1. Gemzar [package insert]. Indianapolis, IN: Lilly USA, LLC; May 2019.
2. Infugem [package insert]. Cranbury, NJ: Sun Pharmaceutical Industries, Inc.; January 2020.
3. Gemcitabine [package insert]. Chicago, IL: Meitheal Pharmaceuticals; August 2019.
4. The NCCN Drugs & Biologics Compendium® © 2023 National Comprehensive Cancer Network, Inc. Available at: https://www.nccn.org. Accessed October 9, 2023.
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6. Clinical Pharmacology [database online]. Tampa, FL: Elsevier; https://www.clinicalkey.com/pharmacology [available with subscription]. Accessed July 14, 2023.
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POLICY Document for GEMZAR (gemcitabine) gemcitabine

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, and overall, clinically appropriate use. This document provides specific information to both sections of the overall policy.

Section 1: Clinical Criteria

- Policy information specific to the clinical appropriateness for the medication

Section 2: Oncology Clinical Policy

- Policy information specific to regimen review per NCCN Guidelines.

Section 1: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

GEMZAR (gemcitabine)
INFUGEM (gemcitabine)
gemcitabine

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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
   In combination with carboplatin for the treatment of patients with advanced ovarian cancer that has relapsed at least 6 months after completion of platinum-based therapy
2. Breast cancer
   In combination with paclitaxel for the first-line treatment of patients with metastatic breast cancer after failure of prior anthracycline-containing adjuvant chemotherapy, unless anthracyclines were clinically contraindicated
3. Non-small cell lung cancer
   In combination with cisplatin for the first-line treatment of patients with inoperable, locally advanced (Stage IIIA or IIIB), or metastatic (Stage IV) non-small cell lung cancer (NSCLC)
4. Pancreatic cancer
   As first-line treatment for patients with locally advanced (nonresectable Stage II or Stage III) or metastatic (Stage IV) adenocarcinoma of the pancreas. Gemzar, Infugem or gemcitabine is indicated for patients previously treated with fluorouracil.

B. Compendial Uses
1. Ampullary adenocarcinoma
2. Bladder cancer, primary carcinoma of the urethra, upper genitourinary tract tumors, transitional cell carcinoma of the urinary tract, urothelial carcinoma of the prostate, non-urothelial and urothelial cancer with variant histology
3. Bone cancer

   a. Ewing's sarcoma
   b. Osteosarcoma
4. Breast cancer
5. Cervical cancer
6. Head and neck cancers (including very advanced head and neck cancer, cancer of the nasopharynx, and salivary gland tumors)
7. Biliary tract cancer
   a. Extrahepatic cholangiocarcinoma
   b. Intrahepatic cholangiocarcinoma
   c. Gallbladder cancer
8. Hodgkin lymphoma
   a. Classic Hodgkin lymphoma
   b. Nodular lymphocyte-predominant Hodgkin lymphoma
9. Kidney cancer
10. Pleural or peritoneal mesothelioma
11. Non-small cell lung cancer (NSCLC)
12. Occult primary tumors (cancer of unknown primary)
13. Ovarian cancer, fallopian tube cancer, and primary peritoneal cancer: epithelial ovarian cancer, fallopian tube cancer, and primary peritoneal cancer
14. Pancreatic adenocarcinoma
15. Small cell lung cancer (SCLC)
16. Soft tissue sarcoma
   a. Angiosarcoma
   b. Extremity/Body wall, head/neck
   c. Retroperitoneal/intra-abdominal
   d. Rhabdomyosarcoma
   e. Solitary fibrous tumor
   f. Dedifferentiated chordoma
   g. Dermatofibrosarcoma protuberans (DFSP) with fibrosarcomatous transformation
17. Testicular cancer
18. Thymomas and thymic carcinomas
19. Uterine neoplasms (including uterine sarcoma and uterine leiomyosarcoma)
20. Kaposi Sarcoma
21. Primary cutaneous lymphomas
   a. Mycosis fungoides/Sezary syndrome
   b. Primary cutaneous CD30+ T-Cell lymphoproliferative disorders
22. T-Cell lymphomas
   a. Peripheral T-Cell lymphomas
   b. Adult T-Cell leukemia/lymphoma
   c. Breast implant-associated anaplastic large cell lymphoma
   d. Extranodal natural killer (NK)/T-Cell lymphoma
   e. Hepatosplenic T-Cell lymphoma
23. Gestational trophoblastic neoplasia
24. B-Cell lymphomas
   a. Follicular lymphoma (grade 1-2)
   b. Histologic transformation of indolent lymphomas to diffuse large B-Cell lymphoma
   c. Mantle cell lymphoma
   d. Diffuse large B-Cell lymphoma
   e. High-Grade B-Cell lymphomas
   f. Burkitt lymphoma
   g. Human immunodeficiency virus (HIV)-Related B-Cell lymphomas
   h. Post-Transplant lymphoproliferative disorders
25. Small bowel adenocarcinoma
26. Malignant germ cell tumor
27. Vulvar cancer

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

II. CRITERIA FOR INITIAL APPROVAL

A. Pancreatic Adenocarcinoma
Authorization of 6 months may be granted for treatment of pancreatic adenocarcinoma.

B. Breast Cancer
Authorization of 6 months may be granted for treatment of members with no response to preoperative systemic therapy, recurrent, or metastatic breast cancer.

C. Biliary Tract Cancer
Authorization of 6 months may be granted for treatment of biliary tract cancer (including intrahepatic and extrahepatic cholangiocarcinoma, and gallbladder cancer).

D. Ampullary Adenocarcinoma
Authorization of 6 months may be granted for treatment of ampullary adenocarcinoma.

E. Ovarian Cancer, Fallopian Tube Cancer, and Primary Peritoneal Cancer
Authorization of 6 months may be granted for treatment of advanced, 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 carcinoma/ovarian borderline epithelial tumors (low malignant potential), mucinous carcinoma of the ovary, or malignant germ cell tumor residual disease.

F. Non-Small Cell Lung Cancer (NSCLC)
Authorization of 6 months may be granted for treatment of NSCLC.

G. Cervical Cancer
Authorization of 6 months may be granted for treatment of cervical cancer.

H. Bladder Cancer, Primary Carcinoma of the Urethra, Upper Genitourinary Tract Tumors, Transitional Cell Carcinoma of the Urinary Tract, Urothelial Carcinoma of the Prostate, and Non-Urothelial and Urothelial Cancer with Variant Histology
Authorization of 6 months may be granted for treatment of bladder cancer, primary carcinoma of the urethra, upper genitourinary tract tumors, transitional cell carcinoma of the urinary tract, urothelial carcinoma of the prostate, and non-urothelial and urothelial cancer with variant histology.

I. Small Cell Lung Cancer (SCLC)
Authorization of 6 months may be granted for treatment of SCLC.

J. Soft Tissue Sarcoma
Authorization of 6 months may be granted for treatment of soft tissue sarcoma (including angiosarcoma, extremity/body wall, head/neck, retroperitoneal/intra-abdominal, rhabdomyosarcoma, solitary fibrous tumor, dedifferentiated chordoma, and dermatofibrosarcoma protuberans (DFSP) with fibrosarcomatous transformation).

K. Bone Cancer

1. Ewing's Sarcoma
Authorization of 6 months may be granted for treatment of relapsed, progressive, or metastatic Ewing's sarcoma.

2. **Osteosarcoma**
   Authorization of 6 months may be granted for treatment of relapsed/refractory or metastatic osteosarcoma.

L. Head and Neck Cancer
Authorization of 6 months may be granted for treatment of head and neck cancer (including very advanced head and neck cancer, cancer of the nasopharynx, and salivary gland tumors).

M. Hodgkin Lymphoma

1. **Hodgkin Lymphoma**
   Authorization of 6 months may be granted for treatment of Hodgkin lymphoma including classic Hodgkin lymphoma and pediatric Hodgkin lymphoma.

2. **Nodular Lymphocyte-Predominant Hodgkin Lymphoma**
   Authorization of 6 months may be granted for treatment of progressive, relapsed, or refractory nodular lymphocyte-predominant Hodgkin lymphoma.

N. Kidney Cancer
Authorization of 6 months may be granted for treatment of relapsed or metastatic kidney cancer.

O. Pleural or Peritoneal Mesothelioma
Authorization of 6 months may be granted for treatment of pleural or peritoneal mesothelioma, including pericardial mesothelioma and tunica vaginalis testis mesothelioma.

P. Occult Primary Tumors (cancer of unknown primary)
Authorization of 6 months may be granted for treatment of occult primary tumors.

Q. Testicular Cancer
Authorization of 6 months may be granted for treatment of testicular cancer.

R. Thymomas and Thymic Carcinomas
Authorization of 6 months may be granted for treatment of thymomas and thymic carcinomas.

S. Uterine Neoplasms
Authorization of 6 months may be granted for treatment of uterine neoplasms (including uterine sarcoma and uterine leiomyosarcoma).

T. Kaposi Sarcoma
Authorization of 6 months may be granted for treatment of Kaposi Sarcoma.

U. Primary Cutaneous Lymphomas
Authorization of 6 months may be granted for treatment of primary cutaneous lymphomas (including mycosis fungoides/Sezary syndrome and primary cutaneous CD30+ T-Cell lymphoproliferative disorders).

V. T-Cell Lymphomas
Authorization of 6 months may be granted for treatment of T-Cell lymphomas (including peripheral T-Cell lymphomas, adult T-Cell leukemia/lymphoma, hepatosplenic T-Cell lymphoma, breast implant-associated anaplastic large cell lymphoma, and extranodal NK/T-Cell lymphoma).

W. Gestational Trophoblastic Neoplasia
Authorization of 6 months may be granted for treatment of gestational trophoblastic neoplasia.

X. B-Cell Lymphomas

Authorization of 6 months may be granted for treatment of B-Cell lymphomas (including follicular lymphoma [grade 1-2], histologic transformation of indolent lymphomas to diffuse large B-Cell lymphoma, mantle cell lymphoma, diffuse large B-Cell lymphoma, high-grade B-Cell lymphomas, Burkitt lymphoma, HIV-Related B-Cell lymphomas, and post-transplant lymphoproliferative disorders).

Y. Small Bowel Adenocarcinoma
Authorization of 6 months may be granted for treatment of small bowel adenocarcinoma.

Z. Malignant Germ Cell Tumor
Authorization of 6 months may be granted for treatment of malignant germ cell tumor.

AA. Vulvar Cancer
Authorization of 6 months may be granted for treatment of vulvar cancer as concurrent chemoradiation as a single agent if cisplatin is unavailable.

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 there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

Section 2: Oncology Clinical Policy

PROGRAM DESCRIPTION

The National Comprehensive Care Network® (NCCN®) is an alliance of leading cancer centers devoted to patient care, research and education dedicated to improving the quality, effectiveness, and efficiency of cancer care so patients can live better lives.[1] It is comprised of oncology experts who convene regularly to establish the best treatments for patients. NCCN develops various resources for use by stakeholders in the health care delivery system. These resources include, but are not limited to, the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®), the NCCN Drugs & Biologics Compendium (NCCN Compendium®) and the NCCN Chemotherapy Order Templates (NCCN Templates®).

NCCN Templates® are based on NCCN Guidelines® and NCCN Compendium®. The NCCN Compendium lists the appropriate drugs and biologics as treatment options for specific cancers using U.S. Food and Drug Administration (FDA)-approved disease indications and specific NCCN panel recommendations. Each recommendation is supported by a level of evidence category.

NCCN Categories of Evidence and Consensus[2]

- Category 1: Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
- Category 2A: Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
- Category 2B: Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.
- Category 3: Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

POLICY

Policy for Regimen Prior Authorization

A regimen prior authorization allows submission of a single prior authorization request for all oncology drugs or biologics within an NCCN template that require prior authorization.

PROCEDURE

This policy provides coverage of a regimen review when all of the following criteria are met:
1. Regimen prior authorization reviews, based on NCCN templates, are initiated through the provider portal.
    - If the prior authorization request is submitted via phone or fax, each drug or biologic will need to be submitted and reviewed as a separate prior authorization request for review with drug-specific criteria.
2. The prior authorization review is requested for an oncology drug or biologic.
3. The member is eligible for regimen review.
4. The indication is for a cancer that is eligible for regimen review. Currently, the cancer types in scope for regimen review include the following:
    - Ampullary Adenocarcinoma
    - Anal Carcinoma
    - B-Cell Lymphomas
    - Basal Cell Skin Cancer
    - Biliary Tract Cancers
    - Bone Cancer
    - Breast Cancer
    - Bladder Cancer
    - Central Nervous System Cancers
    - Cervical Cancer
    - Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma
    - Chronic Myeloid leukemia
    - Colon Cancer
    - Dermatofibrosarcoma Protuberans
    - Esophageal Cancer
    - Gastric Cancer
    - Gastrointestinal Stromal Tumors
    - Gestational Trophoblastic Neoplasms
    - Hairy Cell Leukemia
    - Head and Neck Cancers
    - Hodgkin Lymphoma
    - Hepatocellular Carcinoma
    - Kaposi Sarcoma
    - Kidney Cancer
    - Melanoma: Cutaneous
    - Melanoma: Uveal
    - Merkel Cell Carcinoma
    - Mesothelioma: Peritoneal
    - Mesothelioma: Pleural
    - Myelodysplastic Syndromes
    - Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Gene Fusions
    - Myeloproliferative Neoplasms
    - Neuroendocrine and Adrenal Tumors
    - Non-Small Cell Lung Cancer
    - Occult Primary
    - Ovarian Cancer
    - Pancreatic Cancer
    - Penile Cancer
    - Prostate Cancer
    - Rectal Cancer
    - Small Bowl Adenocarcinoma
    - Small Cell Lung Cancer

- Soft Tissue Sarcoma
- Squamous Cell Skin Cancer
- Systemic Mastocytosis
- Systemic Light Chain Amyloidosis
- Testicular Cancer
- Thymomas and Thymic Carcinomas
- Thyroid Carcinoma
- Uterine Neoplasms
- Vulvar Cancer
- Waldenström Macroglobulinemia / Lymphoplasmacytic Lymphoma

In addition, the following criteria must be met for approval:

1. The requested regimen for the drug(s) or biologic(s) and indication is consistent with an NCCN recommendation with a level of evidence category of 1 or 2A.
2. The NCCN template must be accepted by the provider without modification.

Further review may be indicated when the above criteria are not met.

Authorizations may be granted for 12 months or as medically required, based on the member's condition and provider's assessment.

Supportive Care: Myeloid Growth Factor Therapy
Granulocyte colony stimulating factors are recommended for primary prophylaxis based on the febrile neutropenia risk of the chemotherapy regimen. Febrile neutropenia risk levels vary by NCCN Chemotherapy Order template and are listed at the top of the template. Regimens associated with a high or intermediate risk of febrile neutropenia may include a granulocyte colony stimulating factor as part of the prior authorization.

Continuation of Therapy
To submit a request for continuation of therapy, a new regimen prior authorization review must be requested. Upon template selection, the template must be modified to include the appropriate therapies being used for maintenance treatment. The regimen request will be submitted for further review.

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

REFERENCES:

SECTION 1

1. Gemzar [package insert]. Indianapolis, IN: Lilly USA, LLC; May 2019.
2. Infugem [package insert]. Cranbury, NJ: Sun Pharmaceutical Industries, Inc.; January 2020.
3. Gemcitabine [package insert]. Chicago, IL: Meitheal Pharmaceuticals; August 2019.
4. The NCCN Drugs & Biologics Compendium® © 2023 National Comprehensive Cancer Network, Inc. Available at: https://www.nccn.org. Accessed October 9, 2023.
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SECTION 2

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2. National Comprehensive Cancer Network. NCCN Categories of Evidence and Consensus website, https://www.nccn.org/guidelines/guidelines-process/development-and-update-of-guidelines, accessed June 6, 2023.
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4. National Comprehensive Cancer Network. NCCN Drugs and Biologics Compendium website https://www.nccn.org/compendia-templates/compendia/drugs-and-biologics-compendia, accessed June 6, 2023. (Note: A subscription may be required.)
5. National Comprehensive Cancer Network. NCCN Chemotherapy Order Templates (NCCN Templates) website. https://www.nccn.org/compendia-templates/nccn-templates-main/browse-by-cancer-type, accessed June 6, 2023. (Note: A subscription may be required.)

POLICY Document for GILOTRIF (afatinib)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication. This document provides specific information to each section of the overall policy.

Section 1: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 2: Oncology Clinical Policy
- Policy information specific to regimen review per NCCN Guidelines.

Section 1: Clinical Criteria

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.

Section 2: Oncology Clinical Policy

Oncology Clinical Policy

Program Description

The National Comprehensive Care Network® (NCCN®) is an alliance of leading cancer centers devoted to patient care, research and education dedicated to improving the quality, effectiveness and efficiency of cancer care so patients can live better lives.[1] It is comprised of oncology experts who convene regularly to establish the best treatments for patients. NCCN develops various resources for use by stakeholders in the health care delivery system. These resources include, but are not limited to, the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®), the NCCN Drugs & Biologics Compendium (NCCN Compendium®) and the NCCN Chemotherapy Order Templates (NCCN Templates®).

NCCN templates are based on NCCN Clinical Practice Guidelines and NCCN Compendium. The NCCN Compendium lists the appropriate drugs and biologics for specific cancers using U.S. Food and Drug Administration (FDA)-approved disease indications and specific NCCN panel recommendations. Each recommendation is supported by a level of evidence category.

NCCN Categories of Evidence and Consensus[2]

Category 1: Based on high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2A: Based on lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2B: Based on lower-level evidence, there is NCCN consensus that the intervention is appropriate.
Category 3: Based any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

Policy for Regimen Prior Authorization

A regimen prior authorization allows submission of a single prior authorization request for all oncology drugs or biologics within an NCCN template that require prior authorization.

This policy provides coverage of a regimen review when *all* of the following criteria are met:
a. Regimen prior authorization reviews, based on NCCN templates, are initiated through the provider portal: https://provider.carefirst.com/providers/home.page
b. If the prior authorization request is submitted via phone or fax, each drug or biologic will need to be submitted and reviewed as a separate prior authorization request for review with drug-specific criteria.
2. The prior authorization review is requested for an oncology drug or biologic that requires prior authorization on the medical benefit.
3. The indication is for a cancer that is eligible for regimen review. Currently, the cancer types in scope for regimen review include breast, lung, colon and rectal cancer.
4. The member is eligible for regimen review.

In addition, the following criteria must be met for approval:
1. The requested regimen for the drug(s) or biologic(s) and indication is consistent with an NCCN recommendation with a level of evidence category of 1 or 2A.
2. The NCCN template must be accepted by the provider without modification. Authorizations may be granted for 12 months. Further review may be indicated where the above criteria are not met.

Continuation of Therapy

To submit a request for continuation of therapy, a new regimen prior authorization review must be requested. Upon template selection, the template must be modified to include the appropriate therapies being used for maintenance treatment. The regimen request will be submitted for further review.

Dosage and Administration

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

REFERENCES

SECTION 1

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.

SECTION 2

1. National Comprehensive Cancer Network. About NCCN website. https://www.nccn.org/about/default.aspx, accessed September 16, 2019.
2. National Comprehensive Cancer Network. NCCN Categories of Evidence and Consensus website. https://www.nccn.org/professionals/physician_gls/categories_of_consensus.aspx, accessed September 16, 2019.
3. National Comprehensive Cancer Network. NCCN Guidelines website. http://www.nccn.org/professionals/physician_gls/f_guidelines.asp, accessed September 16, 2019. (Note:An account may be required.)
4. National Comprehensive Cancer Network. NCCN Drugs and Biologics Compendium® website. http://www.nccn.org/professionals/drug_compendium/content/contents.asp, accessed September 16, 2019. (Note: A subscription may be required.)
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POLICY Document for GIVLAARI (givosiran)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, lower cost site of care and overall, clinically appropriate use. This document provides specific information to each of the three sections of the overall policy.

Section 1: Site of Care
- Policy information specific to site of care (outpatient, hospital outpatient, home infusion)

Section 2: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 1: Site of Care

CareFirst Site of Care Criteria
Administration of Subcutaneous Givlaari

POLICY

I. CRITERIA FOR APPROVAL FOR ADMINISTRATION IN OUTPATIENT HOSPITAL SETTING

This policy provides coverage for administration of Givlaari in an outpatient hospital setting for up to 45 days when a member is new to therapy or is reinitiating therapy after not being on therapy for at least 6 months.

This policy provides coverage for administration of Givlaari in an outpatient hospital setting for a longer course of treatment when ANY of the following criteria are met:

A. The member has experienced an adverse reaction that did not respond to conventional interventions (eg, acetaminophen, steroids, diphenhydramine, fluids or other pre-medications) or a severe adverse event (anaphylaxis, anaphylactoid reactions, myocardial infarction, thromboembolism, or seizures) during or immediately after administration.
B. The member is medically unstable (eg respiratory, cardiovascular, or renal conditions).
C. The member has significant behavioral issues and/or physical or cognitive impairment that would impact the safety of drug administration AND the patient does not have access to a caregiver.
D. The member is less than 14 years of age.

For situations where administration of Givlaari does not meet the criteria for outpatient hospital administration, coverage for Givlaari is provided when administered in alternative sites such as; physician office, home infusion or ambulatory care.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the site of care prior authorization review (where applicable):

A. Medical records supporting the member has experienced an adverse reaction that did not respond to conventional interventions or a severe adverse event during or immediately after administration
B. Medical records supporting the member is medically unstable
C. Medical records supporting the member has behavioral issues and/or physical or cognitive impairment and no access to a caregiver

Section 2: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT
GIVLAARI (givosiran)

POLICY

III. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Givlaari is indicated for the treatment of adults with acute hepatic porphyria (AHP).

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

IV. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
Elevated porphobilinogen (PBG) in the urine confirmed by a PBG quantitative, random urine test, or an elevated porphyrin level (plasma or fecal).

V. CRITERIA FOR INITIAL APPROVAL

Acute Hepatic Porphyria
Authorization of 12 months may be granted for treatment of acute hepatic porphyria when all of the following criteria are met:
1. The member is actively symptomatic
2. The member has an elevated urine porphobilinogen (PBG), or an elevated porphyrin level (plasma or fecal).

VI. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment of an indication listed in Section III for members who are experiencing benefit (e.g., reduction in porphyria attacks that required hospitalizations, urgent healthcare visit, or intravenous hemin administration) from therapy while receiving Givlaari.

REFERENCES
SECTION 1
1. Givlaari [package insert]. San Diego, CA: Ajinomoto Althea, Inc.; January 2022.

SECTION 2
1. Givlaari [package insert]. Cambridge, MA: Alnylam Pharmaceuticals; December 2020.

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
   ii. 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
   iii. 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
   iv. 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 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)

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 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

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 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

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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POLICY Document for HALAVEN (eribulin mesylate)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, and overall, clinically appropriate use. This document provides specific information to both sections of the overall policy.

Section 1: Clinical Criteria

- Policy information specific to the clinical appropriateness for the medication

Section 2: Oncology Clinical Policy

- Policy information specific to regimen review per NCCN Guidelines.

Section 1: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

HALAVEN (eribulin mesylate)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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. Halaven is indicated for the treatment of patients with metastatic breast cancer who have previously received at least two chemotherapeutic regimens for the treatment of metastatic disease. Prior therapy should have included an anthracycline and a taxane in either the adjuvant or metastatic setting.
   2. Halaven is indicated for the treatment of patients with unresectable or metastatic liposarcoma who have received a prior anthracycline-containing regimen.

B. Compendial Uses
   1. Breast cancer
   2. Soft tissue sarcoma
      a. Retroperitoneal/intra-abdominal soft tissue sarcoma
      b. Pleomorphic rhabdomyosarcoma
      c. Extremity/body wall, head/neck

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: human epidermal growth factor receptor 2 (HER2) status testing results (where applicable).

III. CRITERIA FOR INITIAL APPROVAL

A. Breast Cancer

Authorization of 12 months may be granted for treatment of recurrent or metastatic breast cancer or breast cancer with no response to preoperative systemic therapy when any of the following criteria is met:

1. The requested medication will be used as a single agent for HER2-negative disease; or
2. The requested medication will be used in combination with margetuximab-cmkb or trastuzumab for HER2-positive disease.

B. Soft Tissue Sarcoma

Authorization of 12 months may be granted for treatment of any of the following types of soft tissue sarcoma, as single-agent therapy:

1. Liposarcoma
2. Pleomorphic rhabdomyosarcoma
3. Retroperitoneal/intra-abdominal soft tissue sarcoma
4. Extremity/ body wall, head/neck

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.

Section 2: Oncology Clinical Policy

PROGRAM DESCRIPTION

The National Comprehensive Care Network® (NCCN®) is an alliance of leading cancer centers devoted to patient care, research and education dedicated to improving the quality, effectiveness, and efficiency of cancer care so patients can live better lives.[1] It is comprised of oncology experts who convene regularly to establish the best treatments for patients. NCCN develops various resources for use by stakeholders in the health care delivery system. These resources include, but are not limited to, the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®), the NCCN Drugs & Biologics Compendium (NCCN Compendium®) and the NCCN Chemotherapy Order Templates (NCCN Templates®).

NCCN Templates® are based on NCCN Guidelines® and NCCN Compendium®. The NCCN Compendium lists the appropriate drugs and biologics as treatment options for specific cancers using U.S. Food and Drug Administration (FDA)-approved disease indications and specific NCCN panel recommendations. Each recommendation is supported by a level of evidence category.

NCCN Categories of Evidence and Consensus[2]

- Category 1: Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
- Category 2A: Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
- Category 2B: Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.
- Category 3: Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

POLICY

Policy for Regimen Prior Authorization

A regimen prior authorization allows submission of a single prior authorization request for all oncology drugs or biologics within an NCCN template that require prior authorization.

PROCEDURE

This policy provides coverage of a regimen review when all of the following criteria are met:
1. Regimen prior authorization reviews, based on NCCN templates, are initiated through the provider portal.
    - If the prior authorization request is submitted via phone or fax, each drug or biologic will need to be submitted and reviewed as a separate prior authorization request for review with drug-specific criteria.
2. The prior authorization review is requested for an oncology drug or biologic.
3. The member is eligible for regimen review.
4. The indication is for a cancer that is eligible for regimen review. Currently, the cancer types in scope for regimen review include the following:
    - Ampullary Adenocarcinoma
    - Anal Carcinoma
    - B-Cell Lymphomas
    - Basal Cell Skin Cancer
    - Biliary Tract Cancers
    - Bone Cancer
    - Breast Cancer
    - Bladder Cancer
    - Central Nervous System Cancers
    - Cervical Cancer
    - Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma
    - Chronic Myeloid leukemia
    - Colon Cancer
    - Dermatofibrosarcoma Protuberans
    - Esophageal Cancer
    - Gastric Cancer
    - Gastrointestinal Stromal Tumors
    - Gestational Trophoblastic Neoplasms
    - Hairy Cell Leukemia
    - Head and Neck Cancers
    - Hodgkin Lymphoma
    - Hepatocellular Carcinoma
    - Kaposi Sarcoma
    - Kidney Cancer
    - Melanoma: Cutaneous
    - Melanoma: Uveal
    - Merkel Cell Carcinoma
    - Mesothelioma: Peritoneal
    - Mesothelioma: Pleural
    - Myelodysplastic Syndromes
    - Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Gene Fusions
    - Myeloproliferative Neoplasms
    - Neuroendocrine and Adrenal Tumors
    - Non-Small Cell Lung Cancer
    - Occult Primary
    - Ovarian Cancer
    - Pancreatic Cancer
    - Penile Cancer
    - Prostate Cancer
    - Rectal Cancer
    - Small Bowl Adenocarcinoma
    - Small Cell Lung Cancer

- Soft Tissue Sarcoma
- Squamous Cell Skin Cancer
- Systemic Mastocytosis
- Systemic Light Chain Amyloidosis
- Testicular Cancer
- Thymomas and Thymic Carcinomas
- Thyroid Carcinoma
- Uterine Neoplasms
- Vulvar Cancer
- Waldenström Macroglobulinemia / Lymphoplasmacytic Lymphoma

In addition, the following criteria must be met for approval:

1. The requested regimen for the drug(s) or biologic(s) and indication is consistent with an NCCN recommendation with a level of evidence category of 1 or 2A.
2. The NCCN template must be accepted by the provider without modification.

Further review may be indicated when the above criteria are not met.

Authorizations may be granted for 12 months or as medically required, based on the member's condition and provider's assessment.

Supportive Care: Myeloid Growth Factor Therapy
Granulocyte colony stimulating factors are recommended for primary prophylaxis based on the febrile neutropenia risk of the chemotherapy regimen. Febrile neutropenia risk levels vary by NCCN Chemotherapy Order template and are listed at the top of the template. Regimens associated with a high or intermediate risk of febrile neutropenia may include a granulocyte colony stimulating factor as part of the prior authorization.

Continuation of Therapy
To submit a request for continuation of therapy, a new regimen prior authorization review must be requested. Upon template selection, the template must be modified to include the appropriate therapies being used for maintenance treatment. The regimen request will be submitted for further review.

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

REFERENCES:

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Reference number
5680-A

SPECIALTY GUIDELINE MANAGEMENT

HEMGENIX (etranacogene dezaparvovec-drlb)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Hemgenix is an adeno-associated virus vector-based gene therapy indicated for treatment of adults with Hemophilia B (congenital Factor IX deficiency) who currently use Factor IX prophylaxis therapy, or have current or historical life-threatening hemorrhage, or have repeated, serious spontaneous bleeding episodes.

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, lab tests documenting all of the following (where applicable):
   1. Severe to moderately severe Factor IX deficiency (≤2% of normal circulating Factor IX)
   2. Absence of Factor IX inhibitors (lab test results required)
   3. Current use of Factor IX prophylaxis therapy
   4. History of life-threatening hemorrhage(s) or repeated, serious spontaneous bleeding episodes.

III. PRESCRIBER SPECIALTIES

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

IV. CRITERIA FOR INITIAL APPROVAL

Hemophilia B
Authorization of 1 month for one dose total may be granted for the treatment of hemophilia B when all of the following criteria are met:
A. Member is 18 years of age or older
B. Member meets either of the following:
   1. Member has a negative Factor IX inhibitor test result within the past 30 days
   2. If member has a positive Factor IX inhibitor test result within the past 30 days, there must be a negative test result within 2 weeks of the initial positive result
C. Member has severe or moderately severe Factor IX deficiency (≤2% of normal circulating Factor IX) and meets any of the following:
   1. Member is currently using Factor IX prophylactic therapy
   2. Member has a current or history of a life-threatening hemorrhage
   3. Member has a history of repeated, serious spontaneous bleeding episodes

D. Member has not previously received gene therapy treatment

V. REFERENCES

1. Hemgenix [package insert]. King of Prussia, PA: CSL Behring LLC; November 2022.

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 Hemlibra 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 Hemlibra.

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 Hemlibra 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.; March 2021.
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 August 2020. MASAC Document #263. https://www.hemophilia.org/sites/default/files/document/files/263_treatment.pdf. Accessed December 20, 2021.
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 20, 2021.

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POLICY Document for
HERCEPTIN (trastuzumab)
OGIVRI (trastuzumab-dkst)
KANJINTI (trastuzumab-anns)
TRAZIMERA (trastuzumab-qyyp)
HERZUMA (trastuzumab-pkrb)
ONTRUZANT (trastuzumab-dttb)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, and overall clinically appropriate use. This document provides specific information to both sections of the overall policy.

Section 1: Preferred Product
- Policy information specific to preferred medications

Section 2: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 3: Oncology Clinical Policy
- Policy information specific to regimen review per NCCN Guidelines.

Section 1: Preferred Product

EXCEPTIONS CRITERIA
TRASTUZUMAB PRODUCTS

PREFERRED PRODUCTS: HERZUMA, KANJINTI, OGIVRI, ONTRUZANT, TRAZIMERA

POLICY
This policy informs prescribers of preferred products and provides an exception process for targeted products through prior authorization.

I. PLAN DESIGN SUMMARY

This program applies to the trastuzumab products specified in this policy. Coverage for targeted products is provided based on clinical circumstances that would exclude the use of the preferred product and may be based on previous use of a product. The coverage review process will ascertain situations where a clinical exception can be made. This program applies to all members requesting treatment with a targeted product.

Each referral is reviewed based on all utilization management (UM) programs implemented for the client.

Table. Trastuzumab Products

	Product(s)
Preferred*	• **Herzuma** (trastuzumab-pkrb) • **Kanjinti** (trastuzumab-anns) • **Ogivri** (trastuzumab-dkst)

	• **Ontruzant** (trastuzumab-dttb) • **Trazimera** (trastuzumab-qyyp)
Targeted	• **Herceptin** (trastuzumab) • **Herceptin Hylecta** (trastuzumab and hyaluronidase-oysk)

*: Medications considered formulary or preferred on your plan may still require a clinical prior authorization review.

II. EXCEPTION CRITERIA

Coverage for a targeted product is provided when the member has had a documented intolerable adverse event to at least three of the preferred products, and the adverse event was not an expected adverse event attributed to the active ingredient as described in the prescribing information (i.e., known adverse reaction for both the reference product and biosimilar products).

Section 2: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

HERCEPTIN (trastuzumab)
OGIVRI (trastuzumab-dkst)
KANJINTI (trastuzumab-anns)
TRAZIMERA (trastuzumab-qyyp)
HERZUMA (trastuzumab-pkrb)
ONTRUZANT (trastuzumab-dttb)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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. Adjuvant breast cancer
   Treatment of human epidermal growth factor receptor 2 (HER2)-overexpressing node positive or node negative (estrogen receptor (ER)/progesterone receptor (PR) negative or with one high risk feature) breast cancer:
   a. As part of a treatment regimen consisting of doxorubicin, cyclophosphamide, and either paclitaxel or docetaxel
   b. As part of a treatment regimen with docetaxel and carboplatin
   c. As a single agent following multi-modality anthracycline based therapy
2. Metastatic breast cancer
   a. In combination with paclitaxel for first-line treatment of HER2-overexpressing metastatic breast cancer
   b. As a single agent for treatment of HER2-overexpressing breast cancer in patients who have received one or more chemotherapy regimens for metastatic disease
3. Metastatic gastric cancer
   In combination with cisplatin and capecitabine or 5-fluorouracil, for the treatment of patients with HER2-overexpressing metastatic gastric or gastroesophageal junction adenocarcinoma, who have not received prior treatment for metastatic disease

B. Compendial Uses
   1. HER2-positive breast cancer
      a. Neoadjuvant therapy
      b. Treatment of recurrent, advanced unresectable, or stage IV (M1) disease
   2. Intra-cerebrospinal fluid (CSF) treatment for leptomeningeal metastases from HER2-positive breast cancer
   3. HER2- positive esophageal and esophagogastric junction cancer
   4. HER2- positive advanced, recurrent, or metastatic uterine serous carcinoma
   5. HER2-amplified and RAS and BRAF wild-type colorectal cancer in combination with pertuzumab or lapatinib
   6. HER2- positive salivary gland tumor
   7. HER2-positive hepatobiliary cancers

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: human epidermal growth factor receptor 2 (HER2) status (where applicable), RAS mutation status (where applicable), BRAF mutation status (where applicable)

III. CRITERIA FOR INITIAL APPROVAL

A. Breast Cancer
1. Authorization of up to 12 months may be granted for neoadjuvant treatment of HER2-positive breast cancer as part of a complete treatment regimen.
2. Authorization of up to 12 months may be granted for adjuvant treatment of HER2-positive breast cancer.
3. Authorization of 12 months may be granted for treatment of HER2-positive recurrent, advanced unresectable, or metastatic (including brain metastases) breast cancer.
4. Authorization of 12 months may be granted for intra-CSF treatment for leptomeningeal metastases from HER2-positive breast cancer.

B. Esophageal, Gastric, or Gastroesophageal Junction Cancer
Authorization of 12 months may be granted for treatment of HER2-positive esophageal, gastric, or gastroesophageal junction cancer in combination with chemotherapy.

C. Uterine Serous Carcinoma
Authorization of 12 months may be granted for treatment of HER2-positive advanced, recurrent, or metastatic uterine serous carcinoma in combination with carboplatin and paclitaxel.

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 pertuzumab or lapatinib when either of the following are met:
1. Member is not appropriate for intensive therapy
2. Trastuzumab will be used as subsequent therapy for progression of advanced or metastatic disease

E. Salivary Gland Tumor
Authorization of 12 months may be granted for treatment of HER2-positive salivary gland tumors.

F. Hepatobiliary Cancers
Authorization of 12 months may be granted for subsequent treatment of unresectable or metastatic HER2-positive hepatobiliary cancers (including intrahepatic and extrahepatic cholangiocarcinoma and gallbladder cancer) when used in combination with pertuzumab.

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. Adjuvant and neoadjuvant treatment of breast cancer will be approved for a total of 12 months of therapy.

Section 3: Oncology Clinical Policy

Oncology Clinical Policy

Program Description

The National Comprehensive Care Network® (NCCN®) is an alliance of leading cancer centers devoted to patient care, research and education dedicated to improving the quality, effectiveness and efficiency of cancer care so patients can live better lives.[1] It is comprised of oncology experts who convene regularly to establish the best treatments for patients. NCCN develops various resources for use by stakeholders in the health care delivery system. These resources include, but are not limited to, the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®), the NCCN Drugs & Biologics Compendium (NCCN Compendium®) and the NCCN Chemotherapy Order Templates (NCCN Templates®).

NCCN templates are based on NCCN Clinical Practice Guidelines and NCCN Compendium. The NCCN Compendium lists the appropriate drugs and biologics for specific cancers using U.S. Food and Drug Administration (FDA)-approved disease indications and specific NCCN panel recommendations. Each recommendation is supported by a level of evidence category.

NCCN Categories of Evidence and Consensus[2]
Category 1: Based on high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2A: Based on lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2B: Based on lower-level evidence, there is NCCN consensus that the intervention is appropriate.
Category 3: Based any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

Policy for Regimen Prior Authorization

A regimen prior authorization allows submission of a single prior authorization request for all oncology drugs or biologics within an NCCN template that require prior authorization.

This policy provides coverage of a regimen review when *all* the following criteria are met:
a. Regimen prior authorization reviews, based on NCCN templates, are initiated through the provider portal: https://provider.carefirst.com/providers/home.page

b. If the prior authorization request is submitted via phone or fax, each drug or biologic will need to be submitted and reviewed as a separate prior authorization request for review with drug-specific criteria.
2. The prior authorization review is requested for an oncology drug or biologic that requires prior authorization on the medical benefit.

3. The indication is for a cancer that is eligible for regimen review. Currently, the cancer types in scope for regimen review include breast, lung, colon and rectal cancer.
4. The member is eligible for regimen review.

In addition, the following criteria must be met for approval:
1. The requested regimen for the drug(s) or biologic(s) and indication is consistent with an NCCN recommendation with a level of evidence category of 1 or 2A.
2. The NCCN template must be accepted by the provider without modification.

Authorizations may be granted for 12 months.
Further review may be indicated where the above criteria are not met.

Continuation of Therapy

To submit a request for continuation of therapy, a new regimen prior authorization review must be requested. Upon template selection, the template must be modified to include the appropriate therapies being used for maintenance treatment. The regimen request will be submitted for further review.

Dosage and Administration

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

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POLICY Document for
HERCEPTIN HYLECTA (trastuzumab and hyaluronidase-oysk)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, and overall clinically appropriate use. This document provides specific information to both sections of the overall policy.

Section 1: Preferred Product
- Policy information specific to preferred medications

Section 2: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 3: Oncology Clinical Policy
- Policy information specific to regimen review per NCCN Guidelines.

Section 1: Preferred Product

EXCEPTIONS CRITERIA
TRASTUZUMAB PRODUCTS

PREFERRED PRODUCTS: HERZUMA, KANJINTI, OGIVRI, ONTRUZANT, TRAZIMERA

POLICY
This policy informs prescribers of preferred products and provides an exception process for targeted products through prior authorization.

I. PLAN DESIGN SUMMARY

This program applies to the trastuzumab products specified in this policy. Coverage for targeted products is provided based on clinical circumstances that would exclude the use of the preferred product and may be based on previous use of a product. The coverage review process will ascertain situations where a clinical exception can be made. This program applies to all members requesting treatment with a targeted product.

Each referral is reviewed based on all utilization management (UM) programs implemented for the client.

Table. Trastuzumab Products

	Product(s)
Preferred*	• **Herzuma** (trastuzumab-pkrb) • **Kanjinti** (trastuzumab-anns) • **Ogivri** (trastuzumab-dkst) • **Ontruzant** (trastuzumab-dttb) • **Trazimera** (trastuzumab-qyyp)
Targeted	• **Herceptin** (trastuzumab) • **Herceptin Hylecta** (trastuzumab and hyaluronidase-oysk)

*: Medications considered formulary or preferred on your plan may still require a clinical prior authorization review.

II. EXCEPTION CRITERIA

Coverage for a targeted product is provided when the member has had a documented intolerable adverse event to at least three of the preferred products, and the adverse event was not an expected adverse event attributed to the active ingredient as described in the prescribing information (i.e., known adverse reaction for both the reference product and biosimilar products).

Section 2: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

HERCEPTIN HYLECTA (trastuzumab and hyaluronidase-oysk)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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. Herceptin Hylecta is indicated for adjuvant treatment of adults with HER2 overexpressing node positive or node negative (ER/PR negative or with one high risk feature) breast cancer:
      a. As part of a treatment regimen consisting of doxorubicin, cyclophosphamide, and either paclitaxel or docetaxel
      b. As part of a treatment regimen with docetaxel and carboplatin
      c. As a single agent following multi-modality anthracycline based therapy

   2. Herceptin Hylecta is indicated in adults:
      a. In combination with paclitaxel for first-line treatment of HER2-overexpressing metastatic breast cancer
      b. As a single agent for treatment of HER2-overexpressing breast cancer in patients who have received one or more chemotherapy regimens for metastatic disease

B. Compendial Uses
   HER2-positive breast cancer: may be substituted for intravenous trastuzumab and used as a single agent or in combination with other systemic therapies

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 APPROVAL

Breast Cancer

1. Authorization of up to 12 months may be granted for adjuvant treatment of HER2-positive breast cancer.
2. Authorization of 12 months may be granted for treatment of HER2-positive recurrent, unresectable advanced, or metastatic breast cancer.
3. Authorization of up to 12 months may be granted for neoadjuvant treatment of HER2-positive breast cancer as part of a complete treatment regimen.

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 and neoadjuvant treatment of breast cancer will be approved for a total of 12 months of therapy.

Section 3: Oncology Clinical Policy

Oncology Clinical Policy

Program Description

The National Comprehensive Care Network® (NCCN®) is an alliance of leading cancer centers devoted to patient care, research and education dedicated to improving the quality, effectiveness and efficiency of cancer care so patients can live better lives.[1] It is comprised of oncology experts who convene regularly to establish the best treatments for patients. NCCN develops various resources for use by stakeholders in the health care delivery system. These resources include, but are not limited to, the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®), the NCCN Drugs & Biologics Compendium (NCCN Compendium®) and the NCCN Chemotherapy Order Templates (NCCN Templates®).

NCCN templates are based on NCCN Clinical Practice Guidelines and NCCN Compendium. The NCCN Compendium lists the appropriate drugs and biologics for specific cancers using U.S. Food and Drug Administration (FDA)-approved disease indications and specific NCCN panel recommendations. Each recommendation is supported by a level of evidence category.

NCCN Categories of Evidence and Consensus[2]

Category 1: Based on high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2A: Based on lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2B: Based on lower-level evidence, there is NCCN consensus that the intervention is appropriate.
Category 3: Based any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

Policy for Regimen Prior Authorization

A regimen prior authorization allows submission of a single prior authorization request for all oncology drugs or biologics within an NCCN template that require prior authorization.

This policy provides coverage of a regimen review when *all* the following criteria are met:
a. Regimen prior authorization reviews, based on NCCN templates, are initiated through the provider portal: https://provider.carefirst.com/providers/home.page
b. If the prior authorization request is submitted via phone or fax, each drug or biologic will need to be submitted and reviewed as a separate prior authorization request for review with drug-specific criteria.
2. The prior authorization review is requested for an oncology drug or biologic that requires prior authorization on the medical benefit.
3. The indication is for a cancer that is eligible for regimen review. Currently, the cancer types in scope for regimen

review include breast, lung, colon and rectal cancer.
4. The member is eligible for regimen review.

In addition, the following criteria must be met for approval:
1. The requested regimen for the drug(s) or biologic(s) and indication is consistent with an NCCN recommendation with a level of evidence category of 1 or 2A.
2. The NCCN template must be accepted by the provider without modification.

Authorizations may be granted for 12 months.
Further review may be indicated where the above criteria are not met.

Continuation of Therapy

To submit a request for continuation of therapy, a new regimen prior authorization review must be requested. Upon template selection, the template must be modified to include the appropriate therapies being used for maintenance treatment. The regimen request will be submitted for further review.

Dosage and Administration

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

REFERENCES:

SECTION 1

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2. Herceptin Hylecta [package insert]. South San Francisco, CA: Genentech, Inc.; February 2019.
3. Herzuma [package insert]. Incheon, Republic of Korea: Celltrion, Inc; May 2019.
4. Kanjinti [package insert]. Thousand Oaks, CA: Amgen Inc; October 2019.
5. Ogivri [package insert]. Steinhausen, Switzerland: Mylan GmbH; February 2021.
6. Ontruzant [package insert]. Whitehouse Station, NJ: Merk Sharp & Dohme Corp.; June 2021.
7. Trazimera [package insert]. Cork, Ireland: Pfizer; November 2020.

SECTION 2

1. Herceptin Hylecta [package insert]. South San Francisco, CA: Genentech, Inc.; February 2019.
2. The NCCN Drugs & Biologics Compendium © 2021 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed December 2, 2021.
3. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Breast Cancer. Version 1.2022. https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed December 8, 2021.

SECTION 3

1. National Comprehensive Cancer Network. About NCCN website. https://www.nccn.org/about/default.aspx, accessed September 16, 2019.
2. National Comprehensive Cancer Network. NCCN Categories of Evidence and Consensus website. https://www.nccn.org/professionals/physician_gls/categories_of_consensus.aspx, accessed September 16, 2019.
3. National Comprehensive Cancer Network. NCCN Guidelines website. http://www.nccn.org/professionals/physician_gls/f_guidelines.asp, accessed September 16, 2019. *(Note: An account may be required.)*
4. National Comprehensive Cancer Network. NCCN Drugs and Biologics Compendium® website. http://www.nccn.org/professionals/drug_compendium/content/contents.asp, accessed September 16, 2019. *(Note: A subscription may be required.)*
5. National Comprehensive Cancer Network. NCCN Chemotherapy Order Templates (NCCN Templates)

website. https://www.nccn.org/professionals/OrderTemplates/Default.aspx, accessed September 16, 2019. *(Note: A subscription may be required.)*

POLICY Document for

DUROLANE (hyaluronic acid)
EUFLEXXA (1% sodium hyaluronate)
GEL-ONE (cross-linked hyaluronate)
GELSYN-3 (sodium hyaluronate 0.84%)
GENVISC 850 (sodium hyaluronate)
HYALGAN (sodium hyaluronate)
HYMOVIS (high molecular weight viscoelastic hyaluronan)
MONOVISC (high molecular weight hyaluronan)
ORTHOVISC (high molecular weight hyaluronan)
SUPARTZ FX (sodium hyaluronate)
SYNOJOYNT (1% sodium hyaluronate)
SYNVISC (hylan G-F 20)
SYNVISC ONE (hylan G-F 20)
TRILURON (sodium hyaluronate)
TRIVISC (sodium hyaluronate)
VISCO-3 (sodium hyaluronate)
1% sodium hyaluronate

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, and overall, clinically appropriate use. This document provides specific information to both sections of the overall policy.

Section 1: Preferred Product
- Policy information specific to preferred medications

Section 2: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 1: Preferred Product

EXCEPTIONS CRITERIA
HYALURONATES

PREFERRED PRODUCTS: EUFLEXXA, MONOVISC AND ORTHOVISC

POLICY
This policy informs prescribers of preferred products and provides an exception process for targeted products through prior authorization.

I. PLAN DESIGN SUMMARY

This program applies to the hyaluronate products specified in this policy. Coverage for targeted products is provided based on clinical circumstances that would exclude the use of the preferred products and may be based on previous use of a product. The coverage review process will ascertain situations where a clinical exception can be made. This program applies to members who are initiating a new treatment course with a targeted product.

Each referral is reviewed based on all utilization management (UM) programs implemented for the client.

Table. Hyaluronate products

	Products
Preferred*	• **Euflexxa** (1% sodium hyaluronate) • **Monovisc** (high molecular weight hyaluronan) • **Orthovisc** (high molecular weight hyaluronan)
Targeted	• **Durolane** (hyaluronic acid) • **Gel-One** (cross-linked hyaluronate) • **Gelsyn-3** (sodium hyaluronate) • **GenVisc 850** (sodium hyaluronate) • **Hyalgan** (sodium hyaluronate) • **Hymovis** (high molecular weight viscoelastic hyaluronan) • **Supartz FX** (sodium hyaluronate) • **Synvisc** (hylan G-F 20) • **Synvisc One** (hylan G-F 20) • **Trivisc** (sodium hyaluronate) • **Visco-3** (sodium hyaluronate)

*: Medications considered formulary or preferred on your plan may still require a clinical prior authorization review.

II. EXCEPTION CRITERIA

This program applies to members requesting treatment for an indication that is FDA-approved for the preferred product.

Coverage for a targeted product is provided when either of the following criteria is met:

A. There is documentation that the member is currently undergoing treatment and coverage is required to complete the current course of treatment.

Number of injections per treatment course

- Gelsyn-3: 3 injections (2 mL each, 6 mL total) per course
- GenVisc 850: 3 to 5 injections (2.5 mL each; 12.5 mL total) per course
- Hyalgan: 3 to 5 injections (2 mL each; 10 mL total) per course
- Hymovis: 2 injections (3 mL each; 6 mL total) per course
- Supartz FX: 3 to 5 injections (2.5 mL each; 12.5 mL total) per course
- Synvisc: 3 injections (2 mL each; 6 mL total) per course
- Trivisc: 3 injections (2.5 mL each, 7.5 mL total) per course
- Visco-3: 3 injections (2.5 mL each, 7.5 mL total) per course

A. Member has a documented intolerable adverse event to all of the preferred products.

Section 2: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

DUROLANE (hyaluronic acid)
EUFLEXXA (1% sodium hyaluronate)

GEL-ONE (cross-linked hyaluronate)
GELSYN-3 (sodium hyaluronate 0.84%)
GENVISC 850 (sodium hyaluronate)
HYALGAN (sodium hyaluronate)
HYMOVIS (high molecular weight viscoelastic hyaluronan)
MONOVISC (high molecular weight hyaluronan)
ORTHOVISC (high molecular weight hyaluronan)
SUPARTZ FX (sodium hyaluronate)
SYNOJOYNT (1% sodium hyaluronate)
SYNVISC (hylan G-F 20)
SYNVISC ONE (hylan G-F 20)
TRILURON (sodium hyaluronate)
TRIVISC (sodium hyaluronate)
VISCO-3 (sodium hyaluronate)
1% sodium hyaluronate

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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 pain in osteoarthritis of the knee in patients who have failed to respond adequately to conservative non-pharmacologic therapy and simple analgesics (e.g., acetaminophen)

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

II. CRITERIA FOR INITIAL APPROVAL

Osteoarthritis (OA) of the Knee
Authorization of 12 months may be granted for treatment of osteoarthritis (OA) in the knee when all of the following criteria are met:

A. The diagnosis is supported by radiographic evidence of osteoarthritis of the knee (e.g., joint space narrowing, subchondral sclerosis, osteophytes and sub-chondral cysts) or the member has at least 5 of the following signs and symptoms:
   1. Bony enlargement
   2. Bony tenderness
   3. Crepitus (noisy, grating sound) on active motion
   4. Erythrocyte sedimentation rate (ESR) less than 40 mm/hr
   5. Less than 30 minutes of morning stiffness
   6. No palpable warmth of synovium
   7. Over 50 years of age
   8. Rheumatoid factor less than 1:40 titer (agglutination method)
   9. Synovial fluid signs (clear fluid of normal viscosity and WBC less than 2000/mm^3)
B. The member has knee pain which interferes with functional activities (e.g., ambulation, prolonged standing).
C. The member has experienced an inadequate response or adverse effects with non-pharmacologic treatment options (e.g., physical therapy, regular exercise, insoles, knee bracing, weight reduction).

D. The member has experienced an inadequate response or intolerance or has a contraindication to a trial of an analgesic (e.g., acetaminophen up to 3 to 4 grams per day, non-steroidal anti-inflammatory drugs [NSAIDs], topical capsaicin cream) for at least 3 months.
E. The member has experienced an inadequate response or intolerance or has a contraindication to a trial of intraarticular steroid injections for at least 3 months.
F. The member is not scheduled to undergo a total knee replacement within 6 months of starting treatment.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment of osteoarthritis in the knee when all of the following criteria are met:
A. Member meets all criteria for initial approval.
B. Member has experienced improvement in pain and functional capacity following the previous injections.
C. At least 6 months has elapsed since the last injection in the prior completed series of injections.

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SECTION 1

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2. Euflexxa [package insert]. Parsippany, NJ: Ferring Pharmaceuticals, Inc.; July 2016.
3. Gel-One [package insert]. Warsaw, IN: Zimmer, Inc.; May 2011.
4. Gelsyn-3 [package insert]. Durham, NC: Bioventus LLC; December 2017.
5. GenVisc 850 [package insert]. Doylestown, PA: OrthogenRx, Inc.; November 2019.
6. Hyalgan [package insert]. Parsippany, NJ: Fidia Pharma USA Inc.; May 2014.
7. Hymovis [package insert]. Parsippany, NJ: Fidia Pharma USA Inc.; September 2017.
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12. Synvisc One [package insert]. Ridgefield, NJ: Genzyme Biosurgery; September 2014.
13. Trivisc [package insert]. Doylestown, PA: OrthogenRx, Inc.; September 2018.
14. Visco-3 [package insert]. Warsaw, IN: Zimmer Inc.; December 2015.

SECTION 2

1. Durolane [package insert]. Durham, NC: Bioventus LLC; September 2017.
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3. Gel-One [package insert]. Warsaw, IN: Zimmer, Inc.; May 2011.
4. Gelsyn-3 [package insert]. Durham, NC: Bioventus LLC; December 2017.
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13. Synvisc One [package insert]. Ridgefield, NJ: Genzyme Biosurgery; September 2014.
14. Triluron [package insert]. Florham Park, NJ: Fidia Pharma USA Inc.: July 2019.
15. Trivisc [package insert]. Doylestown, PA: OrthogenRx, Inc.; November 2019.
16. Visco-3 [package insert]. Warsaw, IN: Zimmer; May 2017.
17. 1% Sodium Hyaluronate [package insert]. North Wales, PA: Teva Pharmaceuticals USA, Inc.; March 2019.

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Reference number(s)
1780-A

SPECIALTY GUIDELINE MANAGEMENT

MAKENA (hydroxyprogesterone caproate)
hydroxyprogesterone caproate (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
Makena is indicated to reduce the risk of preterm birth in women with a singleton pregnancy who have a history of singleton spontaneous preterm birth. The effectiveness of Makena is based on improvement in the proportion of women who delivered < 37 weeks of gestation. There are no controlled trials demonstrating a direct clinical benefit, such as improvement in neonatal mortality and morbidity.

Limitation of use: While there are many risk factors for preterm birth, safety and efficacy of Makena has been demonstrated only in women with a prior spontaneous singleton preterm birth. **It is not intended for use in women with multiple gestations or other risk factors for preterm birth.**

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. Current or history of thrombosis or thromboembolic disorders
B. Known or suspected breast cancer, other hormone-sensitive cancer, or a history of these conditions
C. Undiagnosed abnormal vaginal bleeding unrelated to pregnancy
D. Cholestatic jaundice of pregnancy
E. Liver tumors, benign or malignant, or active liver disease
F. Uncontrolled hypertension

III. CRITERIA FOR INITIAL APPROVAL

Prevention of preterm birth
Authorization of 21 weeks or through 36 weeks, 6 days of gestational age, whichever is less, may be granted for the prevention of preterm birth when all of the following criteria are met:
A. The current pregnancy is a singleton pregnancy (i.e., member is currently pregnant with only one baby).
B. The member has a history of singleton spontaneous preterm birth, defined as delivery at less than 37 weeks gestation following preterm labor, preterm rupture of membranes, and cervical insufficiency.
C. Makena will be initiated between 16 weeks, 0 days and 24 weeks, 6 days of gestation.

IV. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

V. REFERENCES

1. Makena [package insert]. Waltham, MA: AMAG Pharmaceuticals; February 2018.
2. Hydroxyprogesterone caproate [package insert]. Shirley, NY. American Regent, Inc; July 2018.
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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
1801-A

SPECIALTY GUIDELINE MANAGEMENT

ILARIS (canakinumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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. Periodic Fever Syndromes:
      a. Cryopyrin-Associated Periodic Syndromes (CAPS)
         Ilaris is indicated for the treatment of Cryopyrin-Associated Periodic Syndromes (CAPS), in adults and children 4 years of age and older including Familial Cold Autoinflammatory Syndrome (FCAS) and Muckle-Wells Syndrome (MWS).
      b. Tumor Necrosis Factor Receptor Associated Periodic Syndrome (TRAPS)
         Ilaris is indicated for the treatment of TRAPS in adult and pediatric patients.
      c. Hyperimmunoglobulin D Syndrome (HIDS)/Mevalonate Kinase Deficiency (MKD)
         Ilaris is indicated for the treatment of HIDS and MKD in adult and pediatric patients.
      d. Familial Mediterranean Fever (FMF)
         Ilaris is indicated for the treatment of FMF in adult and pediatric patients.
   2. Still's disease (Adult-onset Still's Disease [AOSD] and systemic Juvenile Idiopathic Arthritis [sJIA]):
      Ilaris is indicated for the treatment of active Still's disease, including AOSD and sJIA in patients aged 2 years and older.

B. Compendial Use
   Gout and pseudogout

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. Tumor Necrosis Factor Receptor Associated Periodic Syndrome (TRAPS) and 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.

B. Familial Mediterranean Fever (FMF): For initial requests:
   1. Chart notes or medical record documentation indicating number of active flares within the last 6 months.
   2. Laboratory results, chart notes, or medical record documentation of CRP level.

3. 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.

C. Systemic Juvenile Idiopathic Arthritis (sJIA) and Adult-onset Still's disease (AOSD)
   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. Gout and pseudogout flares: 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. Cryopyrin-associated periodic syndromes (CAPS), TRAPS, HIDS/MKD, and FMF: rheumatologist or immunologist
B. Systemic juvenile idiopathic arthritis (sJIA), AOSD, gout, and pseudogout: rheumatologist

IV. CRITERIA FOR INITIAL APPROVAL

A. Periodic fever syndromes

1. Authorization of 12 months may be granted for members 4 years of age or older for treatment of CAPS when both of the following criteria are met:
   a. 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).
   b. Member has functional impairment limiting the activities of daily living.

2. Authorization of 12 months may be granted for treatment of TRAPS when both of the following criteria are met:
   a. Member has chronic or recurrent disease activity with active flares within the last 6 months.
   b. Physician's Global Assessment (PGA) score greater than or equal to 2 or C-reactive protein (CRP) greater than 10 mg/L.

3. Authorization of 12 months may be granted for treatment of HIDS/MKD when both of the following criteria are met:
   a. Member has had active flares within the last 6 months.
   b. Physician's Global Assessment (PGA) score greater than or equal to 2 or C-reactive protein (CRP) greater than 10 mg/L.

4. Authorization of 12 months may be granted for treatment of FMF when all of the following criteria are met:
   a. Member has active disease with flares within the last 6 months.
   b. C-reactive protein (CRP) greater than 10 mg/L.

c. Member has had an inadequate response or intolerance to or has a contraindication to colchicine.

B. 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:
   a. Member has active systemic features (e.g., fever, evanescent rash, lymphadenopathy, hepatomegaly, splenomegaly, serositis).
   b. Member has had an inadequate response to non-steroidal anti-inflammatory drugs (NSAIDs) or systemic glucocorticoids.

C. Adult-onset Still's disease (AOSD)

1. Authorization of 12 months may be granted for adult members who have previously received a biologic indicated for active AOSD.

2. Authorization of 12 months may be granted for adult members for treatment of active AOSD when both of the following criteria are met:
   a. Member has active systemic features (e.g., fever, arthralgia/arthritis, evanescent rash, lymphadenopathy, hepatomegaly, splenomegaly, sore throat).
   b. Member meets any of the following:
      i. Member has had an inadequate response to a trial of nonsteroidal anti-inflammatory drugs (NSAIDs).
      ii. Member has had an inadequate response to a trial of corticosteroids.
      iii. Member has had an inadequate response to a trial of a conventional synthetic drug (e.g., methotrexate).

D. Management of gout and pseudogout flares

Authorization of 6 months may be granted for the 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.

V. CONTINUATION OF THERAPY

A. 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)

B. Adult-onset Still's disease (AOSD)
Authorization of 12 months may be granted for all adult members (including new members) who are using the requested medication for AOSD 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)

C. Cryopyrin-Associated Periodic Syndromes (CAPS), including Familial Cold Autoinflammatory Syndrome (FCAS) and Muckle-Wells Syndrome (MWS)
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 CAPS, including FCAS and MWS, and who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition.

D. 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 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.

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Reference number
2538-A

SPECIALTY GUIDELINE MANAGEMENT

ILUMYA (tildrakizumab-asmn)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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 adult patients with moderate to severe plaque psoriasis (PsO) 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. Initial requests:
   1. Chart notes or medical record documentation of affected area(s) and body surface area (BSA) affected (if applicable).
   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. PRESCRIBER SPECIALTIES

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

IV. CRITERIA FOR INITIAL APPROVAL

Plaque psoriasis (PsO)

A. 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.

B. 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:
   1. Crucial body areas (e.g., hands, feet, face, neck, scalp, genitals/groin, intertriginous areas) are affected.
   2. At least 10% of 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).

V. CONTINUATION OF THERAPY

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:
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)

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 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, or Acitretin

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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POLICY Document for IMFINZI (durvalumab)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, and overall, clinically appropriate use. This document provides specific information to both sections of the overall policy.

Section 1: Site of Care
- Policy information specific to site of care (outpatient, hospital outpatient, home infusion)

Section 2: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 3: Oncology Clinical Policy
- Policy information specific to regimen review per NCCN Guidelines.

Section 1: Site of Care

CareFirst Site of Care Criteria
Administration of Intravenous Checkpoint Inhibitors
Bavencio, Imfinzi, Jemperli, Keytruda, Libtayo, Opdivo, Opdualag, Tecentriq, Yervoy and Zynyz

POLICY

I. CRITERIA FOR APPROVAL FOR ADMINISTRATION IN OUTPATIENT HOSPITAL SETTING

This policy provides coverage for administration of a checkpoint inhibitor in an outpatient hospital setting for the initial 6 months approval and up to 45 days for renewal of therapy.

This policy provides coverage for administration of a checkpoint inhibitor in an outpatient hospital setting for a longer course of treatment when ANY of the following criteria are met:

A. The member has experienced an adverse reaction that did not respond to conventional interventions (eg, acetaminophen, steroids, diphenhydramine, fluids, other pre-medications or slowing of infusion rate) or a severe adverse event (anaphylaxis, anaphylactoid reactions, myocardial infarction, thromboembolism, or seizures) during or immediately after an infusion or has experienced severe toxicity requiring continuous monitoring (e.g. Grade 2-4 bullous dermatitis, transaminitis, pneumonitis, Stevens-Johnson syndrome, acute pancreatitis, primary adrenal insufficiency aseptic meningitis, encephalitis, transverse myelitis, myocarditis, pericarditis, arrhythmias, impaired ventricular function, conduction abnormalities).
B. The member is medically unstable (eg respiratory, cardiovascular, or renal conditions).
C. The member has severe venous access issues that require the use of a special interventions only available in the outpatient hospital setting.
D. The member has significant behavioral issues and/or physical or cognitive impairment that would impact the safety of the infusion therapy AND the patient does not have access to a caregiver.
E. The member is receiving provider administered combination chemotherapy.
F. The member is less than 14 years of age.

For situations where administration of a checkpoint inhibitor does not meet the criteria for outpatient hospital infusion, coverage for a checkpoint inhibitor is provided when administered in alternative sites such as physician office, home infusion or ambulatory care.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the site of care prior authorization review (where applicable):

A. Medical records supporting the member has experienced an adverse reaction that did not respond to conventional interventions or a severe adverse event during or immediately after an infusion or a severe toxicity requiring continuous monitoring
B. Medical records supporting the member is medically unstable
C. Medical records supporting the member has severe venous access issues that require specialized interventions only available in the outpatient hospital setting
D. Medical records supporting the member has behavioral issues and/or physical or cognitive impairment and no access to a caregiver
E. Medical records supporting the member is receiving provider administered combination therapy.

Section 2: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

IMFINZI (durvalumab)

POLICY

III. INDICATIONS

The indications below including FDA-approved indications and compendial 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. Imfinzi is indicated for the treatment of adult patients with unresectable, Stage III non-small cell lung cancer (NSCLC) whose disease has not progressed following concurrent platinum-based chemotherapy and radiation therapy.
   2. Imfinzi, in combination with etoposide and either carboplatin or cisplatin, is indicated for the first-line treatment of adult patients with extensive-stage small cell lung cancer (ES-SCLC).
   3. Imfinzi, in combination with gemcitabine and cisplatin, is indicated for the treatment of adult patients with locally advanced or metastatic biliary tract cancer (BTC).
   4. Imfinzi, in combination with tremelimumab-actl, is indicated for the treatment of adult patients with unresectable hepatocellular carcinoma (uHCC).
   5. Imfinzi, in combination with tremelimumab-actl and platinum-based chemotherapy, is indicated for the treatment of adult patients with metastatic non-small cell lung cancer (NSCLC) with no sensitizing epidermal growth factor receptor (EGFR) mutations or anaplastic lymphoma kinase (ALK) genomic tumor aberrations.

B. Compendial Uses
   1. Cervical Cancer
   2. Non-small cell lung cancer-unresectable stage II disease, recurrent and advanced
   3. Ampullary Adenocarcinoma
   4. Hepatobiliary Cancers
      a. Intrahepatic Cholangiocarcinoma
      b. Extrahepatic Cholangiocarcinoma
      c. Gallbladder Cancer
      d. Hepatocellular Carcinoma

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

IV. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
Documentation of the absence of EGFR exon 19 deletion and L858R mutations and ALK rearrangements, where applicable (unless testing is not feasible due to insufficient tissue).

V. EXCLUSIONS

Coverage will not be provided for members who have experienced disease progression while on PD-1 or PD-L1 inhibitor therapy.

VI. CRITERIA FOR INITIAL APPROVAL

A. Non-small cell lung cancer (NSCLC)

Authorization of 6 months may be granted for treatment of NSCLC when either of the following criteria are met:

1. The member has unresectable stage II or III NSCLC that has not progressed following concurrent platinum-based chemotherapy and radiation therapy.
2. The member has recurrent, advanced or metastatic NSCLC and meets all of the following criteria:
   a. The requested medication will be used in combination with tremelimumab-actl (Imjudo) and platinum-based chemotherapy
   b. The tumor is negative for EGFR exon 19 deletion and L858R mutations and ALK gene mutations.

B. Extensive-stage small cell lung cancer (ES-SCLC)

Authorization of 6 months may be granted for first-line treatment of extensive-stage small cell lung cancer in combination with etoposide and either carboplatin or cisplatin followed by single agent maintenance.

C. Cervical Cancer

Authorization of 6 months may be granted for treatment of persistent, recurrent or metastatic small cell neuroendocrine carcinoma of the cervix (NECC) when used in combination with etoposide and either cisplatin or carboplatin.

D. Ampullary Adenocarcinoma

Authorization of 6 months may be granted for treatment of unresectable or metastatic ampullary adenocarcinoma when both of the following criteria are met:

1. The disease is pancreatobiliary or mixed type
2. The requested medication will be used in combination with cisplatin and gemcitabine

E. Hepatobiliary Cancers

Authorization of 6 months may be granted for hepatobiliary cancers when one of the following criteria are met:

1. The requested medication will be used in combination with cisplatin and gemcitabine to treat locally advanced, unresectable, or metastatic biliary tract cancer (intrahepatic cholangiocarcinoma, extrahepatic cholangiocarcinoma, or gallbladder cancer) or for disease recurrence after surgery and adjuvant therapy.
2. The requested medication will be used for first-line single agent treatment of unresectable or metastatic hepatocellular carcinoma.
3. The requested medication will be used in combination with tremelimumab-actl (Imjudo) for treatment of unresectable hepatocellular carcinoma.

VII. CONTINUATION OF THERAPY

A. NSCLC

Authorization of 6 months may be granted for continued treatment in members requesting reauthorization for NSCLC when either of the following criteria are met:

1. The member has unresectable stage II or III NSCLC and there is no evidence of unacceptable toxicity or disease progression while on the current regimen. **(up to 12 months total)**
2. The member has recurrent, advanced or metastatic NSCLC and there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

B. All other indications

Authorization of 6 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.

Section 3: Oncology Clinical Policy

Oncology Clinical Policy

Program Description

The National Comprehensive Care Network® (NCCN®) is an alliance of leading cancer centers devoted to patient care, research and education dedicated to improving the quality, effectiveness and efficiency of cancer care so patients can live better lives.[1] It is comprised of oncology experts who convene regularly to establish the best treatments for patients. NCCN develops various resources for use by stakeholders in the health care delivery system. These resources include, but are not limited to, the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®), the NCCN Drugs & Biologics Compendium (NCCN Compendium®) and the NCCN Chemotherapy Order Templates (NCCN Templates®).

NCCN templates are based on NCCN Clinical Practice Guidelines and NCCN Compendium. The NCCN Compendium lists the appropriate drugs and biologics for specific cancers using U.S. Food and Drug Administration (FDA)-approved disease indications and specific NCCN panel recommendations. Each recommendation is supported by a level of evidence category.

NCCN Categories of Evidence and Consensus[2]

a. Category 1: Based on high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
b. Category 2A: Based on lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
c. Category 2B: Based on lower-level evidence, there is NCCN consensus that the intervention is appropriate.
d. Category 3: Based any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

Policy for Regimen Prior Authorization

A regimen prior authorization allows submission of a single prior authorization request for all oncology drugs or biologics within an NCCN template that require prior authorization.

This policy provides coverage of a regimen review when *all* of the following criteria are met:

a. Regimen prior authorization reviews, based on NCCN templates, are initiated through the provider portal: https://provider.carefirst.com/providers/home.page
b. If the prior authorization request is submitted via phone or fax, each drug or biologic will need to be submitted and reviewed as a separate prior authorization request for review with drug-specific criteria.

c. The prior authorization review is requested for an oncology drug or biologic that requires prior authorization on the medical benefit.
d. The indication is for a cancer that is eligible for regimen review. Currently, the cancer types in scope for regimen review include breast, lung, colon and rectal cancer.
e. The member is eligible for regimen review.

In addition, the following criteria must be met for approval:

a. The requested regimen for the drug(s) or biologic(s) and indication is consistent with an NCCN recommendation with a level of evidence category of 1 or 2A.
b. The NCCN template must be accepted by the provider without modification.

Authorizations may be granted for 12 months.
Further review may be indicated where the above criteria are not met.

Continuation of Therapy

To submit a request for continuation of therapy, a new regimen prior authorization review must be requested. Upon template selection, the template must be modified to include the appropriate therapies being used for maintenance treatment. The regimen request will be submitted for further review.

Dosage and Administration

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

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SECTION 2

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SECTION 3

1. National Comprehensive Cancer Network. About NCCN website. https://www.nccn.org/about/default.aspx, accessed September 16, 2019.
2. National Comprehensive Cancer Network. NCCN Categories of Evidence and Consensus website. https://www.nccn.org/professionals/physician_gls/categories_of_consensus.aspx, accessed September 16, 2019.
3. National Comprehensive Cancer Network. NCCN Guidelines website.

http://www.nccn.org/professionals/physician_gls/f_guidelines.asp, accessed September 16, 2019. *(Note: An account may be required.)*
4. National Comprehensive Cancer Network. NCCN Drugs and Biologics Compendium® website. http://www.nccn.org/professionals/drug_compendium/content/contents.asp, accessed September 16, 2019. *(Note: A subscription may be required.)*
5. National Comprehensive Cancer Network. NCCN Chemotherapy Order Templates (NCCN Templates) website. https://www.nccn.org/professionals/OrderTemplates/Default.aspx, accessed September 16, 2019. *(Note: A subscription may be required.)*

POLICY Document for IMLYGIC (talimogene laherparepvec)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, and overall, clinically appropriate use. This document provides specific information to both sections of the overall policy.

Section 1: Clinical Criteria

- Policy information specific to the clinical appropriateness for the medication

Section 2: Oncology Clinical Policy

- Policy information specific to regimen review per NCCN Guidelines.

Section 1: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

IMLYGIC (talimogene laherparepvec)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Imlygic is indicated for the local treatment of unresectable cutaneous, subcutaneous, and nodal lesions in patients with melanoma recurrent after initial surgery.

B. Compendial Uses
1. Limited resectable or unresectable stage III melanoma with clinical satellite/in-transit metastases or with nodal lesions
2. Widely disseminated distant metastatic melanoma
3. Limited resectable or unresectable local satellite/in-transit recurrence of melanoma

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

II. CRITERIA FOR INITIAL APPROVAL

Melanoma
Authorization of 12 months may be granted for treatment of unresectable, limited resectable, or incompletely resectable cutaneous, subcutaneous, and nodal lesions in melanoma.

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.

Section 2: Oncology Clinical Policy

Oncology Clinical Policy

Program Description

The National Comprehensive Care Network® (NCCN®) is an alliance of leading cancer centers devoted to patient care, research and education dedicated to improving the quality, effectiveness and efficiency of cancer care so patients can live better lives.[1] It is comprised of oncology experts who convene regularly to establish the best treatments for patients. NCCN develops various resources for use by stakeholders in the health care delivery system. These resources include, but are not limited to, the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®), the NCCN Drugs & Biologics Compendium (NCCN Compendium®) and the NCCN Chemotherapy Order Templates (NCCN Templates®).

NCCN templates are based on NCCN Clinical Practice Guidelines and NCCN Compendium. The NCCN Compendium lists the appropriate drugs and biologics for specific cancers using U.S. Food and Drug Administration (FDA)-approved disease indications and specific NCCN panel recommendations. Each recommendation is supported by a level of evidence category.

NCCN Categories of Evidence and Consensus

Category 1: Based on high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2A: Based on lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2B: Based on lower-level evidence, there is NCCN consensus that the intervention is appropriate.
Category 3: Based any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

Policy for Regimen Prior Authorization

A regimen prior authorization allows submission of a single prior authorization request for all oncology drugs or biologics within an NCCN template that require prior authorization.

This policy provides coverage of a regimen review when *all* of the following criteria are met:

a. Regimen prior authorization reviews, based on NCCN templates, are initiated through the provider portal: https://provider.carefirst.com/providers/home.page
b. If the prior authorization request is submitted via phone or fax, each drug or biologic will need to be submitted and reviewed as a separate prior authorization request for review with drug-specific criteria.
c. 2. The prior authorization review is requested for an oncology drug or biologic that requires prior authorization on the medical benefit.
d. The indication is for a cancer that is eligible for regimen review. Currently, the cancer types in scope for regimen review include breast, lung, colon and rectal cancer.
e. The member is eligible for regimen review.

In addition, the following criteria must be met for approval:

a. The requested regimen for the drug(s) or biologic(s) and indication is consistent with an NCCN recommendation with a level of evidence category of 1 or 2A.
b. The NCCN template must be accepted by the provider without modification.

Authorizations may be granted for 12 months.
Further review may be indicated where the above criteria are not met.

Continuation of Therapy

To submit a request for continuation of therapy, a new regimen prior authorization review must be requested. Upon template selection, the template must be modified to include the appropriate therapies being used for maintenance treatment. The regimen request will be submitted for further review.

Dosage and Administration

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

REFERENCES:

SECTION 1

1. Imlygic [package insert]. Thousand Oaks, CA: Amgen Inc.; June 2022.
2. The NCCN Drugs & Biologics Compendium® © 2022 National Comprehensive Cancer Network, Inc. Available at: https://www.nccn.org. Accessed November 1, 2022.

SECTION 2

1. National Comprehensive Cancer Network. About NCCN website. https://www.nccn.org/about/default.aspx, accessed September 16, 2019.
2. National Comprehensive Cancer Network. NCCN Categories of Evidence and Consensus website. https://www.nccn.org/professionals/physician_gls/categories_of_consensus.aspx, accessed September 16, 2019.
3. National Comprehensive Cancer Network. NCCN Guidelines website. http://www.nccn.org/professionals/physician_gls/f_guidelines.asp, accessed September 16, 2019. *(Note: An account may be required.)*
4. National Comprehensive Cancer Network. NCCN Drugs and Biologics Compendium® website. http://www.nccn.org/professionals/drug_compendium/content/contents.asp, accessed September 16, 2019. *(Note: A subscription may be required.)*
5. National Comprehensive Cancer Network. NCCN Chemotherapy Order Templates (NCCN Templates) website. https://www.nccn.org/professionals/OrderTemplates/Default.aspx, accessed September 16, 2019. *(Note: A subscription may be required.)*

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 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.

CVS/caremark

POLICY Document for
REMICADE (infliximab)
AVSOLA (infliximab-axxq)
INFLECTRA (infliximab-dyyb)
RENFLEXIS (infliximab-abda)
infliximab

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, lower cost site of care and overall, clinically appropriate use. This document provides specific information to each of the three sections of the overall policy.

Section 1: Preferred Product
- Policy information specific to preferred medications

Section 2: Site of Care
- Policy information specific to site of care (outpatient, hospital outpatient, home infusion)

Section 3: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 1: Preferred Product

EXCEPTIONS CRITERIA
INFLIXIMAB

PREFERRED PRODUCTS: AVSOLA, INFLECTRA AND RENFLEXIS

POLICY
This policy informs prescribers of preferred products and provides an exception process for targeted products through prior authorization.

I. PLAN DESIGN SUMMARY

This program applies to the infliximab products specified in this policy. Coverage for targeted products is provided based on clinical circumstances that would exclude the use of the preferred product and may be based on previous use of a product. The coverage review process will ascertain situations where a clinical exception can be made. This program applies to all members requesting treatment with a targeted product.

Each referral is reviewed based on all utilization management (UM) programs implemented for the client.

Table. Infliximab products

	Product(s)
Preferred*	• **Avsola** (infliximab-axxq) • **Inflectra** (infliximab-dyyb) • **Renflexis** (infliximab-abda)
Targeted	• infliximab • **Remicade** (infliximab)

*: Medications considered formulary or preferred on your plan may still require a clinical prior authorization review.

II. EXCEPTION CRITERIA

Coverage for the targeted product is provided when the member has a documented intolerable adverse event to all of the preferred products, and the adverse event was not an expected adverse event attributed to the active ingredient as described in the prescribing information (i.e., known adverse reaction for both the reference product and biosimilar products).

Section 2: Site of Care

CareFirst Site of Care Criteria
Administration of Intravenous Infliximab

Avsola, Inflectra, Remicade, Renflexis, infliximab (unbranded)

POLICY

I. CRITERIA FOR APPROVAL FOR ADMINISTRATION IN OUTPATIENT HOSPITAL SETTING

This policy provides coverage for administration of infliximab in an outpatient hospital setting 3 months when ANY of the following criteria are met:

A. The member is new to infliximab therapy or is reinitiating therapy after not being on therapy for at least 6 months
B. The member is switching to an infliximab product that he/she has not received before.
C. The member has experienced a gap in therapy of greater than 2 infusions.

This policy provides coverage for administration of infliximab in an outpatient hospital setting for a longer course of treatment when ANY of the following criteria are met:

A. The member has experienced an adverse reaction that did not respond to conventional interventions (eg, acetaminophen, steroids, diphenhydramine, fluids, other pre-medications or slowing of infusion rate) or a severe adverse event (anaphylaxis, anaphylactoid reactions, myocardial infarction, thromboembolism, or seizures) during or immediately after an infusion.
B. The member has developed antibodies to infliximab which increases the risk for infusion related reactions.
C. The member is medically unstable (eg respiratory, cardiovascular, or renal conditions).
D. The member has severe venous access issues that require the use of a special interventions only available in the outpatient hospital setting.
E. The member has significant behavioral issues and/or physical or cognitive impairment that would impact the safety of the infusion therapy AND the patient does not have access to a caregiver.
F. The member is less than 14 years of age.

For situations where administration of infliximab does not meet the criteria for outpatient hospital infusion, coverage for infliximab is provided when administered in alternative sites such as; physician office, home infusion or ambulatory care.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the site of care prior authorization review (where applicable):

A. Medical records supporting the member has experienced an adverse reaction that did not respond to conventional interventions or a severe adverse event during or immediately after an infusion

B. Medical records supporting the member has developed antibodies to infliximab
C. Medical records supporting the member is medically unstable
D. Medical records supporting the member has severe venous access issues that require specialized interventions only available in the outpatient hospital setting
E. Medical records supporting the member has behavioral issues and/or physical or cognitive impairment and no access to a caregiver

Section 3: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

REMICADE (infliximab)
AVSOLA (infliximab-axxq)
INFLECTRA (infliximab-dyyb)
RENFLEXIS (infliximab-abda)
infliximab

POLICY

III. INDICATIONS

The indications below including FDA-approved indications and compendial 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 Crohn's disease (CD) and fistulizing CD who have had an inadequate response to conventional therapy
2. Pediatric patients 6 years of age and older with moderately to severely active Crohn's disease who have had an inadequate response to conventional therapy
3. Moderately to severely active ulcerative colitis (UC) in patients 6 years of age or older who have had an inadequate response to conventional therapy
4. Adult patients with moderately to severely active rheumatoid arthritis (RA), in combination with methotrexate
5. Adult patients with active ankylosing spondylitis (AS)
6. Adult patients with active psoriatic arthritis (PsA)
7. Adult patients with chronic severe plaque psoriasis (PsO) who are candidates for systemic therapy and when other systemic therapies are medically less appropriate

B. Compendial Uses
1. Non-radiographic axial spondyloarthritis
2. Behcet's disease
3. Hidradenitis suppurativa
4. Pyoderma gangrenosum
5. Sarcoidosis
6. Takayasu's arteritis
7. Uveitis
8. Reactive arthritis
9. Immune checkpoint inhibitor toxicity
10. Acute graft versus host disease

11. Moderate to severe plaque psoriasis

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

IV. DOCUMENTATION

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

A. Crohn's disease (CD) and ulcerative colitis (UC)
Continuation requests: Chart notes or medical record documentation supporting positive clinical response to therapy or remission.

B. 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.

C. Ankylosing spondylitis (AS), non-radiographic axial spondyloarthritis (nr-axSpA), psoriatic arthritis (PsA), reactive arthritis, hidradenitis suppurativa, and uveitis
   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. 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.

E. Behcet's disease (initial requests only)
Chart notes, medical record documentation, or claims history supporting previous medications tried, including response to therapy (if applicable).

F. Pyoderma gangrenosum, sarcoidosis, Takayasu's arteritis, immune checkpoint inhibitor toxicity, and acute graft versus host disease (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.

V. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with one of the following:
A. Crohn's disease and ulcerative colitis: gastroenterologist
B. Rheumatoid arthritis, ankylosing spondylitis, non-radiographic axial spondyloarthritis, Behcet's disease, Takayasu's arteritis, and reactive arthritis: rheumatologist
C. Psoriatic arthritis and hidradenitis suppurativa:[60] rheumatologist or dermatologist
D. Plaque psoriasis and pyoderma gangrenosum: dermatologist
E. Sarcoidosis: dermatologist or pulmonologist
F. Uveitis: ophthalmologist or rheumatologist
G. Immune checkpoint inhibitor toxicity and acute graft versus host disease: oncologist or hematologist

VI. CRITERIA FOR INITIAL APPROVAL

A. 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.

B. Ulcerative colitis (UC)
Authorization of 12 months may be granted for members 6 years of age or older for treatment of moderately to severely active UC.

C. 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).

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. 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.

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 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).

G. 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).

H. Hidradenitis suppurativa

1. Authorization of 12 months may be granted for members who have previously received a biologic indicated for 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 an oral antibiotic for at least 90 days.
   ii. Member has an intolerance or contraindication to oral antibiotics.

I. 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).

J. Sarcoidosis

Authorization of 12 months may be granted for treatment of sarcoidosis in members when either of the following criteria is met:

1. Member has experienced an inadequate response to corticosteroids or immunosuppressive therapy.
2. Member has an intolerance or contraindication to corticosteroids and immunosuppressive therapy.

K. Takayasu's arteritis

Authorization of 12 months may be granted for treatment of refractory Takayasu's arteritis when either of the following criteria is met:

1. Member has experienced an inadequate response to corticosteroids or immunosuppressive therapy (e.g., methotrexate, azathioprine, or mycophenolate mofetil).
2. Member has an intolerance or contraindication to corticosteroids and immunosuppressive therapy (e.g., methotrexate, azathioprine, or mycophenolate mofetil).

L. Uveitis

1. Authorization of 12 months may be granted for members who have previous received a biologic indicated for uveitis.

2. Authorization of 12 months may be granted for treatment of uveitis when either of the following criteria is met:
   i. Member has experienced an inadequate response to corticosteroids or immunosuppressive therapy (e.g., methotrexate, azathioprine, or mycophenolate mofetil).
   ii. Member has an intolerance or contraindication to corticosteroids and immunosuppressive therapy (e.g., methotrexate, azathioprine, or mycophenolate mofetil).

M. 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 either of the following criteria is met:
   i. Member has experienced an inadequate response to at least a 3-month trial of one of the following despite adequate dosing or maximally tolerated dose:
      a. Sulfasalazine (i.e., titrated to 1000 mg twice daily)
      b. Methotrexate (i.e., titrated to at least 15 mg/week)

ii. Member has an intolerance or contraindication to methotrexate (see Appendix) and sulfasalazine (e.g., porphyria, intestinal or urinary obstruction).

N. Immune checkpoint inhibitor toxicity

1. Authorization of 6 months may be granted for treatment of immune checkpoint inhibitor toxicity when either of the following criteria is met:
   i. Member has experienced an inadequate response, intolerance, or contraindication to corticosteroids.
   ii. Member has moderate or severe diarrhea or colitis.

2. Authorization of 12 months may be granted for treatment of immune checkpoint inhibitor toxicity when the member has severe inflammatory arthritis and has experienced an inadequate response, intolerance, or contraindication to corticosteroids.

O. 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.

VII. CONTINUATION OF THERAPY

A. 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)

B. Ulcerative colitis (UC)

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 ulcerative colitis 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 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)

C. 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.

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. 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

F. 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)

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. Uveitis

Authorization of 12 months may be granted for all members (including new members) who are using the requested medication for uveitis 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 recurrence compared to baseline
2. Zero anterior chamber inflammation or reduction in anterior chamber inflammation compared to baseline
3. Decreased reliance on topical corticosteroids

I. 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, pain).

J. Immune checkpoint inhibitor toxicity and acute graft versus host disease

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.

VIII. 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.

IX. DOSAGE AND ADMINISTRATION

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

X. 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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POLICY Document for INLYTA (axitinib)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication. This document provides specific information to each section of the overall policy.

Section 1: Clinical Criteria
Policy information specific to the clinical appropriateness for the medication
Section 2: Oncology Clinical Policy
Policy information specific to regimen review per NCCN Guidelines.

Section 1: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

INLYTA (axitinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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. First-Line Advanced Renal Cell Carcinoma
   a. Inlyta in combination with avelumab is indicated for the first-line treatment of patients with advanced renal cell carcinoma (RCC).
   b. Inlyta in combination with pembrolizumab is indicated for the first-line treatment of patients with advanced renal cell carcinoma.
2. Second-Line Advanced Renal Cell Carcinoma
   Inlyta as a single agent is indicated for the treatment of advanced renal cell carcinoma (RCC) after failure of one prior systemic therapy.

B. Compendial Uses
1. Relapsed or stage IV renal cell carcinoma
2. Papillary, Hürthle cell, or follicular thyroid carcinoma
3. Soft tissue sarcomas: alveolar soft part sarcoma (ASPS)

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

II. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with an oncologist.

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 any of the following criteria is met:
1. Inlyta will be used as a single agent for subsequent therapy
2. Inlyta will be used in combination with pembrolizumab
3. Inlyta will be used as first-line treatment in combination with avelumab

B. 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 that is not amenable to radioactive iodine (RAI) therapy.

C. Soft Tissue Sarcomas
Authorization of 12 months may be granted for treatment of alveolar soft part sarcoma (ASPS) subtype of soft tissue sarcoma when used 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.

Section 2: Oncology Clinical Policy

Oncology Clinical Policy

Program Description

The National Comprehensive Care Network® (NCCN®) is an alliance of leading cancer centers devoted to patient care, research and education dedicated to improving the quality, effectiveness and efficiency of cancer care so patients can live better lives.[1] It is comprised of oncology experts who convene regularly to establish the best treatments for patients. NCCN develops various resources for use by stakeholders in the health care delivery system. These resources include, but are not limited to, the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®), the NCCN Drugs & Biologics Compendium (NCCN Compendium®) and the NCCN Chemotherapy Order Templates (NCCN Templates®).

NCCN templates are based on NCCN Clinical Practice Guidelines and NCCN Compendium. The NCCN Compendium lists the appropriate drugs and biologics for specific cancers using U.S. Food and Drug Administration (FDA)-approved disease indications and specific NCCN panel recommendations. Each recommendation is supported by a level of evidence category.

NCCN Categories of Evidence and Consensus[2]
Category 1: Based on high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2A: Based on lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2B: Based on lower-level evidence, there is NCCN consensus that the intervention is appropriate.
Category 3: Based any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

Policy for Regimen Prior Authorization

A regimen prior authorization allows submission of a single prior authorization request for all oncology drugs or

biologics within an NCCN template that require prior authorization.

This policy provides coverage of a regimen review when *all* of the following criteria are met:
a. Regimen prior authorization reviews, based on NCCN templates, are initiated through the provider portal: https://provider.carefirst.com/providers/home.page

b. If the prior authorization request is submitted via phone or fax, each drug or biologic will need to be submitted and reviewed as a separate prior authorization request for review with drug-specific criteria.
2. The prior authorization review is requested for an oncology drug or biologic that requires prior authorization on the medical benefit.
3. The indication is for a cancer that is eligible for regimen review. Currently, the cancer types in scope for regimen review include breast, lung, colon and rectal cancer.
4. The member is eligible for regimen review.

In addition, the following criteria must be met for approval:
1. The requested regimen for the drug(s) or biologic(s) and indication is consistent with an NCCN recommendation with a level of evidence category of 1 or 2A.
2. The NCCN template must be accepted by the provider without modification. Authorizations may be granted for 12 months. Further review may be indicated where the above criteria are not met.

Continuation of Therapy

To submit a request for continuation of therapy, a new regimen prior authorization review must be requested. Upon template selection, the template must be modified to include the appropriate therapies being used for maintenance treatment. The regimen request will be submitted for further review.

Dosage and Administration

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

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CVS/caremark

POLICY Document for Intravenous Immune Globulin (IVIG):

Asceniv™, Bivigam®, Flebogamma® DIF, Gammagard® Liquid, Gammagard® S/D, Gammaked™, Gammaplex®, Gamunex®-C, Octagam®, Panzyga®, and Privigen®

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, lower cost site of care and overall, clinically appropriate use. This document provides specific information to each of the three sections of the overall policy.

Section 1: Site of Care
- Policy information specific to site of care (outpatient, hospital outpatient, home infusion)

Section 2: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 1: Site of Care

CareFirst Site of Care Criteria
Administration of Intravenous Immune Globulins

Asceniv, Bivigam, Flebogamma DIF, Gammagard Liquid, Gammagard S/D, Gammaked, Gammaplex, Gamunex-C, Octagam, Privigen and Panzyga

POLICY

I. CRITERIA FOR APPROVAL FOR ADMINISTRATION IN OUTPATIENT-HOSPITAL SETTING

This policy provides coverage for administration of Ig therapy in an outpatient hospital setting for 1 month when ANY of the following criteria are met:
- A. The member is new to Ig therapy or is reinitiating therapy after not being on therapy for at least 6 months.
- B. The member is switching to an Ig product that he/she has not received before.
- C. The member has experienced a gap in Ig therapy for greater than 8 weeks.

This policy provides coverage for administration of infused Ig therapy in an outpatient hospital setting for a longer course of treatment when ANY of the following criteria are met:
- A. The member has experienced an adverse reaction that did not respond to conventional interventions (eg, acetaminophen, steroids, diphenhydramine, fluids or other pre-medications) or a severe adverse event (anaphylaxis, anaphylactoid reactions, myocardial infarction, thromboembolism, or seizures) during or immediately after an infusion.
- B. The member has developed IgA autoantibodies which increases the risk of infusion related reactions.
- C. The member is medically unstable (eg respiratory, cardiovascular, or renal conditions).

D. The member has severe venous access issues that require the use of a special interventions only available in the outpatient hospital setting.
E. The member has significant behavioral issues and/or physical or cognitive impairment that would impact the safety of the infusion therapy AND the patient does not have access to a caregiver.
F. The member is less than 14 years of age.

For situations where administration of the Ig does not meet the criteria for outpatient hospital infusion, coverage for the Ig is provided when administered in alternative sites such as; physician office, home infusion or ambulatory care.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the site of care prior authorization review (where applicable):
A. Medical records supporting the member has experienced an adverse reaction that did not respond to conventional interventions or a severe adverse event during or immediately after an infusion
B. Medical records supporting the member has developed IgA autoantibodies
C. Medical records supporting the member is medically unstable
D. Medical records supporting the member has severe venous access issues that require specialized interventions only available in the outpatient hospital setting
E. Medical records supporting the member has behavioral issues and/or physical or cognitive impairment and no access to a caregiver

Section 2: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

Intravenous Immune Globulin (IVIG):

Asceniv™, Bivigam®, Flebogamma® DIF, Gammagard® Liquid, Gammagard® S/D, Gammaked™, Gammaplex®, Gamunex®-C, Octagam®, Panzyga®, and Privigen®

POLICY

III. INDICATIONS

The indications below including FDA-approved indications and compendial 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. Primary immunodeficiency
2. Idiopathic thrombocytopenic purpura (ITP)
3. Chronic inflammatory demyelinating polyneuropathy (CIDP)
4. Multifocal motor neuropathy
5. Kawasaki syndrome
6. B-cell chronic lymphocytic leukemia (CLL)
7. Dermatomyositis

B. Compendial Uses
1. Prophylaxis of bacterial infections in pediatric human immunodeficiency virus (HIV) infection

2. Bone marrow transplant (BMT)/hematopoietic stem cell transplant (HSCT)
3. Polymyositis
4. Myasthenia gravis
5. Guillain-Barré syndrome
6. Lambert-Eaton myasthenic syndrome
7. Fetal/neonatal alloimmune thrombocytopenia
8. Parvovirus B19-induced pure red cell aplasia
9. Stiff-person syndrome
10. Management of immune checkpoint inhibitor-related toxicites
11. Acquired red cell aplasia
12. Acute disseminated encephalomyelitis
13. Autoimmune mucocutaneous blistering diseases
14. Autoimmune hemolytic anemia
15. Autoimmune neutropenia
16. Birdshot retinochoroidopathy
17. BK virus associated nephropathy
18. Churg-Strauss Syndrome
19. Enteroviral meningoencephalitis
20. Hematophagocytic lymphohistiocytosis (HLH) or macrophage activation syndrome (MAS)
21. Hemolytic disease of newborn
22. HIV-associated thrombocytopenia
23. Hyperimmunoglobulinemia E Syndrome
24. Hypogammaglobulinemia from chimeric antigen receptor T (CAR-T) therapy
25. Multiple myeloma
26. Neonatal hemochromatosis, prophylaxis
27. Opsoclonus-myoclonus
28. Paraneoplastic opsonus-myoclonus ataxia associated with neuroblastoma
29. Post-transfusion purpura
30. Rasmussen encephalitis
31. Renal transplantation from a live donor with ABO incompatibility or positive cross match
32. Secondary immunosuppression associated with major surgery, hematological malignancy, major burns, and collagen-vascular diseases
33. Solid organ transplantation, for allosensitized members
34. Toxic epidermal necrolysis and Stevens-Johnson syndrome
35. Toxic shock syndrome
36. Systemic lupus erythematosus (SLE)
37. Toxic necrotizing fasciitis due to group A streptococcus
38. Measles (Rubeola) prophylaxis
39. Tetanus treatment and prophylaxis
40. Varicella prophylaxis

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

IV. DOCUMENTATION

The following information is necessary to initiate the prior authorization review:

A. Primary immunodeficiency
   1. Diagnostic test results
      a. Copy of laboratory report with serum immunoglobulin levels: IgG, IgA, IgM, and IgG subclasses
      b. Vaccine response to pneumococcal polysaccharide vaccine (post-vaccination *Streptococcus pneumoniae* antibody titers)

c. Pertinent genetic or molecular testing in members with a known genetic disorder
d. Copy of laboratory report with lymphocyte subset enumeration by flow cytometry

2. IgG trough level for those continuing with IG therapy

B. Myasthenia gravis
1. Clinical records describing standard treatments tried and failed

C. Secondary hypogammaglobulinemia (e.g., CLL, BMT/HSCT recipients)
1. Copy of laboratory report with pre-treatment serum IgG level

D. Chronic inflammatory demyelinating polyneuropathy (CIDP) and multifocal motor neuropathy (MMN)
1. Pre-treatment electrodiagnostic studies (electromyography [EMG] or nerve conduction studies [NCS])

E. Dermatomyositis and polymyositis
1. Clinical records describing standard treatments tried and failed

F. Lambert-Eaton Myasthenic Syndrome (LEMS)
1. Neurophysiology studies (e.g., electromyography)
2. A positive anti- P/Q type voltage-gated calcium channel antibody test

G. Idiopathic thrombocytopenic purpura
1. Laboratory report with pre-treatment/current platelet count
2. Chronic/persistent ITP: copy of medical records supporting trial and failure with corticosteroid or anti-D therapy (unless contraindicated)

H. Parvovirus B19-indicated Pure Red Cell Aplasia (PRCA)
1. Copy of test result confirming presence of parvovirus B19

I. Stiff-person syndrome
1. Anti-glutamic acid decarboxylase (GAD) antibody testing results
2. Clinical records describing standard treatments tried and failed

J. Toxic shock syndrome or toxic necrotizing fasciitis due to group A streptococcus
1. Documented presence of fasciitis (toxic necrotizing fasciitis due to group A streptococcus only)
2. Microbiological data (culture or Gram stain)

V. CRITERIA FOR INITIAL APPROVAL

A. Primary Immunodeficiency

Initial authorization of 6 months may be granted for members with any of the following diagnoses:

1. Severe combined immunodeficiency (SCID) or congenital agammaglobulinemia (eg, X-linked or autosomal recessive agammaglobulinemia):
   a. Diagnosis confirmed by genetic or molecular testing, or
   b. Pretreatment IgG level < 200 mg/dL, or
   c. Absence or very low number of T cells (CD3 T cells < 300/microliter) or the presence of maternal T cells in the circulation (SCID only)
2. Wiskott-Aldrich syndrome, DiGeorge syndrome, or ataxia-telangiectasia (or other non-SCID combined immunodeficiency):
   a. Diagnosis confirmed by genetic or molecular testing (if applicable), and
   b. History of recurrent bacterial infections (eg, pneumonia, otitis media, sinusitis, sepsis, gastrointestinal), and
   c. Impaired antibody response to pneumococcal polysaccharide vaccine (see Appendix A)
3. Common variable immunodeficiency (CVID):
   a. Age 2 years or older, and
   b. Other causes of immune deficiency have been excluded (eg, drug induced, genetic disorders, infectious diseases such as HIV, malignancy), and
   c. Pretreatment IgG level < 500 mg/dL or ≥ 2 SD below the mean for age, and
   d. History of recurrent bacterial infections, and
   e. Impaired antibody response to pneumococcal polysaccharide vaccine (see Appendix A)

4. Hypogammaglobulinemia (unspecified), IgG subclass deficiency, selective IgA deficiency, selective IgM deficiency, or specific antibody deficiency:
   a. History of recurrent bacterial infections, and
   b. Impaired antibody response to pneumococcal polysaccharide vaccine (see Appendix A), and
   c. Any of the following pre-treatment laboratory findings:
      i. Hypogammaglobulinemia: IgG < 500 mg/dL or ≥ 2 SD below the mean for age
      ii. Selective IgA deficiency: IgA level < 7 mg/dL with normal IgG and IgM levels
      iii. Selective IgM deficiency: IgM level < 30 mg/dL with normal IgG and IgA levels
      iv. IgG subclass deficiency: IgG1, IgG2, or IgG3 ≥ 2 SD below mean for age assessed on at least 2 occasions; normal IgG (total) and IgM levels, normal/low IgA levels
      v. Specific antibody deficiency: normal IgG, IgA and IgM levels
5. Other predominant antibody deficiency disorders must meet a., b., and c.i. in section 4. above.
6. Other combined immunodeficiency must meet criteria in section 2. above.

Re-authorization of 6 months may be granted when the following criteria are met:
1. A reduction in the frequency of bacterial infections has been demonstrated since initiation of IG therapy, AND
2. IgG trough levels are monitored at least yearly and maintained at or above the lower range of normal for age (when applicable for indication), OR
3. The prescriber will re-evaluate the dose of IG and consider a dose adjustment (when appropriate).

B. Myasthenia Gravis

1. Authorization of 1 month may be granted to members who are prescribed IG for worsening weakness, acute exacerbation, or in preparation for surgery.
   a. Worsening weakness includes an increase in any of the following symptoms: diplopia, ptosis, blurred vision, difficulty speaking (dysarthria), difficulty swallowing (dysphagia), difficulty chewing, impaired respiratory status, fatigue, and limb weakness. Acute exacerbations include more severe swallowing difficulties and/or respiratory failure
   b. Pre-operative management (eg, prior to thymectomy)
2. Authorization of 6 months may be granted to members with refractory myasthenia gravis who have tried and failed 2 or more standard therapies (eg, corticosteroids, azathioprine, cyclosporine, mycophenolate mofetil, rituximab).

C. Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)

1. Initial authorization of 3 months may be granted when the following criteria are met:
   a. Disease course is progressive or relapsing/remitting for 2 months or longer
   b. Moderate to severe functional disability
   c. The diagnosis was confirmed by electrodiagnostic studies
2. Re-authorization of 6 months may be granted when the following criteria are met:
   a. Significant improvement in disability and maintenance of improvement since initiation of IG therapy
   b. IG is being used at the lowest effective dose and frequency

D. Dermatomyositis or Polymyositis

1. Initial authorization of 3 months may be granted when the following criteria are met:
   a. Member has at least 4 of the following:
      i. Proximal muscle weakness (upper or lower extremity and trunk)
      ii. Elevated serum creatine kinase (CK) or aldolase level
      iii. Muscle pain on grasping or spontaneous pain
      iv. Myogenic changes on EMG (short-duration, polyphasic motor unit potentials with spontaneous fibrillation potentials)
      v. Positive for anti-synthetase antibodies (e.g., anti-Jo-1, also called histadyl tRNA synthetase)

vi. Non-destructive arthritis or arthralgias
vii. Systemic inflammatory signs (fever: more than 37°C at axilla, elevated serum CRP level or accelerated ESR of more than 20 mm/h by the Westergren method)
viii. Pathological findings compatible with inflammatory myositis (inflammatory infiltration of skeletal evidence of active regeneration may be seen), and

b. Standard first-line treatments (corticosteroids) and second-line treatments (immunosuppressants) have been tried but were unsuccessful or not tolerated, or
c. Member is unable to receive standard first-line and second-line therapy because of a contraindication or other clinical reason.

2. Re-authorization of 6 months may be granted when the following criterion is met:
   a. Significant improvement in disability and maintenance of improvement since initiation of IG therapy

E. Idiopathic Thrombocytopenic Purpura ITP/(Immune Thrombocytopenia)

1. Newly diagnosed ITP (diagnosed within the past 3 months) or initial therapy: authorization of 1 month may be granted when the following criteria are met:
   a. Children (< 18 years of age)
      i. Significant bleeding symptoms (mucosal bleeding or other moderate/severe bleeding) or
      ii. High risk for bleeding* (see Appendix B), or
      iii. Rapid increase in platelets is required* (e.g., surgery or procedure)
   b. Adults (≥ 18 years of age)
      i. Platelet count < 30,000/mcL, or
      ii. Platelet count < 50,000/mcL and significant bleeding symptoms, high risk for bleeding or rapid increase in platelets is required*, and
      iii. Corticosteroid therapy is contraindicated and IG will be used alone or IG will be used in combination with corticosteroid therapy
2. Chronic/persistent ITP (≥ 3 months from diagnosis) or ITP unresponsive to first-line therapy: authorization of 6 months may be granted when the following criteria are met:
   a. Platelet count < 30,000/mcL, or
   b. Platelet count < 50,000/mcL and significant bleeding symptoms, high risk for bleeding* or rapid increase in platelets is required*, and
   c. Relapse after previous response to IG or inadequate response/intolerance/contraindication to corticosteroid or anti-D therapy
3. Adults with refractory ITP after splenectomy: authorization of 6 months may be granted when either of the following criteria is met:
   a. Platelet count < 30,000/mcL, or
   b. Significant bleeding symptoms
4. ITP in pregnant women: authorization through delivery may be granted to pregnant women with ITP.

* The member's risk factor(s) for bleeding (see Appendix B) or reason requiring a rapid increase in platelets must be provided.

F. B-cell Chronic Lymphocytic Leukemia (CLL)

1. Initial authorization of 6 months may be granted when all of the following criteria are met:
   a. IG is prescribed for prophylaxis of bacterial infections.
   b. Member has a history of recurrent sinopulmonary infections requiring intravenous antibiotics or hospitalization.
   c. Member has a pretreatment serum IgG level <500 mg/dL.
2. Re-authorization of 6 months may be granted when a reduction in the frequency of bacterial infections has been demonstrated since initiation of IG therapy.

G. Prophylaxis of Bacterial Infections in HIV-Infected Pediatric Patients

1. Initial authorization of up to 6 months may be granted to pediatric members with HIV infection when any of the following criteria are met:
   a. IG is prescribed for primary prophylaxis of bacterial infections and pretreatment serum IgG < 400 mg/dL, or
   b. IG is prescribed for secondary prophylaxis of bacterial infections for members with a history of recurrent bacterial infections (> 2 serious bacterial infections in a 1-year period), or
   c. Member has failed to form antibodies to common antigens, such as measles, pneumococcal, and/or Haemophilus influenzae type b vaccine, or
   d. Member lives in an area where measles is highly prevalent and who have not developed an antibody response after two doses of measles, mumps, and rubella virus vaccine live, or
   e. Member has been exposed to measles and request is for a single dose, or
   f. Member has chronic bronchiectasis that is suboptimally responsive to antimicrobial and pulmonary therapy
2. Re-authorization of 6 months may be granted when a reduction in the frequency of bacterial infections has been demonstrated since initiation of IG therapy.

H. Bone marrow transplant/hemopoietic stem cell transplant (BMT/HSCT)

1. Initial authorization of 6 months may be granted to members who are BMT/HSCT recipients when the following criteria are met:
   a. Therapy will be used to prevent the risk of acute graft-versus-host disease, associated interstitial pneumonia (infectious or idiopathic), septicemia, and other infections (e.g., cytomegalovirus infections [CMV], recurrent bacterial infection).
   b. Either of the following:
      i. IG is requested within the first 100 days post-transplant.
      ii. Member has a pretreatment serum IgG < 400 mg/dL.
2. Re-authorization of 6 months may be granted when a reduction in the frequency of bacterial infections has been demonstrated since initiation of IG therapy.

I. Multifocal Motor Neuropathy (MMN)

1. Initial authorization of 3 months may be granted when the following criteria are met:
   a. Member experienced progressive, multifocal, asymmetrical weakness without objective sensory loss in 2 or more nerves for at least 1 month
   b. The diagnosis was confirmed by electrodiagnostic studies
2. Re-authorization of 6 months may be granted when significant improvement in disability and maintenance of improvement have occurred since initiation of IG therapy

J. Guillain-Barre Syndrome (GBS)

Authorization of 1 month total may be granted for GBS when the following criteria are met:

1. Member has severe disease with significant weakness (e.g., inability to stand or walk without aid, respiratory weakness)
2. Onset of neurologic symptoms occurred less than 4 weeks from the anticipated start of therapy

K. Lambert-Eaton Myasthenic Syndrome (LEMS)

1. Initial authorization of 6 months may be granted for LEMS when the following criteria are met:
   a. Diagnosis has been confirmed by either of the following:
      i. Neurophysiology studies (e.g., electromyography)
      ii. A positive anti- P/Q type voltage-gated calcium channel antibody test
   b. Anticholinesterases (eg pyridostigmine) and amifampridine (e.g., 3,4-diaminopyridine phosphate, Firdapse) have been tried but were unsuccessful or not tolerated
   c. Weakness is severe or there is difficulty with venous access for plasmapheresis
2. Re-authorization of 6 months may be granted when member is responding to therapy (i.e., there is stability or improvement in symptoms relative to the natural course of LEMS).

L. Kawasaki Syndrome
Authorization of 1 month may be granted for pediatric members with Kawasaki syndrome.

M. Fetal/Neonatal Alloimmune Thrombocytopenia (F/NAIT)
Authorization of 6 months may be granted for treatment of F/NAIT.

N. Parvovirus B19-induced Pure Red Cell Aplasia (PRCA)
Authorization of 6 months may be granted for severe, refractory anemia associated with bone marrow suppression, with parvovirus B19 viremia.

O. Stiff-person Syndrome
Authorization of 6 months may be granted for stiff-person syndrome when the following criteria are met:
1. Diagnosis has been confirmed by anti-glutamic acid decarboxylase (GAD) antibody testing
2. Member had an inadequate response to first-line treatment (benzodiazepines and/or baclofen)

P. Management of immune checkpoint inhibitor-related toxicities
Authorization of 1 month may be granted for management of immune checkpoint-inhibitor toxicities when all of the following criteria are met:
1. Member has experienced a moderate or severe adverse event to a PD-1 or PD-L1 inhibitor (e.g., pembrolizumab, nivolumab, atezolizumab, avelumab, durvalumab)
2. The offending medication has been held or discontinued
3. Member experienced one or more of the following adverse events: myocarditis, bullous dermatitis, Stevens-Johnson syndrome, toxic epidermal necrolysis, pneumonitis, myasthenia gravis, peripheral neuropathy, encephalitis, transverse myelitis, severe inflammatory arthritis, Guillain-Barre syndrome, or steroid-refractory myalgias or myositis

Q. Acquired Red Cell Aplasia
Authorization of 6 months may be granted for acquired red cell aplasia.

R. Acute Disseminated Encephalomyelitis
Authorization of 1 month may be granted for acute disseminated encephalomyelitis in members who have had an insufficient response or a contraindication to intravenous corticosteroid treatment.

S. Autoimmune Mucocutaneous Blistering Disease
Authorization of 6 months may be granted for autoimmune mucocutaneous blistering disease (includes pemphigus vulgaris, pemphigus foliaceus, bullous pemphigoid, mucous membrane pemphigoid, and epidermolysis bullosa acquisita) when the following criteria are met:
1. Diagnosis has been proven by biopsy and confirmed by pathology report, and
2. Condition is rapidly progressing, extensive or debilitating, and
3. Member has failed or experienced significant complications (e.g., diabetes, steroid-induced osteoporosis) from standard treatment (corticosteroids, immunosuppressive agents).

T. Autoimmune Hemolytic Anemia
Authorization of 6 months may be granted for warm-type autoimmune hemolytic anemia in members who do not respond or have a contraindication to corticosteroids or splenectomy.

U. Autoimmune Neutropenia
Authorization of 6 months may be granted for autoimmune neutropenia where treatment with G-CSF (granulocyte colony stimulating factor) is not appropriate.

V. Birdshot Retinochoroidopathy
Authorization of 6 months may be granted for birdshot (vitiliginous) retinochoroidopathy that is not responsive to immunosuppressives (eg corticosteroids, cyclosporine).

W. BK Virus Associated Nephropathy
Authorization of 6 months may be granted for BK virus associated nephropathy.

X. Churg-Strauss Syndrome
Authorization of 6 months may be granted for severe, active Churg-Strauss syndrome as adjunctive therapy for members who have experienced failure, intolerance, or are contraindicated to other interventions.

Y. Enteroviral Meningoencephalitis
Authorization of 6 months may be granted for severe cases of enteroviral meningoencephalitis.

Z. Hematophagocytic Lymphohistiocytosis (HLH) or Macrophage Activation Syndrome (MAS)
Authorization of 6 months may be granted for treatment of hypogammaglobulinemia in HLH or MAS when total IgG is less than 400 mg/dL or two standard deviations below the mean for age.

AA. Hemolytic Disease of Newborn
Authorization of 6 months may be granted for isoimmune hemolytic disease in neonates.

BB. HIV-associated Thrombocytopenia
Authorization of 6 months may be granted for HIV-associated thrombocytopenia when the following criteria are met:

1. Pediatric members with IgG < 400 mg/dL and one of the following:
    a. 2 or more bacterial infections in a 1-year period despite antibiotic chemoprophylaxis with TMP-SMZ or another active agent, or
    b. Received 2 doses of measles vaccine and lives in a region with a high prevalence or measles, or
    c. HIV-associated thrombocytopenia despite anti-retroviral therapy, or
    d. Chronic bronchiectasis that is suboptimally responsive to antimicrobial and pulmonary therapy, or
    e. T4 cell count ≥ 200/mm^3
2. Adult members with significant bleeding, platelet count < 20,000/mcL, and failure of RhIG in Rh-positive patients

CC. Hyperimmunoglobulinemia E Syndrome
Authorization of 6 months may be granted to treat severe eczema in hyperimmunoglobulinemia E syndrome.

DD. Hypogammaglobulinemia from CAR-T therapy
Authorization of 6 months may be granted for members with IgG < 400 mg/dL receiving treatment with CAR-T therapy (including but not limited to idecabtagene vicleucel [Abecma], tisagenlecleucel [Kymriah], or axicabtagene ciloleucel [Yescarta]).

EE. Multiple Myeloma
Authorization of 6 months may be granted for multiple myeloma in members who have recurrent, serious infections despite the use of prophylactic antibiotics.

FF. Neonatal Hemochromatosis
Authorization of 6 months may be granted for prophylaxis in members who are pregnant with a history of pregnancy ending in documented neonatal hemochromatosis.

GG. Opsoclonus-myoclonus
Authorization of 6 months may be granted for treatment of either of the following:

1. Paraneoplastic opsoclonus-myoclonus-ataxia associated with neuroblastoma
2. Refractory opsoclonus-myoclonus, as last-resort treatment

HH. Post-transfusion Purpura
Authorization of 1 month may be granted for post-transfusion purpura.

II. Rasmussen Encephalitis
Authorization of 6 months may be granted for Rasmussen encephalitis in members whose symptoms do not improve with anti-epileptic drugs and corticosteroids.

JJ. Renal Transplantation
Authorization of 6 months may be granted for a member undergoing renal transplantation from a live donor with ABO incompatibility or positive cross match.

KK. Secondary Immunosuppression Associated with Major Surgery, Hematological Malignancy, Major Burns, and Collagen-Vascular Diseases
Authorization of 6 months may be granted to prevent or modify recurrent bacterial or viral infections in members with secondary immunosuppression (IgG < 400 mg/dL) associated with major surgery, hematological malignancy, extensive burns, or collagen-vascular disease.

LL. Solid Organ Transplantation
Authorization of 6 months may be granted for solid organ transplantation for allosensitized members.

MM. Toxic Epidermal Necrolysis and Stevens-Johnson Syndrome
Authorization of 1 month may be granted for severe cases of toxic epidermal necrolysis or Stevens-Johnson syndrome.

NN. Toxic Shock Syndrome
Authorization of 1 month may be granted for staphylococcal or streptococcal toxic shock syndrome when the infection is refractory to several hours of aggressive therapy, an undrainable focus is present, or the member has persistent oliguria with pulmonary edema.

OO. Systemic Lupus Erythematosus
Authorization of 6 months may be granted for severe, active SLE in members who have experienced inadequate response, intolerance or have a contraindication to first and second line therapies.

PP. Measles (Rubeola) prophylaxis
Authorization of 1 month may be granted for postexposure prophylaxis to prevent or modify symptoms of measles (rubeola) in susceptible members exposed to the disease less than 6 days previously.

QQ. Tetanus treatment and prophylaxis
Authorization of 1 month may be granted for treatment or postexposure prophylaxis of tetanus as an alternative when tetanus immune globulin (TIG) is unavailable.

RR. Varicella prophylaxis
Authorization of 1 month may be granted for postexposure prophylaxis of varicella in susceptible individuals when varicella-zoster immune globulin (VZIG) is unavailable.

SS. Toxic Necrotizing Fasciitis Due To Group A Streptococcus
Authorization of 1 month may be granted for members with fasciitis due to invasive streptococcal infection.

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VI. CONTINUATION OF THERAPY

Authorization may be granted for continuation of therapy when either the following criteria is met:

a. For conditions with reauthorization criteria listed under section III: Members who are currently receiving IG therapy must meet the applicable reauthorization criteria for the member's condition.
b. For all other conditions, all members (including new members) must meet initial authorization criteria.

VII. APPENDICES

Appendix A: Impaired Antibody Response to Pneumococcal Polysaccharide Vaccine

- Age 2 years and older: impaired antibody response demonstrated to vaccination with a pneumococcal polysaccharide vaccine
- Not established for children less than 2 years of age
- Excludes the therapy initiated in the hospital setting

Appendix B: Examples of Risk Factors for Bleeding (not all inclusive)

- Undergoing a medical or dental procedure where blood loss is anticipated
- Comorbidity (eg, peptic ulcer disease, hypertension)
- Mandated anticoagulation therapy
- Profession or lifestyle predisposes patient to trauma (eg, construction worker, fireman, professional athlete)

Section 3: State Specific PANDAS Criteria

PRIOR AUTHORIZATION CRITERIA

DRUG CLASS	**IMMUNE GLOBULIN (HUMAN)**
BRAND NAME:	
	ASCENIV
	BIVIGAM
	CUTAQUIG
	CUVITRU
	FLEBOGAMMA
	GAMASTAN
	GAMMAGARD LIQUID
	GAMMAGARD S/D

GAMMAKED

GAMMAPLEX

GAMUNEX -C

HIZENTRA

HYQVIA

OCTAGAM

PANZYGA

PRIVIGEN

XEMBIFY

DRUG CLASS **CD20-DIRECTED CYTOLYTIC ANTIBODY**

BRAND NAME:

RIABNI

RITUXAN

RUXIENCE

TRUXIMA

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 to treat either of the following conditions: A) pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections, B) pediatric acute onset neuropsychiatric syndrome, C) autoimmune encephalitis

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Reference number(s)
1897-A

POLICY Document for IXEMPRA (ixabepilone)

The overall objective of this policy is to support the appropriate and cost effective use of the medication. This document provides specific information to each section of the overall policy.

Section 1: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 2: Oncology Clinical Policy
- Policy information specific to regimen review per NCCN Guidelines.

Section 1: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

IXEMPRA (ixabepilone)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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. In combination with capecitabine for the treatment of metastatic or locally advanced breast cancer resistant to treatment with an anthracycline and a taxane, or whose cancer is taxane resistant and for whom further anthracycline therapy is contraindicated
2. Monotherapy for the treatment of metastatic or locally advanced breast cancer in patients whose tumors are resistant or refractory to anthracyclines, taxanes, and capecitabine

B. Compendial Uses
1. 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: HER2 status testing results, where applicable

III. CRITERIA FOR INITIAL APPROVAL

Breast Cancer
Authorization of 12 months may be granted for treatment of breast cancer when any of the following criteria are met:

1. Member has human epidermal growth factor receptor 2 (HER2)-negative locally advanced, recurrent or metastatic disease, as a single agent; or
2. Member has human epidermal growth factor receptor 2 (HER2)-positive recurrent or metastatic disease, in combination with trastuzumab; or
3. Ixempra will be used in combination with capecitabine for treatment of metastatic or locally advanced disease when the following criteria are met:
   a. Member has failed an anthracycline and a taxane, or whose cancer is taxane resistant and for whom further anthracycline therapy is contraindicated; and
   b. Member does not have aspartate aminotransferase (AST) or alanine aminotransferase (ALT) level greater than 2.5 times the upper limit of normal (ULN) or bilirubin greater than 1 time the ULN.

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.

Section 2: Oncology Clinical Policy

Oncology Clinical Policy

Program Description
The National Comprehensive Care Network® (NCCN®) is an alliance of leading cancer centers devoted to patient care, research and education dedicated to improving the quality, effectiveness and efficiency of cancer care so patients can live better lives.[1] It is comprised of oncology experts who convene regularly to establish the best treatments for patients. NCCN develops various resources for use by stakeholders in the health care delivery system. These resources include, but are not limited to, the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®), the NCCN Drugs & Biologics Compendium (NCCN Compendium®) and the NCCN Chemotherapy Order Templates (NCCN Templates®).

NCCN templates are based on NCCN Clinical Practice Guidelines and NCCN Compendium. The NCCN Compendium lists the appropriate drugs and biologics for specific cancers using U.S. Food and Drug Administration (FDA)-approved disease indications and specific NCCN panel recommendations. Each recommendation is supported by a level of evidence category.

NCCN Categories of Evidence and Consensus[2]
Category 1: Based on high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2A: Based on lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2B: Based on lower-level evidence, there is NCCN consensus that the intervention is appropriate.
Category 3: Based any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

Policy for Regimen Prior Authorization

A regimen prior authorization allows submission of a single prior authorization request for all oncology drugs or biologics within an NCCN template that require prior authorization.

This policy provides coverage of a regimen review when *all* of the following criteria are met:
a. Regimen prior authorization reviews, based on NCCN templates, are initiated through the provider portal: https://provider.carefirst.com/providers/home.page

b. If the prior authorization request is submitted via phone or fax, each drug or biologic will need to be submitted and reviewed as a separate prior authorization request for review with drug-specific criteria.
2. The prior authorization review is requested for an oncology drug or biologic that requires prior authorization on the medical benefit.
3. The indication is for a cancer that is eligible for regimen review. Currently, the cancer types in scope for regimen review include breast, lung, colon and rectal cancer.
4. The member is eligible for regimen review.

In addition, the following criteria must be met for approval:
1. The requested regimen for the drug(s) or biologic(s) and indication is consistent with an NCCN recommendation with a level of evidence category of 1 or 2A.
2. The NCCN template must be accepted by the provider without modification. Authorizations may be granted for 12 months. Further review may be indicated where the above criteria are not met.

Continuation of Therapy

To submit a request for continuation of therapy, a new regimen prior authorization review must be requested. Upon template selection, the template must be modified to include the appropriate therapies being used for maintenance treatment. The regimen request will be submitted for further review.

Dosage and Administration

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

REFERENCES

SECTION 1
1. Ixempra [package insert]. Princeton, NJ: R-Pharm US LLC; January 2016.
2. The NCCN Drugs & Biologics Compendium 2021 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed December 7, 2021.

SECTION 2
1. National Comprehensive Cancer Network. About NCCN website. https://www.nccn.org/about/default.aspx, accessed September 16, 2019.
2. National Comprehensive Cancer Network. NCCN Categories of Evidence and Consensus website. https://www.nccn.org/professionals/physician_gls/categories_of_consensus.aspx, accessed September 16, 2019.
3. National Comprehensive Cancer Network. NCCN Guidelines website. http://www.nccn.org/professionals/physician_gls/f_guidelines.asp, accessed September 16, 2019. (Note:An account may be required.)

4. National Comprehensive Cancer Network. NCCN Drugs and Biologics Compendium® website. http://www.nccn.org/professionals/drug_compendium/content/contents.asp, accessed September 16, 2019. (Note: A subscription may be required.)
5. National Comprehensive Cancer Network. NCCN Chemotherapy Order Templates (NCCN Templates) website. https://www.nccn.org/professionals/OrderTemplates/Default.aspx, accessed September 16, 2019. (Note: A subscription may be required.)

Reference number(s)
3820-A

SPECIALTY GUIDELINE MANAGEMENT

JELMYTO (mitomycin)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Jelmyto (mitomycin) is indicated for the treatment of adult patients with low-grade upper tract urothelial cancer (LG-UTUC).

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

II. DOCUMENTATION

Submission of the following information is necessary to initiate a prior authorization for continuation of therapy review: urine cytology and ureteroscopy report 3 months after the initiation of therapy documenting complete response.

III. CRITERIA FOR INITIAL APPROVAL

Urothelial Cancer
Authorization of 6 doses (3 months) may be granted for treatment of non-metastatic, low-grade, low volume (5-15 mm), upper tract urothelial cancer when all of the following criteria are met:
1. The requested drug will be given via pyelocalyceal administration.
2. The requested drug will be administered once weekly for the first six weeks for initiation.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for a maximum of 11 additional doses for continued treatment in members requesting reauthorization for an indication listed in Section III when there has been a complete response (as defined as a complete absence of tumor lesions by urine cytology and ureteroscopy) at 3 months after the initiation of the requested drug.

V. REFERENCES

1. Jelmyto [package insert]. Princeton, NJ: UroGen Pharma, Inc.; January 2021.
2. The NCCN Drugs & Biologics Compendium® © 2022 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed July 6, 2022.

POLICY Document for JEMPERLI (dostarlimab-gxly)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, and overall, clinically appropriate use. This document provides specific information to both sections of the overall policy.

Section 1: Site of Care
- Policy information specific to site of care (outpatient, hospital outpatient, home infusion)

Section 2: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 3: Oncology Clinical Policy
- Policy information specific to regimen review per NCCN Guidelines.

Section 1: Site of Care

CareFirst Site of Care Criteria
Administration of Intravenous Checkpoint Inhibitors
Bavencio, Imfinzi, Jemperli, Keytruda, Libtayo, Opdivo, Opdualag, Tecentriq, Yervoy and Zynyz

POLICY

I. CRITERIA FOR APPROVAL FOR ADMINISTRATION IN OUTPATIENT HOSPITAL SETTING

This policy provides coverage for administration of a checkpoint inhibitor in an outpatient hospital setting for the initial 6 months approval and up to 45 days for renewal of therapy.

This policy provides coverage for administration of a checkpoint inhibitor in an outpatient hospital setting for a longer course of treatment when ANY of the following criteria are met:

A. The member has experienced an adverse reaction that did not respond to conventional interventions (eg, acetaminophen, steroids, diphenhydramine, fluids, other pre-medications or slowing of infusion rate) or a severe adverse event (anaphylaxis, anaphylactoid reactions, myocardial infarction, thromboembolism, or seizures) during or immediately after an infusion or has experienced severe toxicity requiring continuous monitoring (e.g. Grade 2-4 bullous dermatitis, transaminitis, pneumonitis, Stevens-Johnson syndrome, acute pancreatitis, primary adrenal insufficiency aseptic meningitis, encephalitis, transverse myelitis, myocarditis, pericarditis, arrhythmias, impaired ventricular function, conduction abnormalities).
B. The member is medically unstable (eg respiratory, cardiovascular, or renal conditions).
C. The member has severe venous access issues that require the use of a special interventions only available in the outpatient hospital setting.
D. The member has significant behavioral issues and/or physical or cognitive impairment that would impact the safety of the infusion therapy AND the patient does not have access to a caregiver.
E. The member is receiving provider administered combination chemotherapy.
F. The member is less than 14 years of age.

For situations where administration of a checkpoint inhibitor does not meet the criteria for outpatient hospital infusion, coverage for a checkpoint inhibitor is provided when administered in alternative sites such as physician office, home infusion or ambulatory care.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the site of care prior authorization review (where applicable):

A. Medical records supporting the member has experienced an adverse reaction that did not respond to conventional interventions or a severe adverse event during or immediately after an infusion or a severe toxicity requiring continuous monitoring
B. Medical records supporting the member is medically unstable
C. Medical records supporting the member has severe venous access issues that require specialized interventions only available in the outpatient hospital setting
D. Medical records supporting the member has behavioral issues and/or physical or cognitive impairment and no access to a caregiver
E. Medical records supporting the member is receiving provider administered combination therapy.

Section 2: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

JEMPERLI (dostarlimab-gxly)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Jemperli is indicated for the treatment of adult patients with mismatch repair deficient (dMMR) recurrent or advanced:
1. Endometrial cancer (EC), as determined by an FDA-approved test, that has progressed on or following prior treatment with a platinum-containing regimen in any setting and are not candidates for curative surgery or radiation.
2. Solid tumors, as determined by an FDA-approved test, that have progressed on or following prior treatment and who have no satisfactory alternative treatment options.

B. Compendial Uses
1. Breast cancer
2. Colorectal cancer
3. Esophageal and esophagogastric junction cancers
4. Gastric cancer
5. Occult primary cancer
6. Ovarian cancer
   a. Epithelial ovarian cancer
   b. Fallopian tube cancer
   c. Primary peritoneal cancer
   d. Carcinosarcoma (malignant mixed Mullerian tumors)
   e. Clear cell carcinoma of the ovary
   f. Mucinous carcinoma of the ovary
   g. Grade 1 endometrioid carcinoma
   h. Low-grade serous carcinoma/ovarian borderline epithelial tumors
7. Endometrial carcinoma
8. Small bowel adenocarcinoma
9. Ampullary 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 laboratory report confirming microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) tumor status, where applicable.

III. EXCLUSIONS

Coverage will not be provided for members who have experienced disease progression while on PD-1 or PD-L1 inhibitor therapy.

IV. CRITERIA FOR INITIAL APPROVAL

A. Endometrial Carcinoma

1. Authorization of 6 months may be granted for treatment of recurrent or advanced microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) endometrial cancer that has progressed on or following prior treatment with a platinum-containing regimen.
1. Authorization of 6 months may be granted for treatment of endometrial carcinoma in combination with carboplatin and paclitaxel in members with stage III-IV or recurrent disease

B. Solid tumors

Authorization of 6 months may be granted as a single agent for treatment of mismatch repair deficient (dMMR) solid tumors in members with recurrent, or advanced disease that have progressed on or following prior treatment and for whom there are no satisfactory alternative treatment options.

C. Breast cancer

Authorization of 6 months may be granted as a single agent for treatment of recurrent unresectable or stage IV breast cancer that is microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) and has progressed on or following prior treatment and has no satisfactory alternative treatment options.

D. Colorectal cancer

Authorization of 6 months may be granted as a single agent for treatment of advanced or metastatic colorectal cancer, including appendiceal adenocarcinoma, that is microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR).

E. Esophageal, esophagogastric junction and gastric cancer

Authorization of 6 months may be granted for treatment of esophageal, esophagogastric junction, or gastric carcinoma when all 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 subsequent treatment as palliative therapy for patients who are not surgical candidates or have unresectable locally advanced, recurrent, or metastatic disease.
3. The requested medication will be used for microsatellite instability-high (MSI-H) or deficient mismatch repair (dMMR) tumors.
4. The requested medication will be used in patients whose cancer is progressing on or following prior treatment and who have no satisfactory alternative treatment options.

F. Occult primary cancer

Authorization of 6 months may be granted as a single agent for treatment of occult primary cancer that is microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) and has progressed on or following prior treatment and has no satisfactory alternative treatment options.

G. Ovarian cancer
Authorization of 6 months may be granted as a single agent for treatment of epithelial ovarian cancer, fallopian tube cancer, primary peritoneal cancer, carcinosarcoma (malignant mixed Mullerian tumors), clear cell carcinoma of the ovary, mucinous carcinoma of the ovary, grade 1 endometrioid carcinoma, and low-grade serous carcinoma/ovarian borderline epithelial tumors for recurrent, persistent, or advanced microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) tumors.

H. Small bowel adenocarcinoma
Authorization of 6 months may be granted as a single agent for treatment of advanced or metastatic small bowel adenocarcinoma for microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) tumors.

I. Ampullary adenocarcinoma
Authorization of 6 months may be granted as a single agent for subsequent treatment of recurrent or advanced microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) ampullary adenocarcinoma that has progressed on or following prior treatment and has no satisfactory alternative treatment options.

V. CONTINUATION OF THERAPY

Authorization of 6 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.

Section 3: Oncology Clinical Policy

Oncology Clinical Policy

Program Description

The National Comprehensive Care Network® (NCCN®) is an alliance of leading cancer centers devoted to patient care, research and education dedicated to improving the quality, effectiveness and efficiency of cancer care so patients can live better lives.[1] It is comprised of oncology experts who convene regularly to establish the best treatments for patients. NCCN develops various resources for use by stakeholders in the health care delivery system. These resources include, but are not limited to, the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®), the NCCN Drugs & Biologics Compendium (NCCN Compendium®) and the NCCN Chemotherapy Order Templates (NCCN Templates®).

NCCN templates are based on NCCN Clinical Practice Guidelines and NCCN Compendium. The NCCN Compendium lists the appropriate drugs and biologics for specific cancers using U.S. Food and Drug Administration (FDA)-approved disease indications and specific NCCN panel recommendations. Each recommendation is supported by a level of evidence category.

NCCN Categories of Evidence and Consensus[2]

a. Category 1: Based on high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
b. Category 2A: Based on lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.

c. Category 2B: Based on lower-level evidence, there is NCCN consensus that the intervention is appropriate.
d. Category 3: Based any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

Policy for Regimen Prior Authorization

A regimen prior authorization allows submission of a single prior authorization request for all oncology drugs or biologics within an NCCN template that require prior authorization.

This policy provides coverage of a regimen review when *all* of the following criteria are met:

a. Regimen prior authorization reviews, based on NCCN templates, are initiated through the provider portal: https://provider.carefirst.com/providers/home.page
b. If the prior authorization request is submitted via phone or fax, each drug or biologic will need to be submitted and reviewed as a separate prior authorization request for review with drug-specific criteria.
c. The prior authorization review is requested for an oncology drug or biologic that requires prior authorization on the medical benefit.
d. The indication is for a cancer that is eligible for regimen review. Currently, the cancer types in scope for regimen review include breast, lung, colon and rectal cancer.
e. The member is eligible for regimen review.

In addition, the following criteria must be met for approval:

a. The requested regimen for the drug(s) or biologic(s) and indication is consistent with an NCCN recommendation with a level of evidence category of 1 or 2A.
b. The NCCN template must be accepted by the provider without modification.

Authorizations may be granted for 12 months.
Further review may be indicated where the above criteria are not met.

Continuation of Therapy

To submit a request for continuation of therapy, a new regimen prior authorization review must be requested. Upon template selection, the template must be modified to include the appropriate therapies being used for maintenance treatment. The regimen request will be submitted for further review.

Dosage and Administration

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

REFERENCES:

SECTION 1

1. Opdivo [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; February 2023.
2. Bavencio [package insert]. Rockland, MA: EMD Serono, Inc; July 2020.
3. Imfinzi [prescribing information]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; November 2022.
4. Jemperli [prescribing information]. Philadelphia, PA: GlaxoSmithKline LLC; February 2023.
5. Keytruda [prescribing information]. Rahway, NJ: Merck Sharp & Dome LLC.; April 2023.
6. Libtayo [prescribing information]. Tarrytown, NY: Regeneron Pharmaceuticals, Inc.; April 2023.
7. Tecentriq [package insert]. South San Francisco, CA: Genentech, Inc.; December 2022.
8. Yervoy [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; February 2023.

9. Opdualag [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; March 2022.
10. Zynyz [package insert]. Wilmington, DE: Incyte Corporation; March 2023.

SECTION 2

1. Jemperli [package insert]. Research Triangle Park, NC: GlaxoSmithKline; February 2023.
2. The NCCN Drugs & Biologics Compendium® © 2023 National Comprehensive Cancer Network, Inc. Available at: https://www.nccn.org. Accessed May 2, 2023.

SECTION 3

1. National Comprehensive Cancer Network. About NCCN website. https://www.nccn.org/about/default.aspx, accessed September 16, 2019.
2. National Comprehensive Cancer Network. NCCN Categories of Evidence and Consensus website. https://www.nccn.org/professionals/physician_gls/categories_of_consensus.aspx, accessed September 16, 2019.
3. National Comprehensive Cancer Network. NCCN Guidelines website. http://www.nccn.org/professionals/physician_gls/f_guidelines.asp, accessed September 16, 2019. *(Note: An account may be required.)*
4. National Comprehensive Cancer Network. NCCN Drugs and Biologics Compendium® website. http://www.nccn.org/professionals/drug_compendium/content/contents.asp, accessed September 16, 2019. *(Note: A subscription may be required.)*
5. National Comprehensive Cancer Network. NCCN Chemotherapy Order Templates (NCCN Templates) website. https://www.nccn.org/professionals/OrderTemplates/Default.aspx, accessed September 16, 2019. *(Note: A subscription may be required.)*

Reference number(s)
3000-A

SPECIALTY GUIDELINE MANAGEMENT

JETREA (ocriplasmin intravitreal 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
Jetrea is indicated for the treatment of symptomatic vitreomacular adhesion.

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

II. CRITERIA FOR INITIAL APPROVAL

Vitreomacular adhesion
Authorization of 90 days for a single dose (for each eye) may be granted for treatment of symptomatic vitreomacular adhesion.

III. REFERENCES

1. Jetrea [package insert]. Iselin, NJ: ThromboGenics, Inc; February 2017.

POLICY Document for JEVTANA (cabazitaxel)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication. This document provides specific information to each section of the overall policy.

Section 1: Clinical Criteria
Policy information specific to the clinical appropriateness for the medication
Section 2: Oncology Clinical Policy
Policy information specific to regimen review per NCCN Guidelines.

Section 1: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

JEVTANA (cabazitaxel)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Jevtana is indicated in combination with prednisone for the treatment of patients with metastatic castration-resistant prostate cancer previously treated with a docetaxel-containing treatment regimen.

Compendial Uses
1. Subsequent treatment for castration-resistant distant metastatic disease previously treated with a docetaxel-based regimen or in patients who are not candidates for, or are intolerant of docetaxel
2. Subsequent treatment for castration-resistant distant metastatic disease previously treated with novel hormone therapy (e.g., enzalutamide [Xtandi] or abiraterone [Zytiga])

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

II. CRITERIA FOR INITIAL APPROVAL

Metastatic castration-resistant prostate cancer (CRPC)
Authorization of 6 months may be granted for the treatment of metastatic castration-resistant prostate cancer when previously treated with any of the following:
A. A docetaxel-containing regimen or in patients who are not candidates for or who are intolerant to docetaxel
B. Novel hormone therapy (e.g., enzalutamide [Xtandi], abiraterone [Zytiga])

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 there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

Section 2: Oncology Clinical Policy

Oncology Clinical Policy

Program Description

The National Comprehensive Care Network® (NCCN®) is an alliance of leading cancer centers devoted to patient care, research and education dedicated to improving the quality, effectiveness and efficiency of cancer care so patients can live better lives.[1] It is comprised of oncology experts who convene regularly to establish the best treatments for patients. NCCN develops various resources for use by stakeholders in the health care delivery system. These resources include, but are not limited to, the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®), the NCCN Drugs & Biologics Compendium (NCCN Compendium®) and the NCCN Chemotherapy Order Templates (NCCN Templates®).

NCCN templates are based on NCCN Clinical Practice Guidelines and NCCN Compendium. The NCCN Compendium lists the appropriate drugs and biologics for specific cancers using U.S. Food and Drug Administration (FDA)-approved disease indications and specific NCCN panel recommendations. Each recommendation is supported by a level of evidence category.

NCCN Categories of Evidence and Consensus[2]

Category 1: Based on high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2A: Based on lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2B: Based on lower-level evidence, there is NCCN consensus that the intervention is appropriate.
Category 3: Based any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

Policy for Regimen Prior Authorization

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This policy provides coverage of a regimen review when *all* of the following criteria are met:

a. Regimen prior authorization reviews, based on NCCN templates, are initiated through the provider portal: https://provider.carefirst.com/providers/home.page
b. If the prior authorization request is submitted via phone or fax, each drug or biologic will need to be submitted and reviewed as a separate prior authorization request for review with drug-specific criteria.
c. The prior authorization review is requested for an oncology drug or biologic that requires prior authorization on the medical benefit.
d. The indication is for a cancer that is eligible for regimen review. Currently, the cancer types in scope for regimen review include breast, lung, colon and rectal cancer.
e. The member is eligible for regimen review.

In addition, the following criteria must be met for approval:

a. The requested regimen for the drug(s) or biologic(s) and indication is consistent with an NCCN recommendation with a level of evidence category of 1 or 2A.
b. The NCCN template must be accepted by the provider without modification. Authorizations may be granted for 12 months. Further review may be indicated where the above criteria are not met.

Continuation of Therapy

To submit a request for continuation of therapy, a new regimen prior authorization review must be requested. Upon template selection, the template must be modified to include the appropriate therapies being used for maintenance treatment. The regimen request will be submitted for further review.

Dosage and Administration

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

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POLICY Document for KADCYLA (ado-trastuzumab emtansine)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, and overall, clinically appropriate use. This document provides specific information to both sections of the overall policy.

Section 1: Clinical Criteria

- Policy information specific to the clinical appropriateness for the medication

Section 2: Oncology Clinical Policy

- Policy information specific to regimen review per NCCN Guidelines.

Section 1: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

KADCYLA (ado-trastuzumab emtansine)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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. Metastatic Breast Cancer (MBC)

   Kadcyla, as a single agent, is indicated for the treatment of patients with human epidermal growth factor receptor 2 (HER2)-positive, metastatic breast cancer who previously received trastuzumab and a taxane, separately or in combination. Patients should have either received prior therapy for metastatic disease, or developed disease recurrence during or within six months of completing adjuvant therapy.

2. Early Breast Cancer (EBC)

   Kadcyla, as a single agent, is indicated for the adjuvant treatment of patients with HER2-positive early breast cancer who have residual invasive disease after neoadjuvant taxane and trastuzumab-based treatment.

B. Compendial Uses

1. Single-agent therapy for recurrent or stage IV (M1) HER2-positive breast cancer
2. Non-small cell lung cancer with HER2 mutations
3. HER2-positive recurrent salivary gland tumors

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

A. Breast cancer

1. Authorization of 12 months may be granted for subsequent treatment of HER2-positive metastatic or recurrent breast cancer or for HER2-positive breast cancer with no response to preoperative systemic therapy when used as a single agent.
2. Authorization of up to 12 months may be granted for adjuvant treatment of HER2-positive early breast cancer when used as a single agent.

B. Non-small cell lung cancer

Authorization of 12 months may be granted for subsequent treatment of non-small cell lung cancer with HER2 (ERBB2) mutations when both of the following criteria are met:

1. The disease is recurrent, advanced or metastatic
2. The requested medication will be used as a single agent

C. Salivary Gland Tumor

Authorization of 12 months may be granted for treatment of recurrent HER2-positive salivary gland tumors 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. Adjuvant treatment of breast cancer will be approved for a total of 12 months of therapy.

Section 2: Oncology Clinical Policy

Oncology Clinical Policy

Program Description

The National Comprehensive Care Network® (NCCN®) is an alliance of leading cancer centers devoted to patient care, research and education dedicated to improving the quality, effectiveness and efficiency of cancer care so patients can live better lives.[1] It is comprised of oncology experts who convene regularly to establish the best treatments for patients. NCCN develops various resources for use by stakeholders in the health care delivery system. These resources include, but are not limited to, the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®), the NCCN Drugs & Biologics Compendium (NCCN Compendium®) and the NCCN Chemotherapy Order Templates (NCCN Templates®).

NCCN templates are based on NCCN Clinical Practice Guidelines and NCCN Compendium. The NCCN Compendium lists the appropriate drugs and biologics for specific cancers using U.S. Food and Drug Administration (FDA)-approved disease indications and specific NCCN panel recommendations. Each recommendation is supported by a level of evidence category.

NCCN Categories of Evidence and Consensus

Category 1: Based on high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2A: Based on lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2B: Based on lower-level evidence, there is NCCN consensus that the intervention is appropriate.

Category 3: Based any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

Policy for Regimen Prior Authorization

A regimen prior authorization allows submission of a single prior authorization request for all oncology drugs or biologics within an NCCN template that require prior authorization.

This policy provides coverage of a regimen review when *all* of the following criteria are met:

a. Regimen prior authorization reviews, based on NCCN templates, are initiated through the provider portal: https://provider.carefirst.com/providers/home.page
b. If the prior authorization request is submitted via phone or fax, each drug or biologic will need to be submitted and reviewed as a separate prior authorization request for review with drug-specific criteria.
c. 2. The prior authorization review is requested for an oncology drug or biologic that requires prior authorization on the medical benefit.
d. The indication is for a cancer that is eligible for regimen review. Currently, the cancer types in scope for regimen review include breast, lung, colon and rectal cancer.
e. The member is eligible for regimen review.

In addition, the following criteria must be met for approval:

a. The requested regimen for the drug(s) or biologic(s) and indication is consistent with an NCCN recommendation with a level of evidence category of 1 or 2A.
b. The NCCN template must be accepted by the provider without modification.

Authorizations may be granted for 12 months.
Further review may be indicated where the above criteria are not met.

Continuation of Therapy

To submit a request for continuation of therapy, a new regimen prior authorization review must be requested. Upon template selection, the template must be modified to include the appropriate therapies being used for maintenance treatment. The regimen request will be submitted for further review.

Dosage and Administration

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

REFERENCES:

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1. Kadcyla [package insert]. South San Francisco, CA: Genentech, Inc.; February 2022.
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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.

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POLICY Document for KANUMA (sebelipase alfa)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, lower cost site of care and overall, clinically appropriate use. This document provides specific information to each of the three sections of the overall policy.

Section 1: Site of Care

- Policy information specific to site of care (outpatient, hospital outpatient, home infusion)

Section 2: Clinical Criteria

- Policy information specific to the clinical appropriateness for the medication

Section 1: Site of Care

CareFirst Site of Care Criteria
Administration of Intravenous Kanuma

POLICY

I. CRITERIA FOR APPROVAL FOR ADMINISTRATION IN OUTPATIENT HOSPITAL SETTING

This policy provides coverage for administration of Kanuma in an outpatient hospital setting for up to 50 days when a member is new to therapy or is reinitiating therapy after not being on therapy for at least 6 months.

This policy provides coverage for administration of Kanuma in an outpatient hospital setting for a longer course of treatment when ANY of the following criteria are met:

A. The member has experienced an adverse reaction to the drug that did not respond to conventional interventions (eg, acetaminophen, steroids, diphenhydramine, fluids, other pre-medications or slowing of infusion rate) or a severe adverse event (anaphylaxis, anaphylactoid reactions, myocardial infarction, thromboembolism, or seizures) during or immediately after an infusion.
B. The member has developed laboratory confirmed sebelipase alfa antibodies which increases the risk for infusion related reactions
C. The member is medically unstable (eg respiratory, cardiovascular, or renal conditions).
D. The member has severe venous access issues that require the use of special interventions only available in the outpatient hospital setting.
E. The member has significant behavioral issues and/or physical or cognitive impairment that would impact the safety of the infusion therapy AND the patient does not have access to a caregiver.
F. The member is less than 14 years of age.

For situations where administration of Kanuma does not meet the criteria for outpatient hospital infusion, coverage for Kanuma is provided when administered in alternative sites such as; physician office, home infusion or ambulatory care.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the site of care prior authorization review (where applicable):

A. Medical records supporting the member has experienced an adverse reaction that did not respond to conventional interventions or a severe adverse event during or immediately after an infusion
B. Medical records supporting the member has developed sebelipase alfa antibodies
C. Medical records supporting the member is medically unstable
D. Medical records supporting the member has severe venous access issues that requires specialized interventions only available in the outpatient hospital setting
E. Medical records supporting the member has behavioral issues and/or physical or cognitive impairment and no access to a caregiver

Section 2: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

KANUMA (sebelipase 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
Kanuma is indicated for the treatment of patients with a diagnosis of Lysosomal Acid Lipase (LAL) 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: lysosomal acid lipase enzyme assay or genetic testing results supporting diagnosis.
B. Continuation requests: lab values or chart notes documenting a positive response to therapy (e.g., improvement, stabilization, or slowing of disease progression for weight-for-age z-score if exhibiting growth failure, LDL, HDL, triglycerides, or ALT).

III. CRITERIA FOR INITIAL APPROVAL

Lysosomal acid lipase (LAL) deficiency
Authorization of 12 months may be granted for treatment of LAL deficiency when both of the following criteria are met:
A. Diagnosis of LAL deficiency was confirmed by enzyme assay demonstrating a deficiency of lysosomal acid lipase enzyme activity or by genetic testing; AND
B. Member has alanine aminotransferase level (ALT) ≥ 1.5 times the upper limit of normal (based on the age- and gender-specific normal ranges) on two consecutive ALT measurements obtained at least one week apart.

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., improvement, stabilization, or slowing of disease progression for weight-for-age z-score if exhibiting growth failure, low-density lipoprotein [LDL], high-density lipoprotein [HDL], triglycerides, or alanine aminotransferase [ALT]).

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POLICY Document for KEYTRUDA (pembrolizumab)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, and overall, clinically appropriate use. This document provides specific information to both sections of the overall policy.

Section 1: Site of Care
- Policy information specific to site of care (outpatient, hospital outpatient, home infusion)

Section 2: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 3: Oncology Clinical Policy
- Policy information specific to regimen review per NCCN Guidelines.

Section 1: Site of Care

CareFirst Site of Care Criteria
Administration of Intravenous Checkpoint Inhibitors
Bavencio, Imfinzi, Jemperli, Keytruda, Libtayo, Opdivo, Opdualag, Tecentriq, Yervoy and Zynyz

POLICY

I. CRITERIA FOR APPROVAL FOR ADMINISTRATION IN OUTPATIENT HOSPITAL SETTING

This policy provides coverage for administration of a checkpoint inhibitor in an outpatient hospital setting for the initial 6 months approval and up to 45 days for renewal of therapy.

This policy provides coverage for administration of a checkpoint inhibitor in an outpatient hospital setting for a longer course of treatment when ANY of the following criteria are met:

A. The member has experienced an adverse reaction that did not respond to conventional interventions (eg, acetaminophen, steroids, diphenhydramine, fluids, other pre-medications or slowing of infusion rate) or a severe adverse event (anaphylaxis, anaphylactoid reactions, myocardial infarction, thromboembolism, or seizures) during or immediately after an infusion or has experienced severe toxicity requiring continuous monitoring (e.g. Grade 2-4 bullous dermatitis, transaminitis, pneumonitis, Stevens-Johnson syndrome, acute pancreatitis, primary adrenal insufficiency aseptic meningitis, encephalitis, transverse myelitis, myocarditis, pericarditis, arrhythmias, impaired ventricular function, conduction abnormalities).
B. The member is medically unstable (eg respiratory, cardiovascular, or renal conditions).
C. The member has severe venous access issues that require the use of a special interventions only available in the outpatient hospital setting.
D. The member has significant behavioral issues and/or physical or cognitive impairment that would impact the safety of the infusion therapy AND the patient does not have access to a caregiver.
E. The member is receiving provider administered combination chemotherapy.
F. The member is less than 14 years of age.

For situations where administration of a checkpoint inhibitor does not meet the criteria for outpatient hospital infusion, coverage for a checkpoint inhibitor is provided when administered in alternative sites such as physician office, home infusion or ambulatory care.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the site of care prior authorization review (where applicable):

A. Medical records supporting the member has experienced an adverse reaction that did not respond to conventional interventions or a severe adverse event during or immediately after an infusion or a severe toxicity requiring continuous monitoring
B. Medical records supporting the member is medically unstable
C. Medical records supporting the member has severe venous access issues that require specialized interventions only available in the outpatient hospital setting
D. Medical records supporting the member has behavioral issues and/or physical or cognitive impairment and no access to a caregiver
E. Medical records supporting the member is receiving provider administered combination therapy.

Section 2: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

KEYTRUDA (pembrolizumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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. Melanoma
      i. Keytruda (pembrolizumab) is indicated for the treatment of patients with unresectable or metastatic melanoma.
      ii. Keytruda is indicated for the adjuvant treatment of adult and pediatric (12 years and older) patients with Stage IIB, IIC, or III melanoma following complete resection.

   2. Non-Small Cell Lung Cancer
      i. Keytruda, in combination with pemetrexed and platinum chemotherapy, is indicated for the first-line treatment of patients with metastatic nonsquamous non-small cell lung cancer (NSCLC), with no EGFR or ALK genomic tumor aberrations.
      ii. Keytruda, in combination with carboplatin and either paclitaxel or paclitaxel protein-bound, is indicated for the first-line treatment of patients with metastatic squamous NSCLC.
      iii. Keytruda, as a single agent, is indicated for the first-line treatment of patients with NSCLC expressing PD-L1 [Tumor Proportion Score (TPS) ≥1%] as determined by an FDA-approved test, with no EGFR or ALK genomic tumor aberrations, and is:
         a. stage III where patients are not candidates for surgical resection or definitive chemoradiation, or
         b. metastatic.
      iv. Keytruda, as a single agent, is indicated for the treatment of patients with metastatic NSCLC whose tumors express PD-L1 (TPS ≥1%) as determined by an FDA approved test, with disease progression on or after platinum-containing chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving Keytruda.
      v. Keytruda, as a single agent, is indicated for adjuvant treatment following resection and platinum-based chemotherapy for adult patients with stage 1B (T2a ≥ 4cm), II, or IIIA NSCLC

3. Head and Neck Squamous Cell Cancer
   i. Keytruda, in combination with platinum and fluorouracil (FU), is indicated for the first-line treatment of patients with metastatic or with unresectable, recurrent head and neck squamous cell carcinoma (HNSCC).
   ii. Keytruda, as a single agent, is indicated for the first line treatment of patients with metastatic or with unresectable, recurrent HNSCC whose tumors express PD-L1 [Combined Positive Score (CPS) ≥1] as determined by an FDA-approved test.
   iii. Keytruda, as a single agent, is indicated for the treatment of patients with recurrent or metastatic HNSCC with disease progression on or after platinum-containing chemotherapy.

4. Classical Hodgkin Lymphoma
   i. Keytruda is indicated for the treatment of adult patients with relapsed or refractory classical Hodgkin lymphoma (cHL).
   ii. Keytruda is indicated for the treatment of pediatric patients with refractory cHL, or cHL that has relapsed after 2 or more prior lines of therapy.

5. Primary Mediastinal Large B-cell Lymphoma
   Keytruda is indicated for the treatment of adult and pediatric patients with refractory primary mediastinal large B-cell lymphoma (PMBCL), or who have relapsed after 2 or more prior lines of therapy.

   Limitations of Use: Keytruda is not recommended for treatment of patients with PMBCL who require urgent cytoreductive therapy.

6. Urothelial Carcinoma
   i. Keytruda is indicated for the treatment of patients with locally advanced or metastatic urothelial carcinoma:
      a. who are not eligible for any platinum-containing chemotherapy, or
      b. who have disease progression during or following platinum-containing chemotherapy or within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy.
   ii. Keytruda is indicated for the treatment of patients with Bacillus Calmette-Guerin (BCG)-unresponsive, high-risk, non-muscle invasive bladder cancer (NMIBC) with carcinoma in situ (CIS) with or without papillary tumors who are ineligible for or have elected not to undergo cystectomy.
   iii. Keytruda, in combination with enfortumab vedotin, is indicated for the treatment of adult patients with
   locally advanced or metastatic urothelial carcinoma who are not eligible for cisplatin-containing chemotherapy

7. Microsatellite Instability-High Cancer or Mismatch Repair Deficient Cancer
   Keytruda is indicated for the treatment of adult and pediatric patients with unresectable or metastatic, microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) solid tumors, as determined by an FDA-approved test, that have progressed following prior treatment and who have no satisfactory alternative treatment options.

   Limitations of Use: The safety and effectiveness of Keytruda in pediatric patients with MSI-H central nervous system cancers have not been established.

8. Microsatellite Instability-High or Mismatch Repair Deficient Colorectal Cancer (CRC)
   Keytruda is indicated for the treatment of patients with unresectable or metastatic MSI-H or dMMR colorectal cancer (CRC) as determined by an FDA-approved test.

9. Gastric Cancer
   Keytruda, in combination with trastuzumab, fluoropyrimidine- and platinum-containing chemotherapy, is indicated for the first-line treatment of patients with locally advanced unresectable or metastatic HER2-

positive gastric or gastroesophageal junction (GEJ) adenocarcinoma

10. Esophageal Cancer
    Keytruda is indicated for the treatment of patients with locally advanced or metastatic esophageal or gastroesophageal junction (GEJ) (tumors with epicenter 1 to 5 centimeters above the GEJ) carcinoma that is not amenable to surgical resection or definitive chemoradiation either:
    i. In combination with platinum- and fluoropyrimidine-based chemotherapy, or
    ii. As a single agent after one or more prior lines of systemic therapy for patients with tumors of squamous cell histology that express PD-L1 (CPS ≥ 10) as determined by an FDA-approved test

11. Cervical Cancer
    i. Keytruda in combination with chemotherapy, with or without bevacizumab, is indicated for the treatment of patients with persistent, recurrent, or metastatic cervical cancer whose tumors express PD-L1 (CPS ≥1) as determined by an FDA-approved test.
    ii. Keytruda, as a single agent, is indicated for the treatment of patients with recurrent or metastatic cervical cancer with disease progression on or after chemotherapy whose tumor express PD-L1 (CPS ≥ 1) as determined by an FDA-approved test.

12. Hepatocellular Carcinoma
    Keytruda is indicated for the treatment of patients with hepatocellular carcinoma (HCC) who have been previously treated with sorafenib.

13. Merkel Cell Carcinoma
    Keytruda is indicated for the treatment of adult and pediatric patients with recurrent locally advanced or metastatic Merkel cell carcinoma (MCC).

14. Renal Cell Carcinoma
    i. Keytruda, in combination with axitinib, is indicated for the first-line treatment of patients with advanced renal cell carcinoma (RCC).
    ii. Keytruda, in combination with lenvatinib, is indicated for the first-line treatment of adult patients with advanced RCC
    iii. Keytruda is indicated for the adjuvant treatment of patients with RCC at intermediate-high or high risk of recurrence following nephrectomy, or following nephrectomy and resection of metastatic lesions

15. Endometrial Carcinoma
    i. Keytruda, in combination with lenvatinib, is indicated for the treatment of patients with advanced endometrial carcinoma that is mismatch repair proficient (pMMR) as determined by an FDA-approved test or not MSI-H, who have disease progression following prior systemic therapy in any setting and are not candidates for curative surgery or radiation.
    ii. Keytruda, as a single agent, is indicated for the treatment of patients with advanced endometrial carcinoma that is MSI-H or dMMR, as determined by an FDA-approved test, who have disease progression following prior systemic therapy in any setting and are not candidates for curative surgery or radiation.

16. Tumor Mutational Burden-High Cancer
    Keytruda is indicated for the treatment of adult and pediatric patients with unresectable or metastatic tumor mutational burden-high (TMB-H) [≥10 mutations/megabase (mut/Mb)] solid tumors, as determined by an FDA-approved test, that have progressed following prior treatment and who have no satisfactory alternative treatment options.

    Limitations of use: The safety and effectiveness of Keytruda in pediatric patients with TMB-H central nervous system cancers have not been established.

17. Cutaneous Squamous Cell Carcinoma
    Keytruda is indicated for the treatment of patients with recurrent or metastatic cutaneous squamous cell carcinoma (cSCC) or locally advanced cSCC that is not curable by surgery or radiation.

18. Triple-Negative Breast Cancer
    i. Keytruda, in combination with chemotherapy, is indicated for the treatment of patients with locally recurrent unresectable or metastatic triple-negative breast cancer (TNBC) whose tumors express PD-L1 [Combined Positive Score (CPS) ≥10] as determined by an FDA approved test.
    ii. Keytruda is indicated for the treatment of patients with high-risk early-stage triple-negative breast cancer (TNBC) in combination with chemotherapy as neoadjuvant treatment, and then continued as a single agent as adjuvant treatment after surgery.

19. Adult Classical Hodgkin Lymphoma and Adult Primary Mediastinal Large B-Cell Lymphoma: Additional Dosing Regimen of 400mg Every 6 Weeks
    Keytruda is indicated for use at an additional recommended dosage of 400mg every 6 weeks for classical Hodgkin lymphoma and primary mediastinal large B-cell lymphoma in adults.

B. Compendial Uses
1. Cutaneous melanoma
2. Non-small cell lung cancer
3. Head and neck squamous cell cancer
4. Classical Hodgkin Lymphoma
5. Urothelial carcinoma
    i. Bladder cancer
    ii. Primary carcinoma of the urethra
    iii. Upper genitourinary tract tumors
    iv. Urothelial carcinoma of the prostate
6. Anaplastic thyroid carcinoma
7. Follicular, hürthle cell, or papillary thyroid carcinoma
8. Medullary thyroid carcinoma
9. Colorectal cancer
10. Small bowel adenocarcinoma
11. Gastric cancer and esophagogastric junction cancer
12. Esophageal cancer
13. Cervical cancer
14. Epithelial ovarian cancer/fallopian tube cancer/primary peritoneal cancer
15. Uveal melanoma
16. Testicular cancer
17. Endometrial carcinoma
18. Anal carcinoma
19. Central Nervous System (CNS) brain metastases
20. Primary mediastinal large B-cell lymphoma
21. Pancreatic adenocarcinoma
22. Hepatobiliary cancers
23. Vulvar cancer
24. Renal cell carcinoma
25. Thymic carcinoma
26. Primary Cutaneous Lymphomas
    i. Mycosis Fungoides/Sezary syndrome
    ii. Anaplastic Large Cell Lymphoma (ALCL)
27. Extranodal NK/T-cell lymphoma

28. Gestational trophoblastic neoplasia
29. Neuroendocrine and Adrenal Tumors
    i. Well Differentiated Grade 3 Tumors
    ii. Adrenal Gland Tumors
    iii. Poorly Differentiated/Large or Small Cell Tumors
    iv. Adrenocortical carcinoma
30. Soft tissue sarcomas
    i. alveolar soft part sarcoma (ASPS)
    ii. cutaneous angiosarcoma
    iii. extremity/body wall sarcoma
    iv. head/neck sarcoma
    v. retroperitoneal/intra-abdominal sarcoma
    vi. rhabdomyosarcoma
31. Occult primary cancer
32. Prostate cancer
33. Bone Cancer
    i. Chondrosarcoma
    ii. Chordoma
    iii. Ewing Sarcoma
    iv. Osteosarcoma
34. Breast Cancer
35. Salivary Gland Tumors
36. Merkel Cell Carcinoma
37. Penile Cancer
38. Uterine Sarcoma
39. Small cell lung cancer
40. Ampullary Adenocarcinoma
41. Pediatric Diffuse High-Grade Gliomas
42. Cutaneous squamous cell carcinoma
43. Nasopharyngeal Cancer
44. Kaposi Sarcoma

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 programmed death ligand 1 (PD-L1) tumor expression, where applicable.
B. Documentation of laboratory report confirming MSI-H or mismatch repair deficient (dMMR) tumor status, where applicable.
C. Documentation of laboratory report confirming high tumor mutational burden (≥10 mutations/megabase [mut/Mb]), where applicable.
D. Documentation of laboratory report confirming that the cancer cells are negative for the following receptors, where applicable:
    1. human epidermal growth factor receptor 2 (HER-2)
    2. estrogen
    3. progesterone
E. Documentation of the presence of EGFR exon 19 deletions or L858R mutations or ALK rearrangements, where applicable.

III. EXCLUSIONS

Coverage will not be provided for members with any of the following exclusions:
A. Pediatric members with MSI-H central nervous system cancers.
B. Pediatric members with TMB-H central nervous system cancers.
C. Members who have experienced disease progression while on programmed death receptor-1 (PD-1) or PD-L1 inhibitor therapy (other than when used as second-line or subsequent therapy for metastatic or unresectable melanoma in combination with ipilimumab following progression on single agent anti-PD-1 immunotherapy).

IV. CRITERIA FOR INITIAL APPROVAL

A. Cutaneous Melanoma

Authorization of 6 months may be granted for treatment of cutaneous melanoma in any of the following settings:
1. For unresectable, recurrent, or metastatic disease as a single agent.
2. As subsequent therapy for disease progression of metastatic or unresectable tumors, as a single agent or in combination with ipilimumab.
3. As adjuvant treatment following complete lymph node resection or complete resection of stage IIB, IIC, III, or metastatic disease as a single agent.

B. Non-small Cell Lung Cancer (NSCLC)

1. Authorization of 6 months may be granted for treatment of recurrent, advanced, or metastatic NSCLC when there are no EGFR exon 19 deletions or L858R mutations or ALK rearrangements (unless testing is not feasible due to insufficient tissue) and any of the following criteria are met:
   i. The requested medication will be used as a first-line therapy for PDL1 positive disease.
   ii. The requested medication will be used as single agent maintenance therapy.
   iii. The requested medication will be used in combination with pemetrexed and either carboplatin or cisplatin for nonsquamous cell histology.
   iv. The requested medication will be used in combination with carboplatin and either paclitaxel or albumin-bound paclitaxel for squamous cell histology.
2. Authorization of 6 months may be granted as a single agent for adjuvant treatment following resection and platinum-based chemotherapy for stage IB (T2a ≥4 cm), II, or IIIA NSCLC.
3. Authorization of 6 months may be granted for single agent subsequent treatment of PDL1 positive recurrent, advanced, or metastatic NSCLC.

C. Head and Neck Squamous Cell Cancer

Authorization of 6 months may be granted for treatment of members with very advanced head and neck squamous cell carcinoma with mixed subtypes (HNSCC) and nasopharyngeal cancer when any of the following criteria is met:
i. Keytruda will be used as a single agent for first-line treatment in members whose tumors express PD-L1 (CPS ≥1), are microsatellite instability-high (MSI-H), mismatch repair deficient (dMMR) or tumor mutational burden high (TMB-H [≥ 10 mut/Mb].
ii. Keytruda will be used as a single agent for subsequent therapy (regardless of PD-L1 status).
iii. Keytruda will be used in combination with chemotherapy (regardless of PD-L1 status).

D. Classical Hodgkin Lymphoma

Authorization of 6 months may be granted as a single agent or in combination with GVD (gemcitabine, vinorelbine, liposomal doxorubicin) for treatment of relapsed, refractory or progressive classical Hodgkin lymphoma.

E. Urothelial Carcinoma

1. Authorization of 6 months may be granted as a single agent for treatment of urothelial carcinoma when used in any of the following subtypes:
   i. Urothelial carcinoma of the bladder in any of the following settings:
      a. First line therapy for locally advanced or metastatic disease in members who are not eligible for any platinum containing chemotherapy.
      b. Subsequent therapy.
      c. Subsequent therapy for the treatment of members with high risk, non-muscle invasive bladder cancer (NMIBC) with carcinoma in situ (CIS) when disease is Bacillus Calmette Guerin (BCG) unresponsive, and member will not undergo cystectomy.
   ii. Primary carcinoma of the urethra with locally advanced, recurrent or metastatic disease in members who are not eligible for any platinum-containing chemotherapy.
   iii. Urothelial carcinoma of the upper genitourinary tract or urothelial carcinoma of the prostate with metastatic disease in members who are not eligible for any platinum-containing chemotherapy.
2. Authorization of 6 months may be granted for the treatment of locally advanced or metastatic urothelial carcinoma in combination with enfortumab vedotin-ejfv for members who are ineligible for cisplatin-containing chemotherapy.

F. Solid Tumors
Authorization of 6 months may be granted as a single agent for treatment of solid tumors in members with unresectable or metastatic disease that has progressed following prior treatment and who have no satisfactory alternative treatment options when either of the following criteria is met:
1. Keytruda will be used for microsatellite instability-high or mismatch repair deficient solid tumors.
2. Keytruda will be used for tumor mutational burden-high (≥10 mutations/megabase [mut/Mb]) solid tumors.

G. Anaplastic Thyroid Carcinoma
Authorization of 6 months may be granted as a single agent for treatment of metastatic anaplastic thyroid carcinoma for tumor mutational burden-high (≥10 mutations/megabase [mut/Mb]) tumors.

H. Follicular, Hürthle Cell, or Papillary Thyroid Carcinoma
Authorization of 6 months may be granted for treatment of unresectable or metastatic follicular, hürthle cell, or papillary thyroid carcinoma for tumor mutational burden-high (≥10 mutations/megabase [mut/Mb]) tumors not amenable to radioactive iodine therapy.

I. Medullary Thyroid Carcinoma
Authorization of 6 months may be granted for treatment of unresectable, recurrent, or metastatic medullary thyroid carcinoma for tumor mutational burden-high (≥10 mutations/megabase [mut/Mb]) tumors.

J. Colorectal Cancer
Authorization of 6 months may be granted as a single agent for the treatment of inoperable, advanced, or metastatic colorectal cancer, including appendiceal carcinoma, for microsatellite instability-high or mismatch repair deficient tumors.

K. Small Bowel Adenocarcinoma
Authorization of 6 months may be granted as a single agent for treatment of advanced or metastatic small bowel adenocarcinoma for microsatellite instability-high or mismatch repair deficient tumors.

L. Merkel Cell Carcinoma
Authorization of 6 months may be granted for treatment of Merkel cell carcinoma in members with recurrent or metastatic disease.

M. Gastric Cancer
Authorization of 6 months may be granted for treatment of gastric cancer in members who are not surgical

candidates or have unresectable locally advanced, recurrent, or metastatic disease when any of the following criteria is met:

1. Keytruda will be used as subsequent therapy as a single agent for a tumor with microsatellite instability-high or deficient mismatch repair or tumor mutational burden (TMB) high (≥10 mutations/megabase (mut/Mb)).
2. Keytruda will be used in combination with trastuzumab, platinum and fluoropyrimidine-based chemotherapy in HER2 overexpression positive adenocarcinoma.

N. Esophageal Cancer and Esophagogastric Junction Cancer

Authorization of 6 months may be granted for treatment of esophageal cancer (including esophagogastric junction (EGJ) cancer) in members who are not surgical candidates or have unresectable locally advanced, recurrent, or metastatic disease when any of the following conditions are met:

1. Keytruda will be used as subsequent therapy as a single agent for a tumor with microsatellite instability-high or deficient mismatch repair or tumor mutational burden (TMB) high (≥10 mutations/megabase (mut/Mb)).
2. Keytruda will be used as subsequent therapy with PD-L1 tumor expression by CPS ≥ 10 for squamous cell carcinoma.
3. Keytruda will be used in combination with platinum and fluoropyrimidine-based chemotherapy for squamous cell carcinoma or HER2 overexpression negative adenocarcinoma.
4. Keytruda will be used in combination with trastuzumab, platinum and fluoropyrimidine-based chemotherapy for HER2 overexpression positive members.

O. Cervical Cancer

Authorization of 6 months may be granted for the treatment of cervical cancer when any of the following criteria are met:

1. Persistent, recurrent or metastatic disease in combination with chemotherapy in members whose tumors express PD-L1 (CPS ≥1).
2. Persistent, recurrent or metastatic disease as single agent subsequent therapy in members whose tumors express PD-L1 (CPS ≥1) or are microsatellite instability-high or mismatch repair deficient.
3. Recurrent or metastatic disease and the member has experienced disease progression on or after chemotherapy for tumors that express PD-L1 (CPS ≥ 1), as a single agent.

P. Epithelial Ovarian Cancer, Fallopian Tube Cancer, Primary Peritoneal Cancer

Authorization of 6 months may be granted as a single agent for treatment of epithelial ovarian cancer, fallopian tube cancer, primary peritoneal cancer, carcinosarcoma (malignant mixed Mullerian tumors), clear cell carcinoma of the ovary, mucinous carcinoma of the ovary, grade 1 endometrioid carcinoma, low-grade serous carcinoma for recurrent or persistent microsatellite instability-high or mismatch repair deficient tumors or tumor mutational burden-high (TMB-H) (tumors ≥10 mutations/megabase [mut/Mb]).

Q. Uveal Melanoma

Authorization of 6 months may be granted as a single agent for treatment of uveal melanoma for distant metastatic disease.

R. Testicular Cancer

Authorization of 6 months may be granted as a single agent for third-line therapy for treatment of testicular cancer in members with microsatellite instability-high or mismatch repair deficient or tumor mutational burden-high (TMB-H) (≥10 mutations/megabase [mut/Mb]) tumors.

S. Endometrial Carcinoma

1. Authorization of 6 months may be granted in combination with lenvatinib for treatment of advanced, metastatic or recurrent endometrial carcinoma when either of the following criteria are met:
   i. The disease is mismatch repair proficient (pMMR)

ii. The disease is mismatch repair deficient (dMMR) and has progressed following prior platinum-based chemotherapy

2. Authorization of 6 months may be granted as a single agent for treatment of endometrial carcinoma in members with recurrent unresectable or metastatic microsatellite instability-high (MSI-H), mismatch repair deficient (dMMR), or tumor mutational burden high (TMB-H) [≥ 10 mut/Mb] tumors
3. Authorization of 6 months may be granted for treatment of endometrial carcinoma in combination with carboplatin and paclitaxel in members with stage III-IV or recurrent disease

T. Anal Carcinoma

Authorization of 6 months may be granted as a single agent subsequent treatment of metastatic anal carcinoma.

U. CNS Brain Metastases

Authorization of 6 months may be granted as a single agent for treatment of CNS brain metastases in members with melanoma or PD-L1 positive non-small cell lung cancer.

V. Primary Mediastinal Large B-Cell Lymphoma

Authorization of 6 months may be granted as a single agent or in combination with brentuximab vedotin for treatment of primary mediastinal large B-cell lymphoma in members with relapsed or refractory disease.

W. Pancreatic Adenocarcinoma

Authorization of 6 months may be granted as a single agent for treatment of pancreatic adenocarcinoma in members with microsatellite instability-high (MSI-H), mismatch repair deficient (dMMR), or tumor mutational burden high (TMB-H) [≥ 10 mut/Mb] tumors in any of the following settings:

1. Keytruda will be used as subsequent therapy for locally advanced or metastatic disease and disease progression.
2. For local recurrence in the pancreatic operative bed after resection or recurrent metastatic disease.
3. Keytruda will be used as first-line or maintenance therapy for metastatic disease.

X. Hepatobiliary Cancers

Authorization of 6 months may be granted as a single agent for unresectable or metastatic hepatobiliary cancers, including intrahepatic and extrahepatic cholangiocarcinoma and gallbladder cancer for disease that is microsatellite instability-high or mismatch repair deficient.

Y. Hepatocellular Carcinoma

Authorization of 6 months may be granted for treatment of members with hepatocellular carcinoma who have been previously treated with sorafenib.

Z. Vulvar Cancer

Authorization of 6 months may be granted as a single agent for subsequent treatment of advanced, recurrent or metastatic disease in members with squamous cell vulvar cancer when either of the following criteria is met:

1. Member has microsatellite instability-high (MSI-H), mismatch repair deficient (dMMR) or tumor mutational burden high (TMB-H [≥ 10 mut/Mb] tumors.
2. Member has experienced disease progression on or after chemotherapy and whose tumor expresses PD-L1 (CPS ≥ 1).

AA. Renal Cell Carcinoma

Authorization of 6 months may be granted for treatment of renal cell carcinoma, when any of the following criteria are met:

1. Keytruda will be used as first-line treatment in combination with axitinib or lenvatinib for advanced, relapsed or stage IV disease.

2. Keytruda will be used as subsequent therapy in combination with axitinib or lenvatinib for relapsed or stage IV disease with clear cell histology.
3. Keytruda will be used as a single agent for relapsed or stage IV disease with non-clear cell histology.
4. Keytruda will be used as a single agent for the adjuvant treatment of members with RCC at intermediate-high or high risk of recurrence following nephrectomy or following nephrectomy and resection of metastatic lesions.

BB. Thymic Carcinoma

Authorization of 6 months may be granted as a single agent for treatment of thymic carcinoma for unresectable, locally advanced, or metastatic disease, or as postoperative therapy for residual tumor in members who cannot tolerate first-line combination regimens.

CC. Primary Cutaneous Lymphomas

Authorization of 6 months may be granted for treatment of primary cutaneous lymphomas when either of the following is met:

1. Member has a diagnosis of mycosis fungoides/Sezary syndrome.
2. Member has a diagnosis of relapsed or refractory anaplastic large cell lymphoma (ALCL) and the requested medication will be used as a single agent.

DD. Extranodal NK/T-cell lymphoma

Authorization of 6 months may be granted for treatment of extranodal NK/T-cell lymphoma, in members with relapsed or refractory disease.

EE. Gestational Trophoblastic Neoplasia

Authorization of 6 months may be granted as a single agent for treatment of gestational trophoblastic neoplasia for multi-agent chemotherapy-resistant disease when either of the following criteria is met:

1. Member has recurrent or progressive intermediate trophoblastic tumor (placental site trophoblastic tumor or epithelioid trophoblastic tumor) following treatment with a platinum/etoposide-containing regimen.
2. Member has high-risk disease.

FF. Neuroendocrine and Adrenal Tumors

Authorization of 6 months may be granted for treatment of unresectable or metastatic adrenocortical carcinoma.

GG. Cutaneous Squamous Cell Carcinoma

Authorization of 6 months may be granted as a single agent for treatment of cutaneous squamous cell carcinoma that is not curable by surgery or radiation.

HH. Soft Tissue Sarcoma

Authorization of 6 months may be granted for treatment of the following types of soft tissue sarcoma when either of the following criteria are met:

1. The requested medication will be used as a single agent or in combination with axitinib (Inlyta) for the treatment of alveolar soft part sarcoma (ASPS).
2. The requested medication will be used as a single agent for the treatment of cutaneous angiosarcoma.
3. The requested medication will be used as a single agent for the subsequent treatment of extremity/body wall sarcoma, head/neck sarcoma, retroperitoneal/intra-abdominal sarcoma, and rhabdomyosarcoma.

II. Occult Primary Cancer

Authorization of 6 months may be granted as a single agent for treatment of occult primary cancer in members with microsatellite instability-high or mismatch repair deficient tumors or tumor mutational burden-high (TMB-H) (≥10 mutations/megabase (mut/Mb) tumors).

JJ. Breast Cancer

1. Authorization of 6 months may be granted for treatment of patients with no response to preoperative systemic therapy or for locally recurrent unresectable or metastatic triple-negative breast cancer (TNBC) when all of the following criteria are met:
   i. The diagnosis of triple-negative breast cancer is confirmed by the cancer cells testing negative for ALL of the following receptors:
      a. Human epidermal growth factor receptor 2 (HER-2)
      b. Estrogen
      c. Progesterone
   ii. Tumor must express PD-L1.
   iii. The requested medication will be used in combination with chemotherapy.

2. Authorization of 6 months may be granted for treatment of high-risk early-stage triple-negative breast cancer (TNBC) when all of the following criteria are met:
   i. The diagnosis of triple-negative breast cancer is confirmed by the cancer cells testing negative for ALL of the following receptors:
      a. Human epidermal growth factor receptor 2 (HER-2)
      b. Estrogen
      c. Progesterone
   ii. The requested medication will be used as either:
      a. Neoadjuvant treatment in combination with chemotherapy; or
      b. Continued adjuvant treatment after surgery, as a single agent.

KK. Prostate Cancer

Authorization of 6 months may be granted as single agent subsequent therapy for treatment of castration-resistant distant metastatic prostate cancer in members with microsatellite instability-high, mismatch repair deficient, or tumor mutational burden (TMB) ≥10 mutations/megabase tumors.

LL. Small Cell Lung Cancer

Authorization of 6 months may be granted as a single agent for subsequent therapy of relapsed or progressive disease.

MM. Pediatric Diffuse High-Grade Gliomas

Authorization of 6 months may be granted as adjuvant treatment for hypermutant tumor pediatric diffuse high-grade glioma or for recurrent or progressive disease.

NN. Ampullary Adenocarcinoma

Authorization of 6 months may be granted as a single agent for microsatellite instability-high (MSI-H), mismatch repair deficient (dMMR), or tumor mutational burden-high (TMB-H ≥ 10 mut/Mb) ampullary adenocarcinoma.

OO. Kaposi Sarcoma

Authorization of 6 months may be granted as a single agent for subsequent treatment of relapsed/refractory endemic or classic Kaposi Sarcoma.

V. CONTINUATION OF THERAPY

A. Adjuvant treatment of melanoma, adjuvant high-risk early-stage TNBC, RCC, or NSCLC

Authorization of 6 months may be granted (up to 12 months total) for continued treatment in members requesting reauthorization for adjuvant treatment of cutaneous melanoma, high-risk early-stage TNBC, RCC or NSCLC who have not experienced disease recurrence or an unacceptable toxicity.

B. NSCLC, HNSCC, cHL, PMBCL, MSI-H or dMMR Cancers, Gastric Cancer, Esophageal Cancer, Cervical Cancer, HCC, MCC, RCC, Endometrial carcinoma, cSCC, locally recurrent unresectable or metastatic TNBC, TMB-H Cancer

Authorization of 6 months may be granted (up to 24 months of continuous use) for continued treatment in members requesting reauthorization for NSCLC, HNSCC, cHL, PMBCL, MSI-H or dMMR cancers, gastric cancer, esophageal cancer, cervical cancer, HCC, MCC, RCC, endometrial carcinoma, cSCC, locally recurrent unresectable or metastatic TNBC, and TMB-H cancers who have not experienced disease progression or unacceptable toxicity.

C. Urothelial Carcinoma

Authorization of 6 months may be granted (up to 24 months of continuous use) for continued treatment in members requesting reauthorization for urothelial carcinoma when both of the following criteria are met:

1. Member has not experienced disease progression or unacceptable toxicity.
2. For high-risk BCG-unresponsive non-muscle invasive bladder cancer only: disease is not persistent or recurrent.

D. All other indications

Authorization of 6 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section IV who have not experienced disease progression or an unacceptable toxicity.

Section 3: Oncology Clinical Policy

Oncology Clinical Policy

Program Description

The National Comprehensive Care Network® (NCCN®) is an alliance of leading cancer centers devoted to patient care, research and education dedicated to improving the quality, effectiveness and efficiency of cancer care so patients can live better lives.[1] It is comprised of oncology experts who convene regularly to establish the best treatments for patients. NCCN develops various resources for use by stakeholders in the health care delivery system. These resources include, but are not limited to, the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®), the NCCN Drugs & Biologics Compendium (NCCN Compendium®) and the NCCN Chemotherapy Order Templates (NCCN Templates®).

NCCN templates are based on NCCN Clinical Practice Guidelines and NCCN Compendium. The NCCN Compendium lists the appropriate drugs and biologics for specific cancers using U.S. Food and Drug Administration (FDA)-approved disease indications and specific NCCN panel recommendations. Each recommendation is supported by a level of evidence category.

NCCN Categories of Evidence and Consensus[2]

a. Category 1: Based on high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
b. Category 2A: Based on lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
c. Category 2B: Based on lower-level evidence, there is NCCN consensus that the intervention is appropriate.
d. Category 3: Based any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

Policy for Regimen Prior Authorization

A regimen prior authorization allows submission of a single prior authorization request for all oncology drugs or

biologics within an NCCN template that require prior authorization.

This policy provides coverage of a regimen review when *all* of the following criteria are met:

a. Regimen prior authorization reviews, based on NCCN templates, are initiated through the provider portal: https://provider.carefirst.com/providers/home.page
b. If the prior authorization request is submitted via phone or fax, each drug or biologic will need to be submitted and reviewed as a separate prior authorization request for review with drug-specific criteria.
c. The prior authorization review is requested for an oncology drug or biologic that requires prior authorization on the medical benefit.
d. The indication is for a cancer that is eligible for regimen review. Currently, the cancer types in scope for regimen review include breast, lung, colon and rectal cancer.
e. The member is eligible for regimen review.

In addition, the following criteria must be met for approval:

a. The requested regimen for the drug(s) or biologic(s) and indication is consistent with an NCCN recommendation with a level of evidence category of 1 or 2A.
b. The NCCN template must be accepted by the provider without modification.

Authorizations may be granted for 12 months.
Further review may be indicated where the above criteria are not met.

Continuation of Therapy

To submit a request for continuation of therapy, a new regimen prior authorization review must be requested. Upon template selection, the template must be modified to include the appropriate therapies being used for maintenance treatment. The regimen request will be submitted for further review.

Dosage and Administration

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

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6. Libtayo [prescribing information]. Tarrytown, NY: Regeneron Pharmaceuticals, Inc.; April 2023.
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9. Opdualag [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; March 2022.
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SECTION 2

1. Keytruda [package insert]. Whitehouse Station, NJ: Merck & Co., Inc.; April 2023.
2. The NCCN Drugs & Biologics Compendium® © 2023 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed May 5, 2023.
3. Micromedex (electronic version). Truven Health Analytics. Greenwood Village, Colorado, USA

http://www.micromedexsolutions.com/. Accessed August 10, 2022.
4. Makker V, Colombo N, Casado Herraez A, et al: Lenvatinib plus Pembrolizumab for Advanced Endometrial Cancer. N Engl J Med 2022; 386(5):437-448.

SECTION 3

1. National Comprehensive Cancer Network. About NCCN website. https://www.nccn.org/about/default.aspx, accessed September 16, 2019.
2. National Comprehensive Cancer Network. NCCN Categories of Evidence and Consensus website. https://www.nccn.org/professionals/physician_gls/categories_of_consensus.aspx, accessed September 16, 2019.
3. National Comprehensive Cancer Network. NCCN Guidelines website. http://www.nccn.org/professionals/physician_gls/f_guidelines.asp, accessed September 16, 2019. *(Note: An account may be required.)*
4. National Comprehensive Cancer Network. NCCN Drugs and Biologics Compendium® website. http://www.nccn.org/professionals/drug_compendium/content/contents.asp, accessed September 16, 2019. *(Note: A subscription may be required.)*
5. National Comprehensive Cancer Network. NCCN Chemotherapy Order Templates (NCCN Templates) website. https://www.nccn.org/professionals/OrderTemplates/Default.aspx, accessed September 16, 2019. *(Note: A subscription may be required.)*

Reference number(s)
5149-A

SPECIALTY GUIDELINE MANAGEMENT

KIMMTRAK (tebentafusp-tebn)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Kimmtrak is indicated for the treatment of HLA-A*02:01-positive adult patients with unresectable or metastatic uveal 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: medical record documentation of HLA-A*02:01 phenotype.

III. CRITERIA FOR INITIAL APPROVAL

Uveal Melanoma
Authorization of 12 months may be granted for treatment of uveal melanoma when all of the following criteria are met:
1. The member is HLA-A*02:01-positive
2. The disease is unresectable or metastatic

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. Kimmtrak [package insert]. Conshohocken, PA: Immunocore Commercial LLC; January 2022.

Reference number(s)
C24612-A

CAREFIRST: KRYSTEXXA

Client Requested: The intent of the criteria is to ensure that patients follow selection elements as established by CareFirst.

Section 1: Site of Care
- Policy information specific to site of care (outpatient, hospital outpatient, home infusion)

Section 2: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 1: Site of Care

CareFirst Site of Care Criteria
Administration of Intravenous Krystexxa

POLICY

I. CRITERIA FOR APPROVAL FOR ADMINISTRATION IN OUTPATIENT HOSPITAL SETTING

This policy provides coverage for administration of Krystexxa in an outpatient hospital setting for up to 57 days when a member is new to therapy or is reinitiating therapy after not being on therapy for at least 6 months.

This policy provides coverage for administration of Krystexxa in an outpatient hospital setting for a longer course of treatment when ANY of the following criteria are met:

A. The member has experienced an adverse reaction to the drug that did not respond to conventional interventions (eg, acetaminophen, steroids, diphenhydramine, fluids, other pre-medications or slowing of infusion rate) or a severe adverse event (anaphylaxis, anaphylactoid reactions, myocardial infarction, thromboembolism, or seizures) during or immediately after an infusion.
B. The member has developed laboratory confirmed anti-pegloticase antibodies which increases the risk for infusion related reactions
C. The member is medically unstable (eg respiratory, cardiovascular, or renal conditions).
D. The member has severe venous access issues that require the use of special interventions only available in the outpatient hospital setting.
E. The member has significant behavioral issues and/or physical or cognitive impairment that would impact the safety of the infusion therapy AND the patient does not have access to a caregiver.
F. The member is less than 14 years of age.

For situations where administration of Krystexxa does not meet the criteria for outpatient hospital infusion, coverage for Krystexxa is provided when administered in alternative sites such as; physician office, home infusion or ambulatory care.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the site of care prior authorization review (where applicable):

A. Medical records supporting the member has experienced an adverse reaction that did not respond to conventional interventions or a severe adverse event during or immediately after an infusion
B. Medical records supporting the member has developed anti-pegloticase antibodies
C. Medical records supporting the member is medically unstable
D. Medical records supporting the member has severe venous access issues that requires specialized interventions only available in the outpatient hospital setting
E. Medical records supporting the member has behavioral issues and/or physical or cognitive impairment and no access to a caregiver

Section 2: COVERAGE CRITERIA

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

A. Initial criteria: Authorization of 6 months may be granted for members with a diagnosis of chronic gout when ALL of the following criteria are met:
   1. Member is 18 years of age or older.
   2. Krystexxa will NOT be used concomitantly with oral urate-lowering therapies.
   3. The member has at least 2 gout flares per year that were inadequately controlled by colchicine or NSAIDs or

at least 1 gout tophus or gouty arthritis.

4. Member has had an inadequate response to or a clinical reason for not completing at least a three-month trial (see Appendix) with the following medications at the medically appropriate maximum doses:
   i. Allopurinol or febuxostat
   ii. Probenecid (alone or in combination with allopurinol or febuxostat)

B. Continuation criteria: Authorization of 12 months may be granted for continued treatment in all members (including new members) requesting reauthorization for chronic gout when ALL of the following criteria are met:
1. Member has taken Krystexxa for less than 18 months
2. Member meets ALL initial authorization criteria
3. Member has NOT had two consecutive uric acid levels above 6 mg/dL since starting treatment with Krystexxa
4. Member is experiencing benefit from therapy (e.g., serum uric acid levels < 6 mg/dL, reduction of tophi, reduction of symptoms and/or flares). Documentation (e.g., chart notes, lab test results) of a response to therapy (e.g., serum uric acid levels < 6 mg/dL, reduction of tophi, reduction of symptoms and/or flares) must be submitted.

C. Appendix: Clinical reasons for not completing a three-month trial with allopurinol, febuxostat, and probenecid (examples, not all inclusive):
1. Member experienced a severe allergic reaction to the medication
2. Member experienced toxicity with the medication
3. Member could not tolerate the medication
4. Member's current medication regimen has a significant drug interaction
5. Member has severe renal dysfunction (allopurinol)
6. Member has known blood dyscrasias or uric acid kidney stones (probenecid)
7. Member has renal insufficiency (i.e., glomerular filtration rate 30 mL/minute or less) (probenecid)
8. Member has end stage renal impairment (febuxostat)
9. Member has a history of CVD or a new CV event (febuxostat)

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

REFERENCES

1. Krystexxa [package insert]. Dublin, Ireland: Horizon Therapeutics; July 2022.
2. Calabrese LH, Kavanaugh A, Yeo AE, Lipsky PE. Frequency, distribution and immunologic nature of infusion reactions in subjects receiving pegloticase for chronic refractory gout. *Arthritis Res Ther*. 2017 Aug 17;19(1):191.

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SPECIALTY GUIDELINE MANAGEMENT

KYMRIAH (tisagenlecleucel)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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. Pediatric and Young Adult Relapsed or Refractory (r/r) B-cell Acute Lymphoblastic Leukemia (ALL)
   Kymriah is indicated for the treatment of patients up to 25 years of age with B-cell precursor acute lymphoblastic leukemia (ALL) that is refractory or in second or later relapse.
2. Adult Relapsed or Refractory (r/r) Diffuse Large B-cell Lymphoma (DLBCL)
   Adult patients with relapsed or refractory (r/r) large B-cell lymphoma after two or more lines of systemic therapy including diffuse large B-cell lymphoma (DLBCL) not otherwise specified (NOS), high grade B-cell lymphoma and DLBCL arising from follicular lymphoma.
3. Adult Relapsed or Refractory (r/r) Follicular Lymphoma (FL)
   Adult patients with relapsed or refractory (r/r) follicular lymphoma (FL) after two or more lines of systemic therapy.

   Limitation of Use: Kymriah is not indicated for treatment of patients with primary central nervous system lymphoma.

B. Compendial Uses
1. Pediatric B-cell ALL first relapse post hematopoietic stem cell transplant (HSCT)
2. Histologic transformation of indolent lymphomas to DLBCL
3. Acquired immunodeficiency syndrome (AIDS)-related B-cell lymphomas (including AIDS-related diffuse large B-cell lymphoma, primary effusion lymphoma, and human herpesvirus 8 (HHV8)-positive diffuse large B-cell lymphoma, not otherwise specific)
4. Monomorphic post-transplant lymphoproliferative disorder (B-cell type)

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 all indications: Chart notes, medical record documentation or claims history supporting previous lines of therapy.
B. For Acute Lymphoblastic Leukemia:
1. Testing or analysis confirming CD19 tumor expression in bone marrow or peripheral blood.
2. Testing or analysis confirming at least 5% lymphoblasts in the bone marrow.

III. CRITERIA FOR INITIAL APPROVAL

A. Pediatric and Young Adult Relapsed or Refractory (r/r) B-cell Acute Lymphoblastic Leukemia (ALL)

Authorization of 3 months may be granted for treatment of B-cell precursor acute lymphoblastic leukemia (ALL) in members less than 26 years of age when all of the following criteria are met:

1. The member has not received a previous treatment course of the requested medication or another CD19-directed chimeric antigen receptor (CAR) T-cell therapy.
2. The member has CD19 tumor expression in bone marrow or peripheral blood.
3. The member has at least 5% lymphoblasts in the bone marrow.
4. Member meets either of the following:
    i. Member has Philadelphia chromosome-negative disease that is refractory or has had 2 or more relapses
    ii. Member has Philadelphia chromosome-positive disease and meets any of the following:
        a. Member has refractory disease
        b. Member has had 2 or more relapses and has failed at least 2 tyrosine kinase inhibitors (TKIs) (e.g., bosutinib, dasatinib, imatinib, nilotinib, ponatinib)
        c. Member has relapsed disease and is TKI intolerant
        d. Member has experienced a relapse post-hematopoietic stem cell transplant (HSCT)
5. The member has a Karnofsky (age ≥16 years) or Lansky (age < 16 years) performance status greater than or equal to 50%.
6. The member has adequate and stable kidney, liver, pulmonary and cardiac function.
7. The member does not have active or latent hepatitis B, active hepatitis C or any active uncontrolled infection.
8. The member does not have active graft versus host disease.
9. The member does not have an active inflammatory disorder.

B. Adult B-cell Lymphomas

Authorization of 3 months may be granted for treatment of B-cell lymphomas in members 18 years of age or older when all of the following criteria are met:

1. Member has any of the following B-cell lymphoma subtypes:
    i. Diffuse large B-cell lymphoma (DLBCL) arising from follicular lymphoma
    ii. Follicular lymphoma
    iii. Histologic transformation of indolent lymphomas to DLBCL
    iv. Diffuse large B-cell lymphoma (DLBCL)
    v. High-grade B-cell lymphomas (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)
    vi. Acquired immunodeficiency syndrome (AIDS)-related B-cell lymphomas (including AIDS-related diffuse large B-cell lymphoma, primary effusion lymphoma, and human herpesvirus 8 (HHV8)-positive diffuse large B-cell lymphoma, not otherwise specific)
    vii. Monomorphic post-transplant lymphoproliferative disorder (B-cell type)
2. The member has received prior treatment with two or more lines of systemic therapy.
3. The member does not have primary central nervous system lymphoma.
4. The member has not received a previous treatment course of the requested medication or another CD19-directed chimeric antigen receptor (CAR) T-cell therapy.
5. Member has an ECOG performance status of 0 to 2 (member is ambulatory and capable of all self-care but unable to carry out any work activities. Up and about more than 50% of waking hours).
6. The member has adequate and stable kidney, liver, pulmonary and cardiac function.
7. The member does not have active or latent hepatitis B, active hepatitis C or any active uncontrolled infection.
8. The member does not have active graft versus host disease.
9. The member does not have an active inflammatory disorder.

Reference number(s)
2294-A

IV. REFERENCES

1. Kymriah [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; May 2022.
2. The NCCN Drugs & Biologics Compendium® © 2022 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed April 14, 2022.
3. 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.
4. NCCN Clinical Practice Guidelines in Oncology® B-Cell Lymphomas (Version 2.2022).© 2022 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed April 14, 2022.
5. Maude SL, Laetsch TW, Buechner J, et al. Tisagenlecleucel in Children and Young Adults with B-Cell Lymphoblastic Leukemia. N Engl J Med. 2018;378(5):439-448.
6. Schuster SJ, Bishop MR, Tam CS, et al. Tisagenlecleucel in Adult Relapsed or Refractory Diffuse Large B-Cell Lymphoma. N Engl J Med. 2019;380(1):45-56.

POLICY Document for KYPROLIS (carfilzomib)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, and overall, clinically appropriate use. This document provides specific information to both sections of the overall policy.

Section 1: Preferred Product
- Policy information specific to preferred medications

Section 2: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 1: Preferred Product

EXCEPTIONS CRITERIA

MULTIPLE MYELOMA

PREFERRED PRODUCTS: NINLARO, VELCADE

POLICY
This policy informs prescribers of preferred products and provides an exception process for targeted products through prior authorization.

I. PLAN DESIGN SUMMARY

This program applies to the multiple myeloma products specified in this policy. Coverage for targeted products is provided based on clinical circumstances that would exclude the use of the preferred product and may be based on previous use of a product. The coverage review process will ascertain situations where a clinical exception can be made. This program applies to members who are new to treatment with a targeted product for the first time.

Each referral is reviewed based on all utilization management (UM) programs implemented for the client.

Table. Multiple Myeloma Therapies

	Product(s)
Preferred*	• **Ninlaro** (ixazomib) • **Velcade** (bortezomib)
Targeted	• **Kyprolis** (carfilzomib)

*: Medications considered formulary or preferred on your plan may still require a clinical prior authorization review.

II. EXCEPTION CRITERIA

This program applies to members requesting treatment for an indication that is FDA-approved for the preferred product.

Coverage for a targeted product is provided when either of the following criteria are met:

A. Member is currently receiving treatment with a targeted product, excluding when the requested targeted product is obtained as samples or via manufacturer's patient assistance programs.
B. Member has a documented inadequate response or intolerable adverse event with both of the preferred products.

Section 2: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

KYPROLIS (carfilzomib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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. Kyprolis is indicated for the treatment of adult patients with relapsed or refractory multiple myeloma who have received one to three lines of therapy in combination with:
   - Lenalidomide and dexamethasone; or
   - Dexamethasone; or
   - Daratumumab and dexamethasone; or
   - Daratumumab and hyaluronidase-fihj and dexamethasone; or
   - Isatuximab and dexamethasone.
2. Kyprolis is indicated as a single agent for the treatment of adult patients with relapsed or refractory multiple myeloma who have received one or more lines of therapy.

B. Compendial Uses
1. Multiple Myeloma
2. Waldenström macroglobulinemia/lymphoplasmacytic lymphoma
3. Systemic light chain amyloidosis

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 the requested medication will used in any of the following regimens:
1. In combination with dexamethasone when the member has relapsed, refractory, or progressive disease
2. In combination with cyclophosphamide and dexamethasone
3. In combination with lenalidomide and dexamethasone
4. In combination with daratumumab, lenalidomide and dexamethasone
5. In combination with daratumumab and dexamethasone or daratumumab and hyaluronidase-fihj and dexamethasone when the member has relapsed, refractory, or progressive disease
6. In combination with pomalidomide and dexamethasone when the member has relapsed or progressive disease
7. In combination with cyclophosphamide, thalidomide, and dexamethasone when the member has relapsed or progressive disease
8. In combination with isatuximab-irfc and dexamethasone when the member has relapsed, refractory, or progressive disease
9. In combination with selinexor and dexamethasone when the member has relapsed or progressive disease
10. In combination with lenalidomide as maintenance therapy for symptomatic disease

11. In combination with bendamustine and dexamethasone when the member has received more than 3 prior therapies and has relapsed or progressive disease
12. As a single agent when the member has received one or more lines of therapy

B. Waldenstrom Macroglobulinemia/Lymphoplasmacytic Lymphoma
Authorization of 12 months may be granted for treatment of Waldenström macroglobulinemia/lymphoplasmacytic lymphoma.

C. Systemic Light Chain Amyloidosis
Authorization of 12 months may be granted for treatment of relapsed or refractory systemic light chain amyloidosis.

III. 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 all indications, dosing does not exceed the following:

A. If using twice weekly: 56 mg/m^2 (not to exceed 124 mg) per dose, not to exceed 6 doses per 28 days
B. If using once weekly: 70 mg/m^2 (not to exceed 154 mg) per dose, not to exceed 3 doses per 28 days

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.

REFERENCES:

SECTION 1

1. Ninlaro [package insert]. Lexington, MA: Takeda Pharmaceuticals America, Inc.; May 2022.
2. Velcade [package insert]. Lexington, MA: Takeda Pharmaceuticals America, Inc.; August 2022.
3. Kyprolis [package insert]. Thousand Oaks, CA: Onyx Pharmaceuticals, Inc.; June 2022.

SECTION 2

1. Kyprolis [package insert]. Thousand Oaks, CA: Onyx Pharmaceuticals, Inc.; June 2022.
2. The NCCN Drugs & Biologics Compendium® © 2022 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed October 6, 2022.
3. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Multiple Myeloma. Version 1.2023. https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf. Accessed October 6, 2022.

POLICY Document for LAMZEDE (velmanase alfa-tycv)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, lower cost site of care and overall, clinically appropriate use. This document provides specific information to each of the three sections of the overall policy.

Section 1: Site of Care

- Policy information specific to site of care (outpatient, hospital outpatient, home infusion)

Section 2: Clinical Criteria

- Policy information specific to the clinical appropriateness for the medication

Section 1: Site of Care

CareFirst Site of Care Criteria
Administration of Intravenous Lamzede

POLICY

I. CRITERIA FOR APPROVAL FOR ADMINISTRATION IN OUTPATIENT HOSPITAL SETTING

This policy provides coverage for administration of Lamzede in an outpatient hospital setting for up to 54 days when a member is new to therapy or is reinitiating therapy after not being on therapy for at least 6 months.

This policy provides coverage for administration of Lamzede in an outpatient hospital setting for a longer course of treatment when ANY of the following criteria are met:

A. The member has experienced an adverse reaction to the drug that did not respond to conventional interventions (e.g., acetaminophen, steroids, diphenhydramine, fluids, other pre-medications or slowing of infusion rate) or a severe adverse event (anaphylaxis, anaphylactoid reactions, myocardial infarction, thromboembolism, or seizures) during or immediately after infusion.
B. The member has developed laboratory confirmed anti-velmanase alfa-tycv antibodies which increases the risk for infusion related reactions.
C. The member is medically unstable (e.g., respiratory, cardiovascular, or renal conditions).
D. The member has severe venous access issues that require the use of special interventions only available in the outpatient setting.
E. The member has significant behavioral issues and/or physical or cognitive impairment that would impact the safety of the infusion therapy AND the patient does not have access to a caregiver.
F. The member is less than 14 years of age.

For situations where administration of Lamzede does not meet the criteria for outpatient hospital infusion, coverage for Lamzede is provided when administered in alternative sites such as physician office, home infusion or ambulatory care.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the site of care prior authorization review (where applicable):

A. Medical records supporting the member has experienced an adverse reaction that did not respond to conventional interventions or a severe adverse event during or immediately after an infusion

B. Medical records supporting the member has developed anti-velmanase alfa-tycv antibodies
C. Medical records supporting the member is medically unstable
D. Medical records supporting the member has severe venous access issues that requires specialized interventions only available in the outpatient hospital setting
E. Medical records supporting the member has behavioral issues and/or physical or cognitive impairment and no access to a caregiver

Section 2: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

LAMZEDE (velmanase alfa-tycv)

POLICY

III. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Lamzede is indicated for the treatment of non-central nervous system manifestations of alpha-mannosidosis in adult and pediatric patients.

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

IV. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
A. Initial requests: alpha-mannosidase enzyme assay or genetic testing results supporting the diagnosis.
B. Continuation of therapy requests: documentation (e.g., chart notes, lab results) of a response to therapy (e.g., improvement in 3-minute stair climbing test [3MSCT] from baseline, improvement in 6-minute walking test [6MWT] from baseline, improvement in forced vital capacity [FVC, % predicted] from baseline, reduction in serum or urine oligosaccharide concentration from baseline).

V. CRITERIA FOR INITIAL APPROVAL

Alpha-mannosidosis
Authorization of 12 months may be granted for treatment of non-CNS manifestations of alpha-mannosidosis when the diagnosis is confirmed by either of the following:
A. A documented deficiency of alpha-mannosidase activity as measured in blood leukocytes or fibroblasts, or
B. Genetic testing results documenting a mutation in the *MAN2B1* gene.

VI. 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., improvement in 3-minute stair climbing

test [3MSCT] from baseline, improvement in 6-minute walking test [6MWT] from baseline, improvement in forced vital capacity [FVC, % predicted] from baseline, reduction in serum or urine oligosaccharide concentration from baseline).

REFERENCES

SECTION 1

1. Lamzede [package insert]. Cary, NA: Chiesi USA, Inc.; February 2023.

SECTION 2

2. Lamzede [package insert]. Cary, NC: Chiesi USA Inc.; February 2023.
3. Malm D, Nilssen O. Alpha-Mannosidosis. In: GeneReviews. https://www.ncbi.nlm.nih.gov/books/NBK1396/ (Accessed on February 17, 2023).

CVS/caremark

POLICY Document for RADICAVA (edaravone)
RADICAVA ORS (edaravone)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, lower cost site of care and overall, clinically appropriate use. This document provides specific information to each of the three sections of the overall policy.

Section 1: Site of Care
- Policy information specific to site of care (outpatient, hospital outpatient, home infusion)

Section 2: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 1: Site of Care

CareFirst Site of Care Criteria
Administration of Intravenous Radicava

POLICY

I. CRITERIA FOR APPROVAL FOR ADMINISTRATION IN OUTPATIENT HOSPITAL SETTING

This policy provides coverage for administration of Radicava in an outpatient hospital setting for up to 45 days when a member is new to therapy or is reinitiating therapy after not being on therapy for at least 6 months.

This policy provides coverage for administration of Radicava in an outpatient hospital setting for a longer course of treatment when ANY of the following criteria are met:

A. The member has experienced an adverse reaction to the drug or other sulfite containing product that did not respond to conventional interventions (eg, acetaminophen, steroids, diphenhydramine, fluids or other pre-medications) or a severe adverse event (anaphylaxis, anaphylactoid reactions, myocardial infarction, thromboembolism, or seizures) during or immediately after an infusion.
B. The member is medically unstable (eg respiratory, cardiovascular, or renal conditions).
C. The member has severe venous access issues that require the use of special interventions only available in the outpatient hospital setting.
D. The member has significant behavioral issues and/or physical or cognitive impairment that would impact the safety of the infusion therapy AND the patient does not have access to a caregiver.
E. The member is less than 14 years of age.

For situations where administration of Radicava does not meet the criteria for outpatient hospital infusion, coverage for Radicava is provided when administered in alternative sites such as; physician office, home infusion or ambulatory care.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the site of care prior authorization review (where applicable):

A. Medical records supporting the member has experienced an adverse reaction that did not respond to conventional interventions or a severe adverse event during or immediately after an infusion
B. Medical records supporting the member is medically unstable
C. Medical records supporting the member has severe venous access issues that requires specialized interventions only available in the outpatient hospital setting
D. Medical records supporting the member has behavioral issues and/or physical or cognitive impairment and no access to a caregiver

Section 2: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

RADICAVA (edaravone)
RADICAVA ORS (edaravone)

POLICY

III. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Radicava and Radicava ORS are indicated for the treatment of amyotrophic lateral sclerosis (ALS).

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

IV. REQUIRED DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
Chart notes or medical record documentation supporting use as applicable in section IV and V.
A. Initial Requests:
    1. Diagnosis of definite or probable ALS
    2. Member has scores of at least 2 points on all 12 areas of the revised ALS Functional Rating Scale
B. Continuation Requests:
    1. Documentation of clinical benefit from Radicava therapy

V. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with a neurologist, neuromuscular specialist or physician specializing in the treatment of amyotrophic lateral sclerosis (ALS).

VI. CRITERIA FOR INITIAL APPROVAL

Authorization of 12 months may be granted for treatment of ALS when all of the following criteria are met:
A. Diagnosis of definite or probable ALS

B. Member has scores of at least 2 points on all 12 areas of the revised ALS Functional Rating Scale (ALSFRS-R)
C. Continuous use of ventilatory support during the day and night is not required (noninvasive or invasive)

VII. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for members continuing with Radicava therapy for the treatment of ALS when the following criteria are met:
A. Diagnosis of definite or probable ALS
B. There is a clinical benefit from Radicava therapy
C. Invasive ventilation is not required

REFERENCES

SECTION 1

1. Radicava [package insert]. Jersey City, NJ: Mitsubishi Tanabe Pharma America, Inc, May 2022.

SECTION 2

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2. EFNS Task Force on Diagnosis and Management of Amyotrophic Lateral Sclerosis; Andersen PM, et al. EFNS guidelines on the Clinical Management of Amyotrophic Lateral Sclerosis (MALS) – revised report of an EFNS task force. *Eur J Neurol*. 2012;19(3):360-75.
3. Writing Group, Edaravone (MCI-186) ALS 19 Study Group. Safety and efficacy of edaravone in well defined patients with amyotrophic lateral sclerosis: a randomized, double-blind, placebo-controlled trial. *Lancet Neurol*. 2017; 16:505-512.

POLICY Document for SIGNIFOR LAR (pasireotide injectable suspension)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, and overall, clinically appropriate use. This document provides specific information to both sections of the overall policy.

Section 1: Preferred Product
- Policy information specific to preferred medications

Section 2: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 1: Preferred Product

EXCEPTIONS CRITERIA
ACROMEGALY PRODUCTS

PREFERRED PRODUCTS: SANDOSTATIN LAR, SOMATULINE DEPOT

POLICY
This policy informs prescribers of preferred products and provides an exception process for targeted products through prior authorization.

I. PLAN DESIGN SUMMARY

This program applies to the acromegaly products specified in this policy. Coverage for a targeted product is provided based on clinical circumstances that would exclude the use of the preferred products and may be based on previous use of a product. The coverage review process will ascertain situations where a clinical exception can be made. This program applies to all members requesting treatment with a targeted product.

Each referral is reviewed based on all utilization management (UM) programs implemented for the client.

Table. Acromegaly Products

	Product(s)
Preferred*	• **Sandostatin LAR** (octreotide acetate for injectable suspension) • **Somatuline Depot** (lanreotide)
Targeted	• **lanreotide injection** • **Signifor LAR** (pasireotide injectable suspension) • **Somavert** (pegvisomant)

*: Medications considered formulary or preferred on your plan may still require a clinical prior authorization review.

II. EXCEPTION CRITERIA

This program applies to members requesting treatment for an indication that is FDA-approved for both of the preferred products.

A. lanreotide injection

Coverage for the targeted product is provided when all of the following criteria are met:

1. The member has had a documented intolerable adverse event to Somatuline Depot, and the adverse event was not an unexpected adverse event attributed to the active ingredient as described in the prescribing information.
2. The member has a documented inadequate response or intolerable adverse event to Sandostatin LAR.

B. Signifor LAR, Somavert

Coverage for a targeted product is provided when the member has had a documented inadequate response or intolerable adverse event to any of the preferred products.

Section 2: Clinical Criteria

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)

CVS/caremark

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

REFERENCES:

SECTION 1

1. Somatuline Depot [package insert]. Basking Ridge, NJ: Ipsen Biopharmaceuticals, Inc.; February 2023.
2. Sandostatin LAR Depot [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; March 2021.
3. Signifor LAR [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Company; June 2020.
4. Somavert [package insert]. New York, NY: Pharmacia & Upjohn Co; August 2021.
5. Lanreotide injection [package insert]. Warren, NJ: Cipla USA, Inc.; December 2021.

SECTION 2

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.
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6. 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):2807-31.
7. 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: 847-875.

POLICY Document for
SOMATULINE DEPOT (lanreotide acetate injection)
LANREOTIDE INJECTION (lanreotide acetate injection)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, and overall, clinically appropriate use. This document provides specific information to both sections of the overall policy.

Section 1: Preferred Product
- Policy information specific to preferred medications

Section 2: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 1: Preferred Product

EXCEPTIONS CRITERIA
ACROMEGALY PRODUCTS

PREFERRED PRODUCTS: SANDOSTATIN LAR, SOMATULINE DEPOT

POLICY
This policy informs prescribers of preferred products and provides an exception process for targeted products through prior authorization.

I. PLAN DESIGN SUMMARY

This program applies to the acromegaly products specified in this policy. Coverage for a targeted product is provided based on clinical circumstances that would exclude the use of the preferred products and may be based on previous use of a product. The coverage review process will ascertain situations where a clinical exception can be made. This program applies to all members requesting treatment with a targeted product.

Each referral is reviewed based on all utilization management (UM) programs implemented for the client.

Table. Acromegaly Products

	Product(s)
Preferred*	• **Sandostatin LAR** (octreotide acetate for injectable suspension) • **Somatuline Depot** (lanreotide)
Targeted	• **lanreotide injection** • **Signifor LAR** (pasireotide injectable suspension) • **Somavert** (pegvisomant)

*: Medications considered formulary or preferred on your plan may still require a clinical prior authorization review.

II. EXCEPTION CRITERIA

This program applies to members requesting treatment for an indication that is FDA-approved for both of the preferred products.

A. lanreotide injection

Coverage for the targeted product is provided when all of the following criteria are met:

1. The member has had a documented intolerable adverse event to Somatuline Depot, and the adverse event was not an unexpected adverse event attributed to the active ingredient as described in the prescribing information.
2. The member has a documented inadequate response or intolerable adverse event to Sandostatin LAR.

B. Signifor LAR, Somavert

Coverage for a targeted product is provided when the member has had a documented inadequate response or intolerable adverse event to any of the preferred products.

Section 2: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

SOMATULINE DEPOT (lanreotide acetate injection)
LANREOTIDE INJECTION (lanreotide 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. Somatuline Depot
      i. Long-term treatment of acromegalic patients who have had an inadequate response to or cannot be treated with surgery and/or radiotherapy.
      ii. Treatment of adult patients with unresectable, well- or moderately-differentiated, locally advanced or metastatic gastroenteropancreatic neuroendocrine tumors (GEP-NETs) to improve progression-free survival.
      iii. Treatment of adults with carcinoid syndrome; when used, it reduces the frequency of short-acting somatostatin analog rescue therapy.

   2. Lanreotide Injection
      i. Long-term treatment of acromegalic patients who have had an inadequate response to or cannot be treated with surgery and/or radiotherapy.
      ii. Treatment of adult patients with unresectable, well- or moderately-differentiated, locally advanced or metastatic gastroenteropancreatic neuroendocrine tumors (GEP-NETs) to improve progression-free survival.

B. Compendial Uses
   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. 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 for acromegaly:

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

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.

B. Neuroendocrine tumors (NETs)

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, insulinomas, and VIPomas.
5. Well-differentiated grade 3 NETs with favorable biology
   Authorization of 12 months may be granted for treatment of well-differentiated grade 3 NETs (not of gastroenteropancreatic origin) 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

Authorization of 12 months may be granted for treatment of carcinoid syndrome.

D. Pheochromocytoma and paraganglioma

Authorization of 12 months may be granted for treatment of pheochromocytoma and paraganglioma.

E. Zollinger-Ellison syndrome

Authorization of 12 months may be granted 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, pheochromocytoma/paraganglioma, and Zollinger-Ellison syndrome

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 starting therapy.

REFERENCES:

SECTION 1

1. Somatuline Depot [package insert]. Basking Ridge, NJ: Ipsen Biopharmaceuticals, Inc.; February 2023.
2. Sandostatin LAR Depot [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; March 2021.
3. Signifor LAR [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Company; June 2020.
4. Somavert [package insert]. New York, NY: Pharmacia & Upjohn Co; August 2021.
5. Lanreotide injection [package insert]. Warren, NJ: Cipla USA, Inc.; December 2021.

SECTION 2

1. Somatuline Depot [package insert]. Cambridge, MA: Ipsen Biopharmaceuticals, Inc.; June 2019.
2. The NCCN Drugs & Biologics Compendium® © 2022 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed November 8, 2022.
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7. Lanreotide Injection [package insert]. Warren, NJ: Cipla USA, Inc.; December 2021.

POLICY Document for TYKERB (lapatinib)
Lapatinib

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, and overall, clinically appropriate use. This document provides specific information to both sections of the overall policy.

Section 1: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 2: Oncology Clinical Policy
- Policy information specific to regimen review per NCCN Guidelines.

Section 1: Clinical Criteria

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.

Section 2: Oncology Clinical Policy

Oncology Clinical Policy

Program Description

The National Comprehensive Care Network® (NCCN®) is an alliance of leading cancer centers devoted to patient care, research and education dedicated to improving the quality, effectiveness and efficiency of cancer care so patients can live better lives.[1] It is comprised of oncology experts who convene regularly to establish the best treatments for patients. NCCN develops various resources for use by stakeholders in the health care delivery system. These resources include, but are not limited to, the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®), the NCCN Drugs & Biologics Compendium (NCCN Compendium®) and the NCCN Chemotherapy Order Templates (NCCN Templates®).

NCCN templates are based on NCCN Clinical Practice Guidelines and NCCN Compendium. The NCCN Compendium lists the appropriate drugs and biologics for specific cancers using U.S. Food and Drug Administration (FDA)-approved disease indications and specific NCCN panel recommendations. Each recommendation is supported by a level of evidence category.

NCCN Categories of Evidence and Consensus
Category 1: Based on high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2A: Based on lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2B: Based on lower-level evidence, there is NCCN consensus that the intervention is appropriate.
Category 3: Based any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

Policy for Regimen Prior Authorization

A regimen prior authorization allows submission of a single prior authorization request for all oncology drugs or biologics within an NCCN template that require prior authorization.

This policy provides coverage of a regimen review when *all* of the following criteria are met:

a. Regimen prior authorization reviews, based on NCCN templates, are initiated through the provider portal: https://provider.carefirst.com/providers/home.page
b. If the prior authorization request is submitted via phone or fax, each drug or biologic will need to be submitted and reviewed as a separate prior authorization request for review with drug-specific criteria.
c. 2. The prior authorization review is requested for an oncology drug or biologic that requires prior authorization on the medical benefit.
d. The indication is for a cancer that is eligible for regimen review. Currently, the cancer types in scope for regimen review include breast, lung, colon and rectal cancer.
e. The member is eligible for regimen review.

In addition, the following criteria must be met for approval:

a. The requested regimen for the drug(s) or biologic(s) and indication is consistent with an NCCN recommendation with a level of evidence category of 1 or 2A.
b. The NCCN template must be accepted by the provider without modification.

Authorizations may be granted for 12 months.
Further review may be indicated where the above criteria are not met.

Continuation of Therapy

To submit a request for continuation of therapy, a new regimen prior authorization review must be requested. Upon template selection, the template must be modified to include the appropriate therapies being used for maintenance treatment. The regimen request will be submitted for further review.

Dosage and Administration

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

REFERENCES:

SECTION 1

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.

SECTION 2

1. National Comprehensive Cancer Network. About NCCN website. https://www.nccn.org/about/default.aspx, accessed September 16, 2019.
2. National Comprehensive Cancer Network. NCCN Categories of Evidence and Consensus website. https://www.nccn.org/professionals/physician_gls/categories_of_consensus.aspx, accessed September 16, 2019.
3. National Comprehensive Cancer Network. NCCN Guidelines website. http://www.nccn.org/professionals/physician_gls/f_guidelines.asp, accessed September 16, 2019. *(Note: An account may be required.)*
4. National Comprehensive Cancer Network. NCCN Drugs and Biologics Compendium® website. http://www.nccn.org/professionals/drug_compendium/content/contents.asp, accessed September 16, 2019. *(Note: A subscription may be required.)*
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POLICY Document for LEMTRADA (alemtuzumab)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, lower cost site of care and overall, clinically appropriate use. This document provides specific information to each of the three sections of the overall policy.

Section 1: Preferred Product
- Policy information specific to preferred medications

Section 2: Site of Care
- Policy information specific to site of care (outpatient, hospital outpatient, home infusion)

Section 3: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 1: Preferred Product

EXCEPTIONS CRITERIA
MULTIPLE SCLEROSIS PRODUCTS
PREFERRED PRODUCTS: OCREVUS, TYSABRI

POLICY
This policy informs prescribers of preferred products and provides an exception process for targeted products through prior authorization.

I. PLAN DESIGN SUMMARY

This program applies to the multiple sclerosis products specified in this policy. Coverage for targeted products is provided based on clinical circumstances that would exclude the use of the preferred product and may be based on previous use of a product. The coverage review process will ascertain situations where a clinical exception can be made. This program applies to members who are new to treatment with Lemtrada for the first time.

Each referral is reviewed based on all utilization management (UM) programs implemented for the client.

Table. Multiple sclerosis (MS) products

	Products
Preferred*	• **Ocrevus** (ocrelizumab) • **Tysabri** (natalizumab)
Targeted	• **Lemtrada** (alemtuzumab)

*: Medications considered formulary or preferred on your plan may still require a clinical prior authorization review.

II. EXCEPTION CRITERIA

This program applies to members requesting treatment for an indication that is FDA-approved for the preferred product.

Coverage for the targeted product is provided when either of the following criteria is met:

A. Member is currently receiving treatment with the targeted product, excluding when the requested targeted product is obtained as samples or via manufacturer's patient assistance programs.

B. Member has a documented inadequate response, intolerable adverse event, or contraindication with both of the preferred products (including any of their components).

Section 2: Site of Care

CareFirst Site of Care Criteria
Administration of Intravenous Lemtrada

POLICY

I. CRITERIA FOR APPROVAL FOR ADMINISTRATION IN OUTPATIENT HOSPITAL SETTING

This policy provides coverage for administration of Lemtrada in an outpatient hospital setting for up to 45 days when a member is new to therapy or is reinitiating therapy after not being on therapy for at least 13 months.

This policy provides coverage for administration of Lemtrada in an outpatient hospital setting for subsequent treatment courses when ANY of the following criteria are met:

A. The member has experienced an adverse reaction to the drug that did not respond to conventional interventions (eg, acetaminophen, steroids, diphenhydramine, fluids or other pre-medications) or a severe adverse event (anaphylaxis, anaphylactoid reactions, myocardial infarction, thromboemobolism, or seizures) during or immediately after an infusion.
B. The member is medically unstable (eg respiratory, cardiovascular, or renal conditions).
C. The member has severe venous access issues that require the use of a special intervention only available in the outpatient hospital setting.
D. The member has significant behavioral issues and/or physical or cognitive impairment that would impact the safety of the infusion therapy AND the patient does not have access to a caregiver.
E. The member is less than 14 years of age.

For situations where administration of Lemtrada does not meet the criteria for outpatient hospital infusion, coverage for Lemtrada is provided when administered in alternative sites such as; physician office or ambulatory care. Lemtrada is not indicated for home infusion.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the site of care prior authorization review (where applicable):

A. Medical records supporting the member has experienced an adverse reaction that did not respond to conventional interventions or a severe adverse event during or immediately after an infusion
B. Medical records supporting the member is medically unstable
C. Medical records supporting the member has severe venous access issues that require specialized interventions only available in the outpatient hospital setting
D. Medical records supporting the member has behavioral issues and/or physical or cognitive impairment and no access to a caregiver

Section 3: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

LEMTRADA (alemtuzumab)

POLICY

III. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Lemtrada is indicated for the treatment of patients with relapsing forms of multiple sclerosis (MS), to include relapsing-remitting disease and active secondary progressive disease, in adults. Because of its safety profile, the use of Lemtrada should generally be reserved for patients who have had an inadequate response to two or more drugs indicated for the treatment of MS.

Limitations of Use: Lemtrada 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.

IV. PRESCRIBER SPECIALTIES

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

V. CRITERIA FOR APPROVAL

A. First Course – Relapsing forms of multiple sclerosis
Authorization of 30 days (5 doses) may be granted to members with a diagnosis of a relapsing form of multiple sclerosis (including relapsing-remitting and secondary progressive disease for those who continue to experience relapse) who have had an inadequate response to two or more drugs indicated for multiple sclerosis.

B. Subsequent Courses – Relapsing forms of multiple sclerosis
Authorization of 30 days (3 doses) may be granted to members with a diagnosis of a relapsing form of multiple sclerosis (including relapsing-remitting and secondary progressive disease for those who continue to experience relapse) who have completed at least one previous course of therapy and treatment will start at least 12 months after the last dose of the prior treatment course.

VI. OTHER CRITERIA

A. Members will not use Lemtrada 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.

REFERENCES:

SECTION 1
1. Lemtrada [package insert]. Cambridge, MA: Genzyme Corporation; August 2022.
2. Ocrevus [package insert]. South San Francisco, CA: Genentech, Inc.; August 2022.
3. Tysabri [package insert]. Cambridge, MA: Biogen Inc; June 2022.

SECTION 2
1. Lemtrada [package insert]. Cambridge, MA: Genzyme Corporation; January 2023.

2. Caon C, Namey M, Meyer C, et al. Prevention and Management of Infusion-Associated Reactions in the Comparison of Alemtuzumab and Rebif((R)) Efficacy in Multiple Sclerosis (CARE-MS) Program. *Int J MS Care.* 2015;17(4):191-198.

SECTION 3

1. Lemtrada [package insert]. Cambridge, MA: Genzyme Corporation; January 2023.

Reference number(s)
5116-A

SPECIALTY GUIDELINE MANAGEMENT

LEQVIO (inclisiran)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Leqvio is indicated as an adjunct to diet and maximally tolerated statin therapy for the treatment of adults with heterozygous familial hypercholesterolemia (HeFH) or clinical atherosclerotic cardiovascular disease (ASCVD), who require additional lowering of low-density lipoprotein cholesterol (LDL-C).

Limitations of Use
The effect of Leqvio 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 and continuation requests. The level must be dated within six months preceding the authorization request.
B. For heterozygous familial hypercholesterolemia: genetic testing or medical records confirming the diagnosis of HeFH including untreated (before any lipid lowering therapy) LDL-C level.
C. For clinical atherosclerotic cardiovascular disease (ASCVD), chart notes confirming 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 all of the following criteria are met:
1. Member has a history of clinical ASCVD (See Appendix A)
2. At least one of the following criteria are met:
   i. Member has a current LDL-C level ≥ 70 mg/dL after at least three months of treatment with a high-intensity statin. If the member is unable to tolerate a high-intensity statin dose, a moderate-intensity statin dose may be used.
   ii. Member has a current LDL-C level ≥ 70 mg/dL with a contraindication or intolerance to statins (See Appendix B and C).
3. Member will continue to receive concomitant statin therapy if no contraindication or intolerance. (See Appendix B and C).

B. Heterozygous familial hypercholesterolemia (HeFH)

Authorization of 6 months may be granted for treatment of heterozygous familial hypercholesterolemia (HeFH) when all of the following criteria are met:

1. Member has a history of HeFH with a diagnosis confirmed by either of the following criteria:
   i. An LDL-receptor mutation, familial defective apo B-100, or a PCSK9 mutation
   ii. A documented history of untreated LDL-C of > 190mg/dL and meets at least one of the following criteria:
      a. Presence of tendon xanthoma(s) in the member or first/second-degree relative
      b. Family history of myocardial infarction (MI) at < 60 years in first degree relative or < 50 years in second degree relative
      c. Family history of total cholesterol (TC) > 290 mg/dL in a first/second degree relative
2. At least one of the following criteria are met:
   i. Member has a current LDL-C level ≥ 100 mg/dL after at least three months of treatment with a high-intensity statin. If the member is unable to tolerate a high-intensity statin dose, a moderate-intensity statin dose may be used.
   ii. Member has a current LDL-C level ≥ 100 mg/dL with a contraindication or intolerance to statins. (See Appendix B and C).
3. Member will continue to receive concomitant statin therapy if no contraindication or intolerance. (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 when all of the following criteria are met:

A. Member has achieved or maintained an LDL-C reduction (e.g., LDL-C is now at goal, robust lowering of LDL-C).
B. Member will continue to receive concomitant statin therapy if no contraindication or intolerance. (See Appendix B and 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 (PAD) 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

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CVS/caremark

POLICY Document for LEUKINE (sargramostim)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, and overall, clinically appropriate use. This document provides specific information to both sections of the overall policy.

Section 1: Preferred Product
- Policy information specific to preferred medications

Section 2: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 1: Preferred Product

EXCEPTIONS CRITERIA
Colony Stimulating Factors – Short Acting

PREFERRED PRODUCTS: NIVESTYM, RELEUKO AND ZARXIO

POLICY
This policy informs prescribers of preferred products and provides an exception process for targeted products through prior authorization.

I. PLAN DESIGN SUMMARY

This program applies to the short-acting colony stimulating factor products specified in this policy. Coverage for targeted products is provided based on clinical circumstances that would exclude the use of the preferred products and may be based on previous use of a product. The coverage review process will ascertain situations where a clinical exception can be made. This program applies to all members requesting treatment with Granix or Neupogen and for members who are new to treatment with Leukine for the first time.

Each referral is reviewed based on all utilization management (UM) programs implemented for the client.

Table. Colony Stimulating Factors – Short Acting

	Product(s)
Preferred*	• **Nivestym** (filgrastim-aafi) • **Releuko** (filgrastim-ayow) • **Zarxio** (filgrastim-sndz)
Targeted	• **Granix** (TBO-filgrastim) • **Leukine** (sargramostim) • **Neupogen** (filgrastim)

*: Medications considered formulary or preferred on your plan may still require a clinical prior authorization review.

II. EXCEPTION CRITERIA

A. Coverage for the targeted products, Neupogen or Granix, is provided when one of the following criteria is met:

1. Member has had a documented intolerable adverse event to all of the preferred products and the adverse event was not an expected adverse event attributed to the active ingredient as described in the prescribing information (i.e., known adverse reaction for both the reference products and biosimilar products)
2. Member has a documented latex allergy and the prescriber states that the member must use latex-free products (Neupogen vial, Granix pre-filled syringe, or Granix vial) and the member has had an intolerable adverse effect to Nivestym and Releuko.
3. Neupogen or Granix are requested for doses less than 180 mcg and the member has had an intolerable adverse effect to Nivestym.

B. Coverage for the targeted product, Leukine, is provided when one of the following criteria is met:
1. Member has had a documented inadequate response or an intolerable adverse event to one of the preferred products.
2. Leukine is being requested for an indication that is not FDA-approved for the preferred product.
3. Member is currently receiving treatment with Leukine, excluding when the requested targeted product is obtained as samples or via manufacturer's patient assistance programs.

Section 2: Clinical Criteria

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)
1661-A

SPECIALTY GUIDELINE MANAGEMENT

FUSILEV (levoleucovorin) powder/solution
KHAPZORY (levoleucovorin) powder
levoleucovorin 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 Indications
   1. Levoleucovorin/Fusilev/Khapzory is indicated for rescue after high-dose methotrexate therapy in osteosarcoma.
   2. Levoleucovorin/Fusilev/Khapzory is indicated for diminishing the toxicity associated with overdosage of folic acid antagonists or impaired methotrexate elimination.
   3. Levoleucovorin/Fusilev/Khapzory is indicated for use in combination with fluorouracil for treatment of metastatic colorectal cancer.

B. Compendial Uses
   1. Rescue treatment after high-dose methotrexate therapy
   2. Combination with fluorouracil-based chemotherapy regimens

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

II. CRITERIA FOR INITIAL APPROVAL

Authorization of 3 months may be granted for any of the settings listed below when leucovorin is not an appropriate/available option at this time:
1. Rescue treatment after high-dose methotrexate therapy
2. Treatment of a folate antagonist overdose or impaired methotrexate elimination
3. Combination therapy with fluorouracil-based chemotherapy regimens

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

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POLICY Document for LIBTAYO (cemiplimab-rwlc)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, and overall, clinically appropriate use. This document provides specific information to both sections of the overall policy.

Section 1: Site of Care
- Policy information specific to site of care (outpatient, hospital outpatient, home infusion)

Section 2: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 3: Oncology Clinical Policy
- Policy information specific to regimen review per NCCN Guidelines.

Section 1: Site of Care

CareFirst Site of Care Criteria
Administration of Intravenous Checkpoint Inhibitors
Bavencio, Imfinzi, Jemperli, Keytruda, Libtayo, Opdivo, Opdualag, Tecentriq, Yervoy and Zynyz

POLICY

I. CRITERIA FOR APPROVAL FOR ADMINISTRATION IN OUTPATIENT HOSPITAL SETTING

This policy provides coverage for administration of a checkpoint inhibitor in an outpatient hospital setting for the initial 6 months approval and up to 45 days for renewal of therapy.

This policy provides coverage for administration of a checkpoint inhibitor in an outpatient hospital setting for a longer course of treatment when ANY of the following criteria are met:

A. The member has experienced an adverse reaction that did not respond to conventional interventions (eg, acetaminophen, steroids, diphenhydramine, fluids, other pre-medications or slowing of infusion rate) or a severe adverse event (anaphylaxis, anaphylactoid reactions, myocardial infarction, thromboembolism, or seizures) during or immediately after an infusion or has experienced severe toxicity requiring continuous monitoring (e.g. Grade 2-4 bullous dermatitis, transaminitis, pneumonitis, Stevens-Johnson syndrome, acute pancreatitis, primary adrenal insufficiency aseptic meningitis, encephalitis, transverse myelitis, myocarditis, pericarditis, arrhythmias, impaired ventricular function, conduction abnormalities).
B. The member is medically unstable (eg respiratory, cardiovascular, or renal conditions).
C. The member has severe venous access issues that require the use of a special interventions only available in the outpatient hospital setting.
D. The member has significant behavioral issues and/or physical or cognitive impairment that would impact the safety of the infusion therapy AND the patient does not have access to a caregiver.
E. The member is receiving provider administered combination chemotherapy.
F. The member is less than 14 years of age.

For situations where administration of a checkpoint inhibitor does not meet the criteria for outpatient hospital infusion, coverage for a checkpoint inhibitor is provided when administered in alternative sites such as physician office, home infusion or ambulatory care.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the site of care prior authorization review (where applicable):

A. Medical records supporting the member has experienced an adverse reaction that did not respond to conventional interventions or a severe adverse event during or immediately after an infusion or a severe toxicity requiring continuous monitoring
B. Medical records supporting the member is medically unstable
C. Medical records supporting the member has severe venous access issues that require specialized interventions only available in the outpatient hospital setting
D. Medical records supporting the member has behavioral issues and/or physical or cognitive impairment and no access to a caregiver
E. Medical records supporting the member is receiving provider administered combination therapy.

Section 2: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

LIBTAYO (cemiplimab-rwlc)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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. Cutaneous Squamous Cell Carcinoma (CSCC)
      Libtayo is indicated for the treatment of patients with metastatic CSCC or locally advanced CSCC who are not candidates for curative surgery or curative radiation.
   2. Basal Cell Carcinoma (BCC)
      a. Libtayo is indicated for the treatment of patients with locally advanced BCC previously treated with a hedgehog pathway inhibitor or for whom a hedgehog pathway inhibitor is not appropriate.
      b. Libtayo is indicated for the treatment of patients with metastatic BCC previously treated with a hedgehog pathway inhibitor or for whom a hedgehog pathway inhibitor is not appropriate.
   3. Non-Small Cell Lung Cancer (NSCLC)
      a. Libtayo, as a single agent, is indicated for the first-line treatment of adult patients with non-small cell lung cancer (NSCLC) whose tumors have high PD-L1 expression [Tumor Proportion Score (TPS) ≥ 50%] as determined by an FDA-approved test, with no EGFR, ALK or ROS1 aberrations, and is:
         i. locally advanced where patients are not candidates for surgical resection or definitive chemoradiation or
         ii. metastatic
      b. Libtayo, in combination with platinum-based chemotherapy, is indicated for the first-line treatment of adult patients with NSCLC with no EGFR, ALK, or ROS1 aberrations and is:
         i. locally advanced where patients are not candidates for surgical resection or definitive chemoradiation or
         ii. metastatic

B. Compendial Uses
   1. Squamous cell skin cancer
   2. Basal cell skin cancer
   3. Non-small cell lung cancer

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

II. EXCLUSIONS

Coverage will not be provided for members who have experienced disease progression while on programmed death receptor-1 (PD-1) or programmed death ligand 1 (PD-L1) inhibitor therapy.

III. DOCUMENTATION

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

A. Documentation of programmed death ligand 1 (PD-L1) tumor expression, where applicable.
B. Documentation of molecular testing for EGFR, ALK, and ROS1 genomic tumor aberrations, where applicable.

IV. CRITERIA FOR INITIAL APPROVAL

A. Cutaneous Squamous Cell Carcinoma (CSCC)

Authorization of 6 months may be granted for treatment of cutaneous squamous cell carcinoma when all of the following criteria are met:

1. The disease is one of the following:
    a. Metastatic
    b. Locally advanced
    c. Recurrent
    d. Regional and inoperable or incompletely resected
2. The member is not a candidate for curative surgery or curative radiation
3. The requested medication will be used as a single agent

B. Basal Cell Carcinoma (BCC)

Authorization of 6 months may be granted for single-agent treatment of advanced, recurrent, or metastatic basal cell carcinoma in members who have received a hedgehog pathway inhibitor (e.g., vismodegib [Erivedge], sonidegib [Odomzo]) or for whom a hedgehog pathway inhibitor is not appropriate.

C. Non-Small Cell Lung Cancer (NSCLC)

1. Authorization of 6 months may be granted for treatment of non-small cell lung cancer as a single agent when all of the following criteria are met:
    a. The requested medication will be used as either:
        i. First-line treatment, or
        ii. Maintenance therapy if there is tumor response or stable disease following first-line cemiplimab-rwlc therapy
    b. The tumor has high PD-L1 expression [Tumor Proportion Score (TPS) $\geq$ 50%]
    c. The tumor does not have EGFR exon 19 deletions or L858R mutations, ALK rearrangements, or ROS1 aberrations, unless testing is not feasible due to insufficient tissue
    d. The disease is advanced, recurrent, or metastatic

2. Authorization of 6 months may be granted for treatment of NSCLC when used in combination with platinum-based chemotherapy and all of the following criteria are met:
    a. The requested medication will be used as first-line treatment
    b. The tumor does not have EGFR, ALK, and ROS1 aberrations, unless testing is not feasible due to insufficient tissue

c. The disease is advanced or metastatic

V. CONTINUATION OF THERAPY

Authorization of 6 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.

Section 3: Oncology Clinical Policy

Oncology Clinical Policy

Program Description

The National Comprehensive Care Network® (NCCN®) is an alliance of leading cancer centers devoted to patient care, research and education dedicated to improving the quality, effectiveness and efficiency of cancer care so patients can live better lives.[1] It is comprised of oncology experts who convene regularly to establish the best treatments for patients. NCCN develops various resources for use by stakeholders in the health care delivery system. These resources include, but are not limited to, the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®), the NCCN Drugs & Biologics Compendium (NCCN Compendium®) and the NCCN Chemotherapy Order Templates (NCCN Templates®).

NCCN templates are based on NCCN Clinical Practice Guidelines and NCCN Compendium. The NCCN Compendium lists the appropriate drugs and biologics for specific cancers using U.S. Food and Drug Administration (FDA)-approved disease indications and specific NCCN panel recommendations. Each recommendation is supported by a level of evidence category.

NCCN Categories of Evidence and Consensus[2]

a. Category 1: Based on high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
b. Category 2A: Based on lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
c. Category 2B: Based on lower-level evidence, there is NCCN consensus that the intervention is appropriate.
d. Category 3: Based any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

Policy for Regimen Prior Authorization

A regimen prior authorization allows submission of a single prior authorization request for all oncology drugs or biologics within an NCCN template that require prior authorization.

This policy provides coverage of a regimen review when *all* of the following criteria are met:

a. Regimen prior authorization reviews, based on NCCN templates, are initiated through the provider portal: https://provider.carefirst.com/providers/home.page
b. If the prior authorization request is submitted via phone or fax, each drug or biologic will need to be submitted and reviewed as a separate prior authorization request for review with drug-specific criteria.
c. The prior authorization review is requested for an oncology drug or biologic that requires prior authorization on the medical benefit.
d. The indication is for a cancer that is eligible for regimen review. Currently, the cancer types in scope for regimen review include breast, lung, colon and rectal cancer.
e. The member is eligible for regimen review.

In addition, the following criteria must be met for approval:

a. The requested regimen for the drug(s) or biologic(s) and indication is consistent with an NCCN recommendation with a level of evidence category of 1 or 2A.
b. The NCCN template must be accepted by the provider without modification.

Authorizations may be granted for 12 months.
Further review may be indicated where the above criteria are not met.

Continuation of Therapy

To submit a request for continuation of therapy, a new regimen prior authorization review must be requested. Upon template selection, the template must be modified to include the appropriate therapies being used for maintenance treatment. The regimen request will be submitted for further review.

Dosage and Administration

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

REFERENCES:

SECTION 1

1. Opdivo [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; February 2023.
2. Bavencio [package insert]. Rockland, MA: EMD Serono, Inc; July 2020.
3. Imfinzi [prescribing information]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; November 2022.
4. Jemperli [prescribing information]. Philadelphia, PA: GlaxoSmithKline LLC; February 2023.
5. Keytruda [prescribing information]. Rahway, NJ: Merck Sharp & Dome LLC.; April 2023.
6. Libtayo [prescribing information]. Tarrytown, NY: Regeneron Pharmaceuticals, Inc.; April 2023.
7. Tecentriq [package insert]. South San Francisco, CA: Genentech, Inc.; December 2022.
8. Yervoy [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; February 2023.
9. Opdualag [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; March 2022.
10. Zynyz [package insert]. Wilmington, DE: Incyte Corporation; March 2023.

SECTION 2

1. Libtayo [package insert]. Tarrytown, NY: Regeneron Pharmaceuticals, Inc.; November 2022.
2. The NCCN Drugs & Biologics Compendium® © 2022 National Comprehensive Cancer Network, Inc. Available at: https://www.nccn.org. Accessed November 4, 2022.

SECTION 3

1. National Comprehensive Cancer Network. About NCCN website. https://www.nccn.org/about/default.aspx, accessed September 16, 2019.
2. National Comprehensive Cancer Network. NCCN Categories of Evidence and Consensus website. https://www.nccn.org/professionals/physician_gls/categories_of_consensus.aspx, accessed September 16, 2019.
3. National Comprehensive Cancer Network. NCCN Guidelines website. http://www.nccn.org/professionals/physician_gls/f_guidelines.asp, accessed September 16, 2019. *(Note: An account may be required.)*
4. National Comprehensive Cancer Network. NCCN Drugs and Biologics Compendium® website. http://www.nccn.org/professionals/drug_compendium/content/contents.asp, accessed September 16, 2019. *(Note: A subscription may be required.)*

5. National Comprehensive Cancer Network. NCCN Chemotherapy Order Templates (NCCN Templates) website. https://www.nccn.org/professionals/OrderTemplates/Default.aspx, accessed September 16, 2019. *(Note: A subscription may be required.)*

POLICY Document for
LUCENTIS (ranibizumab)
BYOOVIZ (ranibizumab-nuna)
CIMERLI (ranibizumab-eqrn)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, and overall, clinically appropriate use. This document provides specific information to both sections of the overall policy.

Section 1: Preferred Product
- Policy information specific to preferred medications

Section 2: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 1: Preferred Product

EXCEPTIONS CRITERIA
VEGF INHIBITORS FOR OCULAR INDICATIONS

PREFERRED PRODUCTS: AVASTIN, BYOOVIZ

POLICY
This policy informs prescribers of preferred products and provides an exception process for targeted products through prior authorization.

I. PLAN DESIGN SUMMARY

This program applies to the VEGF inhibitor ocular products specified in this policy. Coverage for targeted products is provided based on clinical circumstances that would exclude the use of the preferred product and may be based on previous use of a product. The coverage review process will ascertain situations where a clinical exception can be made. For Lucentis, this program applies to all members requesting treatment with a targeted product. For Eylea, this program applies to members who are new to treatment with a targeted product for the first time for an ocular indication.

Each referral is reviewed based on all utilization management (UM) programs implemented for the client.

Table. VEGF Inhibitors for Ocular indications

	Product(s)
Preferred*	• **Avastin** (bevacizumab) • **Byooviz** (ranibizumab-nuna)
Targeted	• **Eylea** (aflibercept) • **Lucentis** (ranibizumab)

*: Medications considered formulary or preferred on your plan may still require a clinical prior authorization review.

II. EXCEPTION CRITERIA

This program applies to members requesting treatment for ocular indications.

A. Eylea

Coverage of the targeted product Eylea is provided when any of the following criteria is met:

1. Member is currently receiving treatment with a targeted product, excluding when the requested targeted product is obtained as samples or via manufacturer's patient assistance programs.
2. Member has a documented inadequate response or intolerable adverse event with both preferred products, Avastin and Byooviz.

B. Lucentis

Coverage for the targeted product Lucentis is provided when both of the following criteria are met:

1. Member has failed treatment with the preferred product Byooviz due to a documented intolerable adverse event that was NOT an expected adverse event attributed to the active ingredient as described in the prescribing information (i.e., known adverse reaction for both products).
2. Member has a documented inadequate response or intolerable adverse event with the preferred product, Avastin.

Section 2: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

LUCENTIS (ranibizumab)
BYOOVIZ (ranibizumab-nuna)
CIMERLI (ranibizumab-eqrn)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Lucentis, Byooviz and Cimerli are indicated for:

1. Neovascular (wet) age-related macular degeneration
2. Macular edema following retinal vein occlusion
3. Myopic choroidal neovascularization

Lucentis and Cimerli are also indicated for:

1. Diabetic macular edema
2. Diabetic retinopathy

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

II. CRITERIA FOR INITIAL APPROVAL

A. Diabetic Macular Edema

Authorization of 6 months may be granted for treatment of diabetic macular edema.

B. Neovascular (Wet) Age-Related Macular Degeneration
Authorization of 6 months may be granted for treatment of neovascular (wet) age-related macular degeneration.

C. Macular Edema Following Retinal Vein Occlusion
Authorization of 6 months may be granted for treatment of macular edema following retinal vein occlusion.

D. Diabetic Retinopathy
Authorization of 6 months may be granted for treatment of diabetic retinopathy.

E. Myopic Choroidal Neovascularization
Authorization of 6 months may be granted for treatment of myopic choroidal neovascularization.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment of an indication listed in Section II for members who have demonstrated a positive clinical response to therapy (e.g., improvement or maintenance in best corrected visual acuity [BCVA] or visual field, or a reduction in the rate of vision decline or the risk of more severe vision loss).

REFERENCES:

SECTION 1

1. Avastin [package insert]. South San Francisco, CA: Genentech, Inc.; December 2020.
2. Eylea [package insert]. Tarrytown, NY: Regeneron Pharmaceuticals, Inc.; August 2022.
3. Lucentis [package insert]. San Francisco, CA: Genentech, Inc.; March 2018.
4. Byooviz (ranibizumab) [package insert]. Cambridge, MA: Biogen Inc; June 2022

SECTION 2

1. Lucentis [package insert]. South San Francisco, CA: Genentech, Inc.; March 2018.
2. American Academy of Ophthalmology Retinal/Vitreous Panel. Preferred Practice Pattern® Guidelines. Age-Related Macular Degeneration. San Francisco, CA: American Academy of Ophthalmology; 2019. Available at: https://www.aao.org/preferred-practice-pattern/age-related-macular-degeneration-ppp.
3. American Academy of Ophthalmology Retinal/Vitreous Panel. Preferred Practice Pattern® Guidelines. Diabetic Retinopathy. San Francisco, CA: American Academy of Ophthalmology; 2019. Available at: https://www.aao.org/preferred-practice-pattern/diabetic-retinopathy-ppp.
4. American Academy of Ophthalmology Retinal/Vitreous Panel. Preferred Practice Pattern® Guidelines. Retinal Vein Occlusions. San Francisco, CA: American Academy of Ophthalmology; 2019. Available at: https://www.aao.org/preferred-practice-pattern/retinal-vein-occlusions-ppp.
5. Byooviz [package insert]. Cambridge, MA: Biogen, Inc.; September 2021.
6. Cimerli [package insert]. Redwood City, CA: Coherus BioSciences, Inc.; August 2022.

CVS/caremark

POLICY Document for LUMIZYME (alglucosidase alfa)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, lower cost site of care and overall, clinically appropriate use. This document provides specific information to each of the three sections of the overall policy.

Section 1: Site of Care

- Policy information specific to site of care (outpatient, hospital outpatient, home infusion)

Section 2: Clinical Criteria

- Policy information specific to the clinical appropriateness for the medication

Section 1: Site of Care

CareFirst Site of Care Criteria
Administration of Intravenous Lumizyme

POLICY

I. CRITERIA FOR APPROVAL FOR ADMINISTRATION IN OUTPATIENT HOSPITAL SETTING

This policy provides coverage for administration of Lumizyme in an outpatient hospital setting for up to 106 days when a member is new to therapy or is reinitiating therapy after not being on therapy for at least 6 months.

This policy provides coverage for administration of Lumizyme in an outpatient hospital setting for a longer course of treatment when ANY of the following criteria are met:

A. The member has experienced an adverse reaction to the drug that did not respond to conventional interventions (eg, acetaminophen, steroids, diphenhydramine, fluids, other pre-medications or slowing of infusion rate) or a severe adverse event (anaphylaxis, anaphylactoid reactions, myocardial infarction, thromboembolism, or seizures) during or immediately after an infusion.
B. The member has developed laboratory confirmed alglucosidase alfa antibodies which increases the risk for infusion related reactions
C. The member is medically unstable (eg respiratory, cardiovascular, or renal conditions).
D. The member has severe venous access issues that require the use of special interventions only available in the outpatient hospital setting.
E. The member has significant behavioral issues and/or physical or cognitive impairment that would impact the safety of the infusion therapy AND the patient does not have access to a caregiver.
F. The member is less than 14 years of age.

For situations where administration of Lumizyme does not meet the criteria for outpatient hospital infusion, coverage for Lumizyme is provided when administered in alternative sites such as; physician office, home infusion or ambulatory care.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the site of care prior authorization review (where applicable):

A. Medical records supporting the member has experienced an adverse reaction that did not respond to conventional interventions or a severe adverse event during or immediately after an infusion

B. Medical records supporting the member has developed alglucosidase alfa antibodies
C. Medical records supporting the member is medically unstable
D. Medical records supporting the member has severe venous access issues that requires specialized interventions only available in the outpatient hospital setting
E. Medical records supporting the member has behavioral issues and/or physical or cognitive impairment and no access to a caregiver

Section 2: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

LUMIZYME (alglucosidase 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
Lumizyme is indicated for patients with Pompe disease (acid alpha-glucosidase [GAA] 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: acid alpha-glucosidase enzyme assay or genetic testing results supporting diagnosis.
B. Continuation requests: chart notes documenting a positive response to therapy (e.g., improvement stabilization, or slowing of disease progression for motor function, walking capacity, cardiorespiratory function, decrease in left ventricular mass index [LVMI], delay in death).

III. CRITERIA FOR INITIAL APPROVAL

Pompe disease
Authorization of 12 months may be granted for treatment of Pompe disease when the diagnosis of Pompe disease was confirmed by enzyme assay demonstrating a deficiency of acid alpha-glucosidase enzyme activity or by genetic testing.

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., improvement, stabilization, or slowing of disease progression for motor function, walking capacity, cardiorespiratory function, decrease in left ventricular mass index (LVMI), delay in death).

REFERENCES

SECTION 1

1. Lumizyme [package insert]. Cambridge, MA: Genzyme Corporation; May 2022.
2. Nicolino M, Byrne B, Wraith JE, et al. Clinical outcomes after long-term treatment with alglucosidase alfa in infants and children with advanced Pompe disease. *Genet Med.* 2009;11(3):210-219.
3. Kishnani PS, Corzo D, Leslie ND, et al. Early treatment with alglucosidase alpha prolongs long-term survival of infants with Pompe disease. *Pediatr Res.* 2009;66(3):329-335.
4. van der Ploeg AT, Clemens PR, Corzo D, et al. A randomized study of alglucosidase alfa in late-onset Pompe's disease. *N Engl J Med.* 2010;362(15):1396-1406.

SECTION 2

5. Lumizyme [package insert]. Cambridge, MA: Genzyme Corporation; February 2020.

Reference number(s)
2739-A

SPECIALTY GUIDELINE MANAGEMENT

LUMOXITI (moxetumomab pasudotox-tdfk)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Lumoxiti is indicated for the treatment of adult patients with relapsed or refractory hairy cell leukemia (HCL) who received at least two prior systemic therapies, including treatment with a purine nucleoside analog (PNA).

Limitations of use
Lumoxiti is not recommended in patients with severe renal impairment (CrCl≤29 mL/min).

B. Compendial Uses
Hairy cell leukemia

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

II. CRITERIA FOR INITIAL APPROVAL

Hairy Cell Leukemia
Authorization of 6 months may be granted for treatment of relapsed or refractory hairy cell leukemia as a single agent when all of the following criteria are met:
A. Member has received at least two prior systemic therapies, including treatment with a purine nucleoside analog.
B. Member has not previously received 6 or more cycles of treatment with the requested medication.

III. CONTINUATION OF THERAPY

Authorization of up to 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. Member will receive a maximum of 6 cycles with the requested medication.
B. There is no evidence of disease progression or an unacceptable toxicity while on the current regimen.

IV. REFERENCES

1. Lumoxiti [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; February 2022.
2. The NCCN Drugs & Biologics Compendium 2022 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed May 31, 2022.

Reference number(s)
1994-A

SPECIALTY GUIDELINE MANAGEMENT

LUPANETA PACK-1 Month 3.75 mg
LUPANETA PACK-3 Month 11.25 mg
(leuprolide acetate for depot suspension/norethindrone 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
Lupaneta Pack is indicated for initial management of the painful symptoms of endometriosis and for management of recurrence of symptoms.

Limitations of Use:
Duration of use is limited due to concerns about adverse impact on bone mineral density. The initial treatment course of Lupaneta Pack is limited to six months. A single retreatment course of not more than six months may be administered after the initial course of treatment if symptoms recur. Use of Lupaneta Pack for longer than a total of 12 months is not recommended.

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

II. CRITERIA FOR INITIAL APPROVAL

Endometriosis
Authorization of up to 6 months (one treatment course) may be granted to members for initial treatment of endometriosis.

III. CONTINUATION OF THERAPY

Endometriosis
Authorization of up to 6 months (for a lifetime maximum of 12 months total) may be granted for retreatment of endometriosis when all of the following criteria are met:
A. The member has had a recurrence of symptoms
B. The member has a bone mineral density within normal limits

IV. REFERENCES

1. Lupaneta Pack [package insert]. North Chicago, IL: AbbVie Inc.; June 2015.

CVS caremark®

POLICY Document for
LUPRON DEPOT 3.75 mg
LUPRON DEPOT-3 Month 11.25 mg
(leuprolide acetate for depot suspension)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, and overall, clinically appropriate use. This document provides specific information to both sections of the overall policy.

Section 1: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 2: Oncology Clinical Policy
- Policy information specific to regimen review per NCCN Guidelines.

Section 1: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

LUPRON DEPOT 3.75 mg
LUPRON DEPOT-3 Month 11.25 mg
(leuprolide acetate for depot 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.

A. FDA-Approved Indications

1. Endometriosis
   Lupron Depot 3.75 mg and Lupron Depot-3 Month 11.25 mg are indicated for management of endometriosis, including pain relief and reduction of endometriotic lesions. Lupron Depot 3.75 mg monthly and Lupron Depot-3 Month 11.25 mg with norethindrone acetate 5 mg daily are also indicated for initial management of the painful symptoms of endometriosis and for management of recurrence of symptoms.

   Use of norethindrone acetate in combination with Lupron Depot 3.75 mg and Lupron Depot 11.25 mg is referred to as add-back therapy, and is intended to reduce the loss of bone mineral density (BMD) and reduce vasomotor symptoms associated with use of Lupron Depot 3.75 mg and Lupron Depot 11.25 mg.

2. Uterine Leiomyomata (Fibroids)
   When used concomitantly with iron therapy, Lupron Depot 3.75 mg and Lupron Depot-3 Month 11.25 mg are indicated for preoperative hematologic improvement of women with anemia caused by fibroids for whom three months of hormonal suppression is deemed necessary. The clinician may wish to consider a one-month trial period on iron alone, as some women will respond to iron alone. Lupron Depot may be added if the response to iron alone is considered inadequate.

   Limitations of Use:

For endometriosis: The total duration of therapy with Lupron Depot 3.75 mg and 11.25 mg plus add-back therapy should not exceed 12 months due to concerns about adverse impact on bone mineral density.

For uterine leiomyomata: Lupron Depot 3.75 mg and 11.25 mg are not indicated for combination use with norethindrone acetate add-back therapy for the preoperative hematologic improvement of women with anemia caused by heavy menstrual bleeding due to fibroids.

B. Compendial Uses
1. Breast cancer
2. Ovarian cancer – Epithelial ovarian cancer/fallopian tube cancer/primary peritoneal cancer, and less common ovarian cancers (grade 1 endometrioid carcinoma, low-grade serous carcinoma, carcinosarcoma [malignant mixed Müllerian tumors], mucinous carcinoma of the ovary, or clear cell carcinoma of the ovary)
3. Recurrent androgen receptor positive salivary gland tumors
4. Gender dysphoria (also known as gender non-conforming or transgender persons)
5. Preservation of ovarian function in patients with cancer
6. Prevention of recurrent menstrual related attacks in acute porphyria

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

II. PRESCRIBER SPECIALTIES

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 patients less than 18 years of age.

III. CRITERIA FOR INITIAL APPROVAL

A. Endometriosis
Authorization of up to 6 months (one treatment course) may be granted to members for initial treatment of endometriosis.

B. Uterine leiomyomata (fibroids)
Authorization of up to 3 months may be granted for initial treatment of uterine leiomyomata (fibroids) when either of the following criteria is met:
1. Member has anemia due to uterine leiomyomata, or
2. Lupron Depot will be used prior to surgery for uterine leiomyomata.

C. Breast cancer
Authorization of 12 months may be granted for treatment of hormone receptor-positive breast cancer.

D. Ovarian cancer
Authorization of 12 months may be granted for treatment of persistent disease or recurrence of any of the following types of ovarian cancer when used as a single agent:
1. Epithelial ovarian cancer
2. Fallopian tube cancer
3. Primary peritoneal cancer
4. Grade 1 endometrioid carcinoma
5. Low-grade serous carcinoma
6. Carcinosarcoma (malignant mixed Müllerian tumors)
7. Mucinous carcinoma of the ovary
8. Clear cell carcinoma of the ovary

E. Salivary gland tumors
Authorization of 12 months may be granted for treatment of recurrent salivary gland tumors when the tumor is androgen receptor positive.

F. Gender dysphoria
1. Authorization of 12 months may be granted for pubertal hormonal suppression in an adolescent member when all of the following criteria are met:
   i. The member has a diagnosis of gender dysphoria.
   ii. The member has reached Tanner stage 2 of puberty or greater.
   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 transition when all of the following criteria are met:
   i. The member has a diagnosis of gender dysphoria.
   ii. The member will receive Lupron Depot concomitantly with gender-affirming hormones.
   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.

G. Preservation of ovarian function in patients with cancer
Authorization of 3 months may be granted for preservation of ovarian function when the member is premenopausal and undergoing chemotherapy.

H. Prevention of recurrent menstrual related attacks in acute porphyria
Authorization of 12 months may be granted for prevention of recurrent menstrual related attacks in members with acute porphyria when the requested medication is prescribed by or in consultation with a physician experienced in the management of porphyrias.

IV. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria in addition to the following diagnosis-specific criteria (if applicable).

A. Endometriosis
Authorization of up to 6 months (for a lifetime maximum of 12 months total) may be granted for retreatment of endometriosis when all of the following criteria are met:
1. The member has had a recurrence of symptoms.
2. The member has a bone mineral density within normal limits.

B. Uterine leiomyomata (fibroids)
Authorization of up to 3 months (for a lifetime maximum of 6 months total) may be granted when either of the following criteria is met:
1. Member has anemia due to uterine leiomyomata, or
2. Lupron Depot will be used prior to surgery for uterine leiomyomata.

C. Breast cancer, ovarian cancer, and salivary gland tumors
Authorization of 12 months may be granted for continued treatment of breast cancer, ovarian cancer, and salivary gland tumors in members requesting reauthorization when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

D. Gender dysphoria
1. Authorization of 12 months may be granted for continued treatment for pubertal hormonal suppression in adolescent members requesting reauthorization when all of the following criteria are met:

a. The member has a diagnosis of gender dysphoria.
b. The member has previously reached Tanner stage 2 of puberty or greater.
c. The member's comorbid conditions are reasonably controlled.
d. The member has been educated on any contraindications and side effects to therapy.
e. 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 transition in members requesting reauthorization when all of the following criteria are met:
   i. The member has a diagnosis of gender dysphoria.
   ii. The member will receive Lupron Depot concomitantly with gender-affirming hormones.
   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.

E. All members (including new members) requesting authorization for continuation of therapy for the specified indications below must meet all initial authorization criteria:

1. Preservation of ovarian function in patients with cancer
2. Prevention of recurrent menstrual related attacks in acute porphyria

Section 2: Oncology Clinical Policy

Oncology Clinical Policy

Program Description

The National Comprehensive Care Network® (NCCN®) is an alliance of leading cancer centers devoted to patient care, research and education dedicated to improving the quality, effectiveness and efficiency of cancer care so patients can live better lives.[1] It is comprised of oncology experts who convene regularly to establish the best treatments for patients. NCCN develops various resources for use by stakeholders in the health care delivery system. These resources include, but are not limited to, the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®), the NCCN Drugs & Biologics Compendium (NCCN Compendium®) and the NCCN Chemotherapy Order Templates (NCCN Templates®).

NCCN templates are based on NCCN Clinical Practice Guidelines and NCCN Compendium. The NCCN Compendium lists the appropriate drugs and biologics for specific cancers using U.S. Food and Drug Administration (FDA)-approved disease indications and specific NCCN panel recommendations. Each recommendation is supported by a level of evidence category.

NCCN Categories of Evidence and Consensus

Category 1: Based on high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2A: Based on lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2B: Based on lower-level evidence, there is NCCN consensus that the intervention is appropriate.
Category 3: Based any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

Policy for Regimen Prior Authorization

A regimen prior authorization allows submission of a single prior authorization request for all oncology drugs or biologics within an NCCN template that require prior authorization.

This policy provides coverage of a regimen review when *all* of the following criteria are met:

a. Regimen prior authorization reviews, based on NCCN templates, are initiated through the provider portal: https://provider.carefirst.com/providers/home.page
b. If the prior authorization request is submitted via phone or fax, each drug or biologic will need to be submitted

and reviewed as a separate prior authorization request for review with drug-specific criteria.

c. 2. The prior authorization review is requested for an oncology drug or biologic that requires prior authorization on the medical benefit.
d. The indication is for a cancer that is eligible for regimen review. Currently, the cancer types in scope for regimen review include breast, lung, colon and rectal cancer.
e. The member is eligible for regimen review.

In addition, the following criteria must be met for approval:

a. The requested regimen for the drug(s) or biologic(s) and indication is consistent with an NCCN recommendation with a level of evidence category of 1 or 2A.
b. The NCCN template must be accepted by the provider without modification.

Authorizations may be granted for 12 months.
Further review may be indicated where the above criteria are not met.

Continuation of Therapy

To submit a request for continuation of therapy, a new regimen prior authorization review must be requested. Upon template selection, the template must be modified to include the appropriate therapies being used for maintenance treatment. The regimen request will be submitted for further review.

Dosage and Administration

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

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POLICY Document for
LUPRON DEPOT 1-Month 7.5 mg
LUPRON DEPOT 3-Month 22.5 mg
LUPRON DEPOT 4-Month 30 mg
LUPRON DEPOT 6-Month 45 mg
(leuprolide acetate for depot suspension)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, and overall, clinically appropriate use. This document provides specific information to both sections of the overall policy.

Section 1: Preferred Product
- Policy information specific to preferred medications

Section 2: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 3: Oncology Clinical Policy
- Policy information specific to regimen review per NCCN Guidelines.

Section 1: Preferred Product

EXCEPTIONS CRITERIA
GONADOTROPIN RELEASING HORMONE AGONISTS

PREFERRED PRODUCT: ELIGARD

POLICY
This policy informs prescribers of preferred products and provides an exception process for targeted products through prior authorization.

I. PLAN DESIGN SUMMARY

This program applies to the gonadotropin releasing hormone agonist products specified in this policy. Coverage for targeted products is provided based on clinical circumstances that would exclude the use of the preferred product and may be based on previous use of a product. The coverage review process will ascertain situations where a clinical exception can be made. This program applies to all members requesting treatment with Camcevi and Lupron Depot. This program also applies to members who are new to treatment with Firmagon, Trelstar, or Zoladex for the first time.

Each referral is reviewed based on all utilization management (UM) programs implemented for the client.

Table. Gonadotropin releasing hormone agonists

	Product(s)
Preferred*	• **Eligard** (leuprolide acetate)
Targeted	• **Camcevi** (leuprolide mesylate) • **Firmagon** (degarelix)

	• **Lupron Depot** (leuprolide acetate for depot suspension) • **Trelstar** (triptorelin) • **Zoladex** (goserelin acetate)

*: Medications considered formulary or preferred on your plan may still require a clinical prior authorization review.

II. EXCEPTION CRITERIA

This program applies to members requesting treatment for prostate cancer.

A. Firmagon, Trelstar, and Zoladex

Coverage for the Firmagon, Trelstar, and Zoladex is provided when any of the following criteria is met:

1. Member is currently receiving treatment with the requested targeted product, excluding when the requested targeted product is obtained as samples or via manufacturer's patient assistance programs.
2. Member has a documented hypersensitivity to the preferred product.

B. Camcevi and Lupron Depot

Coverage for Camcevi and Lupron Depot is provided when the member has a documented hypersensitivity to the preferred product.

Section 2: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

LUPRON DEPOT 1-Month 7.5 mg
LUPRON DEPOT 3-Month 22.5 mg
LUPRON DEPOT 4-Month 30 mg
LUPRON DEPOT 6-Month 45 mg
(leuprolide acetate for depot 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.

A. FDA-Approved Indication
Lupron Depot 1-Month 7.5 mg, Lupron Depot 3-Month 22.5 mg, Lupron Depot 4-Month 30 mg, and Lupron Depot 6-Month 45 mg are indicated in the palliative treatment of advanced prostatic cancer.

B. Compendial Uses
1. Prostate cancer
2. Ovarian Cancer - Malignant sex cord-stromal tumors
3. Recurrent androgen receptor positive salivary gland tumors
4. Gender dysphoria (also known as gender non-conforming or transgender persons)

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

II. PRESCRIBER SPECIALTIES

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 patients less than 18 years of age.

III. CRITERIA FOR INITIAL APPROVAL

A. Prostate cancer

Authorization of 12 months may be granted for treatment of prostate cancer.

B. Gender dysphoria

1. Authorization of 12 months may be granted for pubertal hormonal suppression in an adolescent member when all of the following criteria are met:
   i. The member has a diagnosis of gender dysphoria.
   ii. The member has reached Tanner stage 2 of puberty or greater.
   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 transition when all of the following criteria are met:
   i. The member has a diagnosis of gender dysphoria.
   ii. The member will receive Lupron Depot concomitantly with gender-affirming hormones.
   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.

C. Ovarian cancer

Authorization of 12 months may be granted for treatment of malignant sex cord-stromal tumors (granulosa cell tumors) as a single agent.

D. 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.

IV. CONTINUATION OF THERAPY

A. Salivary gland tumors

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization who are experiencing clinical benefit to therapy and who have not experienced an unacceptable toxicity.

B. Ovarian cancer

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. Prostate cancer

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization 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. Gender dysphoria

1. Authorization of 12 months may be granted for continued treatment for pubertal hormonal suppression 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 has previously reached Tanner stage 2 of puberty or greater.
   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.
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Section 3: Oncology Clinical Policy

Oncology Clinical Policy

Program Description

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authorization on the medical benefit.

d. The indication is for a cancer that is eligible for regimen review. Currently, the cancer types in scope for regimen review include breast, lung, colon and rectal cancer.
e. The member is eligible for regimen review.

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a. The requested regimen for the drug(s) or biologic(s) and indication is consistent with an NCCN recommendation with a level of evidence category of 1 or 2A.
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To submit a request for continuation of therapy, a new regimen prior authorization review must be requested. Upon template selection, the template must be modified to include the appropriate therapies being used for maintenance treatment. The regimen request will be submitted for further review.

Dosage and Administration

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

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5. National Comprehensive Cancer Network. NCCN Chemotherapy Order Templates (NCCN Templates) website. https://www.nccn.org/professionals/OrderTemplates/Default.aspx, accessed September 16, 2019. *(Note: A subscription may be required.)*

Reference number(s)
1972-A

SPECIALTY GUIDELINE MANAGEMENT

Lupron Depot-PED (leuprolide acetate for depot 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.

A. FDA-Approved Indication
Lupron Depot-PED is indicated for the treatment of pediatric patients with central precocious puberty (CPP).

B. Compendial Use
Gender dysphoria (also known as gender non-conforming or transgender persons)

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. PRESCRIBER SPECIALTIES

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 patients less than 18 years of age.

IV. 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. Gender dysphoria

1. Authorization of 12 months may be granted for pubertal hormonal suppression in an adolescent member when all of the following criteria are met:
   i. The member has a diagnosis of gender dysphoria.
   ii. The member has reached Tanner stage 2 of puberty or greater.
   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 transition when all of the following criteria are met:
   i. The member has a diagnosis of gender dysphoria.
   ii. The member will receive Lupron Depot-PED concomitantly with gender-affirming hormones.
   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.

V. CONTINUATION OF THERAPY

A. Central precocious puberty (CPP)

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. Gender dysphoria

1. Authorization of 12 months may be granted for continued treatment for pubertal hormonal suppression 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 has previously reached Tanner stage 2 of puberty or greater.
   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 transition in members requesting reauthorization when all of the following criteria are met:
   i. The member has a diagnosis of gender dysphoria.
   ii. The member will receive Lupron Depot-PED concomitantly with gender-affirming hormones.
   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.

VI. REFERENCES

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Reference number(s)
2513-A

SPECIALTY GUIDELINE MANAGEMENT

LUTATHERA (lutetium Lu 177 dotatate)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Lutathera is indicated for the treatment of somatostatin receptor-positive gastroenteropancreatic neuroendocrine tumors (GEP-NETs), including foregut, midgut, and hindgut neuroendocrine tumors in adults.

B. Compendial Uses
1. Carcinoid syndrome
2. Neuroendocrine tumors (NETs) of the lung and thymus (carcinoid tumors)
3. Pheochromocytoma/paraganglioma
4. Well-differentiated grade 3 NETs with favorable biology

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:
Somatostatin receptor status as detected by somatostatin receptor-based imaging

III. CRITERIA FOR INITIAL APPROVAL

A. Neuroendocrine tumors (NETs)

1. Tumors of the gastrointestinal (GI) tract (carcinoid tumors)
Authorization of 12 months and 4 doses total may be granted for treatment of somatostatin receptor-positive NETs of the gastrointestinal tract when the member has recurrent, locoregional advanced disease and/or distant metastases and one of the following criteria is met:
   i. Member has clinically significant tumor burden, or
   ii. Member experienced disease progression on octreotide or lanreotide.

2. Tumors of the pancreas
Authorization of 12 months and 4 doses total may be granted for treatment of somatostatin receptor-positive NETs of the pancreas when both of the following criteria are met:
   i. Member has symptomatic disease, clinically significant tumor burden, or progressive recurrent, locoregional advanced disease and/or distant metastases.
   ii. Member experienced disease progression on octreotide or lanreotide.

3. Neuroendocrine tumors (NETs) of the lung and thymus (carcinoid tumors)

Authorization of 12 months and 4 doses total may be granted for treatment of somatostatin receptor-positive NETs of the lung and thymus when one of the following criteria are met:

i. Member has recurrent or locoregional unresectable disease and has progressed on octreotide or lanreotide
ii. Member has distant metastatic disease, has experienced progression on octreotide or lanreotide, and meets one of the following criteria:
    a. Clinically significant tumor burden and low grade (typical carcinoid) histology
    b. Evidence of disease progression
    c. Intermediate grade (atypical carcinoid) histology
    d. Symptomatic disease

4. Well-differentiated grade 3 NETs with favorable biology
   Authorization of 12 months and 4 doses total may be granted for treatment of well-differentiated grade 3 unresectable locally advanced or metastatic NETs with favorable biology (e.g., relatively low Ki-67 [less than 55%], positive somatostatin receptor [SSTR]-based PET imaging) when member meets one of the following criteria:
    i. Clinically significant tumor burden, or
    ii. Evidence of disease progression

B. Carcinoid Syndrome

Authorization of 12 months and 4 doses total may be granted for treatment of poorly controlled carcinoid syndrome when all of the following criteria are met:

1. Member has somatostatin receptor-positive neuroendocrine tumors of the gastrointestinal tract, lung or thymus.
2. Member experienced progression on octreotide or lanreotide.
3. The requested medication will be used in combination with either a) octreotide LAR or lanreotide for persistent symptoms (i.e., flushing, diarrhea) or b) telotristat for persistent diarrhea in combination with octreotide LAR or lanreotide.

C. Pheochromocytoma/paraganglioma

Authorization of 12 months and 4 doses total may be granted for treatment of somatostatin receptor-positive pheochromocytoma/paraganglioma when the member meets one of the following criteria:

1. Member has locally unresectable disease, or
2. Member has distant metastases

IV. REFERENCES

1. Lutathera [package insert]. Millburn, NJ: Advanced Accelerator Applications USA, Inc.; June 2022.
2. The NCCN Drugs & Biologics Compendium® © 2023 National Comprehensive Cancer Network, Inc. Available at: https://www.nccn.org. Accessed January 03, 2023.

Reference number(s)
2458-A

SPECIALTY GUIDELINE MANAGEMENT

LUXTURNA (voretigene neparvovec-rzyl)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Luxturna is indicated for the treatment of patients with confirmed biallelic RPE65 mutation-associated retinal dystrophy. Patients must have viable retinal cells as determined by the treating physician(s).

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 a genetic diagnosis of pathogenic/likely pathogenic biallelic RPE65 gene mutations.

III. CRITERIA FOR INITIAL APPROVAL

Biallelic RPE65 mutation-associated retinal dystrophy
Authorization of 90 days for a one-time administration per eye may be granted for treatment of biallelic RPE65 mutation-associated retinal dystrophy when all of the following criteria are met:

A. The member has bi-allelic pathogenic and/or likely pathogenic RPE65 mutations via genetic testing (single gene test or multi gene panel test if medically necessary).
B. The RPE65 gene mutations classifications are based on the current American College of Medical Genetics and Genomics (ACMG) standards and guidelines for the interpretation of sequence variants.
C. Pathogenic and/or likely pathogenic classification of the RPE65 mutations has been affirmed within the last 12 months.
D. The member is at least 12 months of age but less than 65 years of age.
E. The member has viable retinal cells in each eye to be treated as determined by optical coherence tomography (OCT) and/or ophthalmoscopy; and must have any of the following:
    1. An area of retina within the posterior pole of greater than 100 µm thickness shown on OCT
    2. Greater than or equal to 3 disc areas of retina without atrophy or pigmentary degeneration within the posterior pole
    3. Remaining visual field within 30 degrees of fixation as measured by a III4e isopter or equivalent
F. The member has not received a previous treatment course of Luxturna.

IV. REFERENCES

1. Luxturna [package insert]. Philadelphia, PA: Spark Therapeutics, Inc.; December 2019.

2. Russel S, Bennet J, Wellman JA, et al. Efficacy and safety of voretigene neparvovec (AAV2-hRPE65v2) in patients with RPE65-mediated inherited retinal dystrophy: a randomized, controlled, open-label phase 3 trial. *Lancet 2017*; 390:849-860.
3. Richards S, Aziz N, Bale S, et al; ACMG Laboratory Quality Assurance Committee. Standards and guidelines for the interpretation of sequence variants: A joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology. Genet Med. 2015;17(5):405-24.

Reference number(s)
2909-A

SPECIALTY GUIDELINE MANAGEMENT

MACUGEN (pegaptanib sodium 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
Macugen is indicated for the treatment of neovascular (wet) age-related macular degeneration.

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

II. CRITERIA FOR INITIAL APPROVAL

Neovascular (wet) age-related macular degeneration
Authorization of 6 months may be granted for treatment of neovascular (wet) age-related macular degeneration.

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III. CONTINUATION OF THERAPY

Authorization of 12 months (with a maximum of 2 years of treatment for each eye) may be granted for continued treatment in members requesting reauthorization for neovascular (wet) age-related macular degeneration who have demonstrated a positive clinical response to Macugen therapy (e.g., improvement or maintenance in best corrected visual acuity [BCVA], or visual field, or a reduction in the rate of vision decline or the risk of more severe vision loss).

IV. REFERENCES

1. Macugen [package insert]. Palm Beach Gardens, FL: Eyetech Inc.; July 2016.

Reference number(s)
4405-A

SPECIALTY GUIDELINE MANAGEMENT

MARGENZA (margetuximab-cmkb)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Margenza is indicated, in combination with chemotherapy, for the treatment of adult patients with human epidermal growth factor receptor 2 (HER2)-positive metastatic breast cancer who have received two or more prior anti-HER2 regimens, at least one of which was for metastatic disease.

B. Compendial Uses
Breast cancer

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
Authorization of 12 months may be granted for treatment of HER2-positive recurrent unresectable or metastatic breast cancer, in combination with chemotherapy, for members who have received two or more prior regimens.

IV. CONTINUATION OF THERAPY

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

V. REFERENCES

1. Margenza [package insert]. Rockville, MD: MacroGenics, Inc.; December 2020.
2. The NCCN Drugs & Biologics Compendium 2021 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed December 22, 2021

Reference number(s)
4405-A

POLICY Document for MEKINIST (trametinib)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, and overall, clinically appropriate use. This document provides specific information to both sections of the overall policy.

Section 1: Clinical Criteria

- Policy information specific to the clinical appropriateness for the medication

Section 2: Oncology Clinical Policy

- Policy information specific to regimen review per NCCN Guidelines.

Section 1: Clinical Criteria

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.

Section 2: Oncology Clinical Policy

Oncology Clinical Policy

Program Description

The National Comprehensive Care Network® (NCCN®) is an alliance of leading cancer centers devoted to patient care, research and education dedicated to improving the quality, effectiveness and efficiency of cancer care so patients can live better lives.[1] It is comprised of oncology experts who convene regularly to establish the best treatments for patients. NCCN develops various resources for use by stakeholders in the health care delivery system. These resources include, but are not limited to, the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®), the NCCN Drugs & Biologics Compendium (NCCN Compendium®) and the NCCN Chemotherapy Order Templates (NCCN Templates®).

NCCN templates are based on NCCN Clinical Practice Guidelines and NCCN Compendium. The NCCN Compendium lists the appropriate drugs and biologics for specific cancers using U.S. Food and Drug Administration (FDA)-approved disease indications and specific NCCN panel recommendations. Each recommendation is supported by a level of evidence category.

NCCN Categories of Evidence and Consensus

Category 1: Based on high-level evidence, there is uniform NCCN consensus that the intervention is

appropriate.
Category 2A: Based on lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2B: Based on lower-level evidence, there is NCCN consensus that the intervention is appropriate.
Category 3: Based any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

Policy for Regimen Prior Authorization

A regimen prior authorization allows submission of a single prior authorization request for all oncology drugs or biologics within an NCCN template that require prior authorization.

This policy provides coverage of a regimen review when *all* of the following criteria are met:

a. Regimen prior authorization reviews, based on NCCN templates, are initiated through the provider portal: https://provider.carefirst.com/providers/home.page
b. If the prior authorization request is submitted via phone or fax, each drug or biologic will need to be submitted and reviewed as a separate prior authorization request for review with drug-specific criteria.
c. 2. The prior authorization review is requested for an oncology drug or biologic that requires prior authorization on the medical benefit.
d. The indication is for a cancer that is eligible for regimen review. Currently, the cancer types in scope for regimen review include breast, lung, colon and rectal cancer.
e. The member is eligible for regimen review.

In addition, the following criteria must be met for approval:

a. The requested regimen for the drug(s) or biologic(s) and indication is consistent with an NCCN recommendation with a level of evidence category of 1 or 2A.
b. The NCCN template must be accepted by the provider without modification.

Authorizations may be granted for 12 months.
Further review may be indicated where the above criteria are not met.

Continuation of Therapy

To submit a request for continuation of therapy, a new regimen prior authorization review must be requested. Upon template selection, the template must be modified to include the appropriate therapies being used for maintenance treatment. The regimen request will be submitted for further review.

Dosage and Administration

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

REFERENCES:

SECTION 1

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.

SECTION 2

1. National Comprehensive Cancer Network. About NCCN website. https://www.nccn.org/about/default.aspx, accessed September 16, 2019.
2. National Comprehensive Cancer Network. NCCN Categories of Evidence and Consensus website. https://www.nccn.org/professionals/physician_gls/categories_of_consensus.aspx, accessed September 16, 2019.
3. National Comprehensive Cancer Network. NCCN Guidelines website. http://www.nccn.org/professionals/physician_gls/f_guidelines.asp, accessed September 16, 2019. *(Note: An account may be required.)*
4. National Comprehensive Cancer Network. NCCN Drugs and Biologics Compendium® website. http://www.nccn.org/professionals/drug_compendium/content/contents.asp, accessed September 16, 2019. *(Note: A subscription may be required.)*
5. National Comprehensive Cancer Network. NCCN Chemotherapy Order Templates (NCCN Templates) website. https://www.nccn.org/professionals/OrderTemplates/Default.aspx, accessed September 16, 2019. *(Note: A subscription may be required.)*

POLICY Document for MEKTOVI (binimetinib)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, and overall, clinically appropriate use. This document provides specific information to both sections of the overall policy.

Section 1: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 2: Oncology Clinical Policy
- Policy information specific to regimen review per NCCN Guidelines.

Section 1: Clinical Criteria

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.

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.

Section 2: Oncology Clinical Policy

Oncology Clinical Policy

Program Description

The National Comprehensive Care Network® (NCCN®) is an alliance of leading cancer centers devoted to patient care, research and education dedicated to improving the quality, effectiveness and efficiency of cancer care so patients can live better lives.[1] It is comprised of oncology experts who convene regularly to establish the best treatments for patients. NCCN develops various resources for use by stakeholders in the health care delivery system. These resources include, but are not limited to, the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®), the NCCN Drugs & Biologics Compendium (NCCN Compendium®) and the NCCN Chemotherapy Order Templates (NCCN Templates®).

NCCN templates are based on NCCN Clinical Practice Guidelines and NCCN Compendium. The NCCN Compendium lists the appropriate drugs and biologics for specific cancers using U.S. Food and Drug Administration (FDA)-approved disease indications and specific NCCN panel recommendations. Each recommendation is supported by a level of evidence category.

NCCN Categories of Evidence and Consensus
Category 1: Based on high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2A: Based on lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2B: Based on lower-level evidence, there is NCCN consensus that the intervention is appropriate.
Category 3: Based any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

Policy for Regimen Prior Authorization

A regimen prior authorization allows submission of a single prior authorization request for all oncology drugs or biologics within an NCCN template that require prior authorization.

This policy provides coverage of a regimen review when *all* of the following criteria are met:

a. Regimen prior authorization reviews, based on NCCN templates, are initiated through the provider portal: https://provider.carefirst.com/providers/home.page
b. If the prior authorization request is submitted via phone or fax, each drug or biologic will need to be submitted and reviewed as a separate prior authorization request for review with drug-specific criteria.
c. 2. The prior authorization review is requested for an oncology drug or biologic that requires prior authorization on the medical benefit.
d. The indication is for a cancer that is eligible for regimen review. Currently, the cancer types in scope for regimen review include breast, lung, colon and rectal cancer.
e. The member is eligible for regimen review.

In addition, the following criteria must be met for approval:
a. The requested regimen for the drug(s) or biologic(s) and indication is consistent with an NCCN recommendation with a level of evidence category of 1 or 2A.
b. The NCCN template must be accepted by the provider without modification.

Authorizations may be granted for 12 months.
Further review may be indicated where the above criteria are not met.

Continuation of Therapy

To submit a request for continuation of therapy, a new regimen prior authorization review must be requested. Upon template selection, the template must be modified to include the appropriate therapies being used for maintenance treatment. The regimen request will be submitted for further review.

Dosage and Administration

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

REFERENCES:

SECTION 1

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.

SECTION 2

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2. National Comprehensive Cancer Network. NCCN Categories of Evidence and Consensus website.

https://www.nccn.org/professionals/physician_gls/categories_of_consensus.aspx, accessed September 16, 2019.
3. National Comprehensive Cancer Network. NCCN Guidelines website. http://www.nccn.org/professionals/physician_gls/f_guidelines.asp, accessed September 16, 2019. *(Note: An account may be required.)*
4. National Comprehensive Cancer Network. NCCN Drugs and Biologics Compendium® website. http://www.nccn.org/professionals/drug_compendium/content/contents.asp, accessed September 16, 2019. *(Note: A subscription may be required.)*
5. National Comprehensive Cancer Network. NCCN Chemotherapy Order Templates (NCCN Templates) website. https://www.nccn.org/professionals/OrderTemplates/Default.aspx, accessed September 16, 2019. *(Note: A subscription may be required.)*

POLICY Document for MEPSEVII (vestronidase alfa-vjbk)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, lower cost site of care and overall, clinically appropriate use. This document provides specific information to each of the three sections of the overall policy.

Section 1: Site of Care
- Policy information specific to site of care (outpatient, hospital outpatient, home infusion)

Section 2: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 1: Site of Care

CareFirst Site of Care Criteria
Administration of Intravenous Mepsevii

POLICY

I. CRITERIA FOR APPROVAL FOR ADMINISTRATION IN OUTPATIENT HOSPITAL SETTING

This policy provides coverage for administration of Mepsevii in an outpatient hospital setting for up to 50 days when a member is new to therapy or is reinitiating therapy after not being on therapy for at least 6 months.

This policy provides coverage for administration of Mepsevii in an outpatient hospital setting for a longer course of treatment when ANY of the following criteria are met:

A. The member has experienced an adverse reaction to the drug that did not respond to conventional interventions (eg, acetaminophen, steroids, diphenhydramine, fluids or other pre-medications) or a severe adverse event (anaphylaxis, anaphylactoid reactions, myocardial infarction, thromboembolism, or seizures) during or immediately (including up to 60 minutes) after an infusion.
B. The member is medically unstable (eg respiratory, cardiovascular, or renal conditions).
C. The member has severe venous access issues that require the use of special interventions only available in the outpatient hospital setting.
D. The member has significant behavioral issues and/or physical or cognitive impairment that would impact the safety of the infusion therapy AND the patient does not have access to a caregiver.
E. The member is less than 14 years of age.

For situations where administration of Mepsevii does not meet the criteria for outpatient hospital infusion, coverage for Mepsevii is provided when administered in alternative sites such as; physician office, home infusion or ambulatory care.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the site of care prior authorization review (where applicable):

A. Medical records supporting the member has experienced an adverse reaction that did not respond to conventional interventions or a severe adverse event during or immediately after an infusion
B. Medical records supporting the member is medically unstable

C. Medical records supporting the member has severe venous access issues that requires specialized interventions only available in the outpatient hospital setting
D. Medical records supporting the member has behavioral issues and/or physical or cognitive impairment and no access to a caregiver

Section 2: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

MEPSEVII (vestronidase alfa-vjbk)

POLICY

III. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Mepsevii is indicated in pediatric and adult patients for the treatment of mucopolysaccharidosis VII (MPS VII, Sly syndrome).

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

IV. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
A. Initial requests: beta-glucuronidase enzyme assay or genetic testing results supporting diagnosis.
B. Continuation requests: chart notes documenting a clinically positive response to therapy, which shall include improvement, stabilization, or slowing of disease progression.

V. CRITERIA FOR INITIAL APPROVAL

Mucopolysaccharidosis VII (MPS VII, Sly syndrome)
Authorization of 12 months may be granted for treatment of MPS VII (Sly syndrome) when both of the following criteria are met:
A. Diagnosis of MPS VII was confirmed by enzyme assay demonstrating a deficiency of beta-glucuronidase enzyme activity or by genetic testing; AND
B. Elevated urinary glycosaminoglycan (uGAG) excretion at a minimum of 2-fold over the mean normal for age at initiation of treatment with Mepsevii.

VI. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for mucopolysaccharidosis VII (MPS VII, Sly syndrome) who have a clinically positive response to therapy, which shall include improvement, stabilization, or slowing of disease progression.

REFERENCES

SECTION 1

1. Mepsevii [package insert]. Novato, CA: Ultragenyx Pharmaceutical Inc.; December 2020.
2. A Phase 3 Study of UX003 Recombinant Human Betaglucuronidase (rhGUS) Enzyme Replacement Therapy in Patients With Mucopolysaccharidosis Type 7 (MPS 7). https://ClinicalTrials.gov/show/NCT02230566.

SECTION 2

1. Mepsevii [package insert]. Novato, CA: Ultragenyx; December 2020.
2. ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). Identifier NCT01856218. An OpenLabel Phase 1/2 Study to Assess the Safety, Efficacy and Dose of Study Drug UX003 Recombinant Human Beta- glucuronidase (rhGUS) Enzyme Replacement Therapy in Patients With Mucopolysaccharidosis Type 7 (MPS 7); January 31, 2018. Available at: https://clinicaltrials.gov/ct2/show/NCT01856218?term=NCT01856218&rank=1.
3. ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). Identifier NCT02230566. A Phase 3 Study of UX003 Recombinant Human Betaglucuronidase (rhGUS) Enzyme Replacement Therapy in Patients With Mucopolysaccharidosis Type 7 (MPS 7); February 16, 2018. Available at: https://clinicaltrials.gov/ct2/show/NCT02230566?term=NCT02230566&rank=1.
4. ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). Identifier NCT02432144. A LongTerm Open-Label Treatment and Extension Study of UX003 rhGUS Enzyme Replacement Therapy in Subjects With MPS 7; November 6, 2017. Available at: https://clinicaltrials.gov/ct2/show/NCT02432144?term=NCT02432144&rank=1.
5. Harmatz P, et al. A novel Blind Start study design to investigate vestronidase alfa for mucopolysaccharidosis VII, an ultra-rare genetic disease. Mol Genet Metab. 2018 Apr;123(4):488-494.

POLICY Document for MIRCERA (methoxy polyethylene glycol-epoetin beta)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, and overall, clinically appropriate use. This document provides specific information to both sections of the overall policy.

Section 1: Preferred Product
- Policy information specific to preferred medications

Section 2: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 1: Preferred Product

EXCEPTIONS CRITERIA
ERYTHROPOIESIS STIMULATING AGENTS
PREFERRED PRODUCTS: ARANESP AND RETACRIT

POLICY
This policy informs prescribers of preferred products and provides an exception process for targeted products through prior authorization.

I. PLAN DESIGN SUMMARY

This program applies to the erythropoiesis stimulating agents specified in this policy. Coverage for targeted products is provided based on clinical circumstances that would exclude the use of the preferred products and may be based on previous use of a product. The coverage review process will ascertain situations where a clinical exception can be made. This program applies to all members who are requesting treatment with the targeted products, Epogen or Procrit. This program also applies to members who are new to treatment with the targeted product, Mircera, for the first time.

Each referral is reviewed based on all utilization management (UM) programs implemented for the client.

Table. Erythropoiesis stimulating agents

	Product(s)
Preferred*	• **Aranesp** (darbepoetin alfa) • **Retacrit** (epoetin alfa-epbx)
Targeted	• **Epogen** (epoetin alfa) • **Mircera** (methoxy polyethylene glycol-epoetin beta) • **Procrit** (epoetin alfa)

*: Medications considered formulary or preferred on your plan may still require a clinical prior authorization review.

II. EXCEPTION CRITERIA

This program applies to members requesting treatment for an indication that is FDA-approved for the preferred products.

A. Mircera

Coverage for the targeted product is provided when the member meets either of the following criteria:

1. Member is currently receiving treatment with a targeted product, excluding when the requested targeted product is obtained as samples or via manufacturer's patient assistance programs.
2. Member has a documented inadequate response or intolerable adverse event with both of the preferred products, Retacrit and Aranesp.

B. Epogen or Procrit

Coverage for the targeted products are provided when both of the following criteria are met:

1. Member has had a documented intolerable adverse event with the preferred product, Retacrit, and the adverse event was not an expected adverse event attributed to the active ingredient as described in the prescribing information.
2. Member has experienced a documented inadequate response or intolerable adverse event with the preferred product, Aranesp, when prescribed for the treatment of anemia due to chronic kidney disease or the treatment of anemia due to myelosuppressive chemotherapy in cancer.

Section 2: Clinical Criteria

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.

REFERENCES:

SECTION 1

1. Aranesp [package insert]. Thousand Oaks, CA: Amgen Inc.; January 2019.
2. Epogen [package insert]. Thousand Oaks, CA: Amgen Inc.; July 2018.
3. Procrit [package insert]. Horsham, PA: Janssen Products, LP; July 2018.
4. Mircera [package insert]. St. Gallen, Switzerland: Vifor (International) Inc.; June 2018.
5. Retacrit [package insert]. Lake Forest, IL: Hospira Inc.; August 2020.

SECTION 2

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.

Reference number(s)
4056-A

SPECIALTY GUIDELINE MANAGEMENT

MONJUVI (tafasitamab-cxix)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Monjuvi, in combination with lenalidomide, 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 low grade lymphoma, and who are not eligible for autologous stem cell transplant (ASCT).

B. Compendial Uses
B-cell lymphomas
1. Human immunodeficiency virus (HIV)-related B-cell lymphoma
2. Histologic transformation of indolent lymphomas to diffuse large B-cell lymphoma
3. Follicular lymphoma
4. Monomorphic post-transplant lymphoproliferative disorders (B-cell type)
5. Diffuse large B-cell lymphoma (DLBCL)
6. High-grade B-cell lymphomas (HGBLs)

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 notes, medical record documentation or claims history supporting previous lines of therapy.

III. CRITERIA FOR INITIAL APPROVAL

B-Cell Lymphomas
Authorization of 12 months may be granted for treatment of relapsed or refractory B-cell lymphomas when all of the following criteria are met:
A. The member has one of the following B-cell lymphoma subtypes:
1. Human immunodeficiency virus (HIV)-related B-cell lymphoma (including HIV-related diffuse large B-cell lymphoma, primary effusion lymphoma, HIV-related plasmablastic lymphoma, and human herpes virus-8 (HHV8)-positive diffuse large B-cell lymphoma)
2. Histologic transformation of indolent lymphomas to diffuse large B-cell lymphoma
3. Follicular lymphoma
4. Monomorphic post-transplant lymphoproliferative disorders (PTLD) (B-cell type)

5. Diffuse large B-cell lymphoma (DLBCL) (including DLBCL arising from low grade lymphoma and DLBCL not otherwise specified)
6. High-grade B-cell lymphomas (HGBLs)

B. The member is not eligible for an autologous stem cell transplant
C. The requested medication will be used in combination with lenalidomide for up to a maximum of 12 cycles

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 and if the member has completed 12 cycles, the requested drug will be used as monotherapy.

V. REFERENCES

1. Monjuvi [package insert]. Boston, MA: Morphosys US, Inc; June 2021.
2. The NCCN Drugs & Biologics Compendium® © 2023 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed June 7, 2023.

Reference number
1860-A

SPECIALTY GUIDELINE MANAGEMENT

MOZOBIL (plerixafor)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Mozobil is indicated in combination with granulocyte-colony stimulating factor (G-CSF) to mobilize hematopoietic stem cells (HSCs) to the peripheral blood for collection and subsequent autologous transplantation in patients with non-Hodgkin's lymphoma or multiple myeloma.

B. Compendial Use
Hematopoietic cell transplantation

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

II. CRITERIA FOR INITIAL APPROVAL

Hematopoietic Stem Cell Mobilization
Authorization of 6 months may be granted when all of the following criteria are met:
A. Mozobil will be used to mobilize hematopoietic stem cells for collection prior to transplantation.
B. Mozobil will be administered after the member has received a G-CSF (e.g., filgrastim) or chemo-mobilization.
C. Mozobil will not be used beyond 4 consecutive days or after completion of stem cell harvest/apheresis.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

1. Mozobil [package insert]. Cambridge, MA: Genzyme Corporation; August 2020.
2. The NCCN Drugs & Biologics Compendium® © 2023 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed January 5, 2023.
3. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Hematopoietic Cell Transplantation (HCT) Version 2.2022. https://www.nccn.org/professionals/physician_gls/pdf/hct.pdf Accessed January 5, 2023.

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

1. Myalept [package insert]. Dublin, Ireland: Amryt Pharmaceuticals DAC; February 2022.
2. Brown RJ, Araujo-Vilar D, Cheung PT, et al. The diagnosis and management of lipodystrophy syndromes: A multi-society practice guideline. *J Clin Endocrinol Metab*. 2016;101(12):4500-4511. doi:10.1210/jc.2016-2466
3. Handelsman Y, Oral AE, Bloomgarden ZT, et al. The clinical approach to the detection of lipodystrophy – an AACE consensus statement. *Endocr Pract.* 2013;19(1):107-116. doi:10.4158/endp.19.1.v767575m65p5mr06
4. Chan JL, Lutz K, Cochran E, et al. Clinical effects of long-term metreleptin treatment in patients with lipodystrophy. *Endocr Pract.* 2011;17(6):922-932. doi:10.4158/EP11229.OR
5. Garg A. Clinical review#: Lipodystrophies: genetic and acquired body fat disorders. *J Clin Endocrinol Metab.* 2011;96(11):3313-3325. doi:10.1210/jc.2011-1159
6. Rodriguez AJ, Mastronardi CA, Paz-Filho GJ. New advances in the treatment of generalized lipodystrophy: role of metreleptin. *Ther Clin Risk Manag.* 2015;11:1391-1400. doi:10.2147/TCRM.S66521
7. Lee HL, Waldman MA, Auh S, et al. Effects of metreleptin on proteinuria in patients with lipodystrophy. [published online ahead of print, 2019 Apr 16]. *J Clin Endocrinol Metab*. 2019;104(9):4169-4177. doi:10.1210/jc.2019-00200
8. Oral EA, Gorden P, Cochran E, et al. Long-term effectiveness and safety of metreleptin in the treatment of patients with partial lipodystrophy. *Endocrine*. 2019;64(3):500-511. doi:10.1007/s12020-019-01862-8

Reference number(s)
2299-A

SPECIALTY GUIDELINE MANAGEMENT

Mylotarg (gemtuzumab ozogamicin)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Acute Myeloid Leukemia (AML)
1. Newly diagnosed CD33-positive acute myeloid leukemia in adults and pediatric patients 1 month and older
2. Relapsed or refractory CD33-positive AML in adults and pediatric patients 2 years and older

B. Compendial Uses
Acute promyelocytic leukemia (APL)

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 AML and APL: medical record documentation of CD33-positive tumor as confirmed by testing or analysis to identify the CD33 antigen.

III. CRITERIA FOR INITIAL APPROVAL

A. Acute Myeloid Leukemia (AML)
Authorization of 12 months may be granted for the treatment of AML when the tumor is CD33-positive as confirmed by testing or analysis to identify the CD33 antigen.

B. Acute Promyelocytic Leukemia (APL)
Authorization of 12 months may be granted for the treatment of APL when the tumor is CD33-positive as confirmed by testing or analysis to identify the CD33 antigen.

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.

Reference number(s)
2299-A

V. REFERENCES

1. Mylotarg [package insert]. Philadelphia, PA: Pfizer; August 2021.
2. The NCCN Drugs & Biologics Compendium® © 2022 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed January 7, 2022.
3. Lo Coco F, Ammatuna E, Noguera N. Treatment of acute promyelocytic leukemia with gemtuzumab ozogamicin. *Clin Adv Hematol Oncol*. 2006;4(1):57-77.

POLICY Document for MYOBLOC (rimabotulinumtoxin B)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, and overall, clinically appropriate use. This document provides specific information to both sections of the overall policy.

Section 1: Preferred Product
- Policy information specific to preferred medications

Section 2: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 1: Preferred Product

EXCEPTIONS CRITERIA
BOTULINUM TOXINS

PREFERRED PRODUCTS: BOTOX, DYSPORT AND XEOMIN

POLICY
This policy informs prescribers of preferred products and provides an exception process for targeted products through prior authorization.

I. PLAN DESIGN SUMMARY

This program applies to the botulinum toxins products specified in this policy. Coverage for targeted products is provided based on clinical circumstances that would exclude the use of the preferred product and may be based on previous use of a product. The coverage review process will ascertain situations where a clinical exception can be made. This program applies to all members requesting treatment with the targeted product.

Each referral is reviewed based on all utilization management (UM) programs implemented for the client.

Table. Botulinum Toxins

	Product(s)
Preferred*	• **Botox** (onabotulinumtoxinA) • **Dysport** (abobotulinumtoxinA) • **Xeomin** (incobotulinumtoxinA)
Targeted	• **Myobloc** (rimabotulinumtoxinB)

*: Medications considered formulary or preferred on your plan may still require a clinical prior authorization review.

II. EXCEPTION CRITERIA

This program applies to members requesting treatment for an indication that is FDA-approved for the preferred product.

Coverage for a targeted product is provided when ANY of the following criteria is met:
A. Member has a documented inadequate response or intolerable adverse event to all of the preferred products.
B. Member is requesting Myobloc for the treatment of chronic sialorrhea and has had a documented inadequate response or an intolerable adverse event to Xeomin.

CVS/caremark

Section 2: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

MYOBLOC (rimabotulinumtoxin B)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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 cervical dystonia in adults to reduce the severity of abnormal head position and neck pain associated with cervical dystonia
   2. Treatment of chronic sialorrhea in adults

B. Compendial Uses
   1. Primary axillary and palmar hyperhidrosis
   2. Upper limb spasticity

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

II. PRESCRIBER SPECIALTIES

The medication must be prescribed by, or in consultation with the following for each indication:
A. Cervical dystonia and upper limb spasticity: neurologist, orthopedist or physiatrist
B. Chronic sialorrhea: neurologist or otolaryngologist
C. Primary axillary and palmar hyperhidrosis: neurologist or dermatologist

III. EXCLUSIONS

Coverage will not be provided for cosmetic use.

IV. CRITERIA FOR INITIAL APPROVAL

A. Cervical dystonia

Authorization of 12 months may be granted for treatment of adults with cervical dystonia (e.g., torticollis) when all of the following are met:
1. Member is 18 years of age or older
2. Member has abnormal placement of the head with limited range of motion in the neck

B. Chronic Sialorrhea (excessive salivation)

Authorization of 12 months may be granted for treatment of excessive salivation (chronic sialorrhea) when all of the following are met:
1. Member is 18 years of age or older
2. Member is refractory to pharmacotherapy (e.g., anticholinergics)

C. Primary axillary and palmar hyperhidrosis
Authorization of 12 months may be granted for treatment of primary axillary or palmer hyperhidrosis when all of the following criteria are met:
1. Significant disruption of professional and/or social life has occurred because of excessive sweating; and
2. Topical aluminum chloride or other extra-strength antiperspirants are ineffective or result in a severe rash.

D. Upper limb spasticity
Authorization of 12 months may be granted for treatment of upper limb spasticity either as a primary diagnosis or as a symptom of a condition causing limb spasticity.

V. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria and be experiencing benefit from therapy.

REFERENCES:

SECTION 1

1. Botox [package insert]. Irvine, CA: Allergan, Inc.; August 2022.
2. Dysport [package insert]. Basking Ridge, NJ: Ipsen Biopharmaceuticals, Inc.; July 2020.
3. Myobloc [package insert]. South San Francisco, CA: Solstice Neurosciences, Inc.; March 2021.
4. Xeomin [package insert]. Frankfurt, Germany: Merz Pharmaceuticals GmbH; August 2021.

SECTION 2

1. Myobloc [package insert]. South San Francisco, CA: Solstice Neurosciences, Inc.; March 2021.
2. DRUGDEX® System (electronic version). Truven Health Analytics, Ann Arbor, MI. Available at http://www.micromedexsolutions.com. Accessed July 28, 2022.
3. AHFS Drug Information. http://online.lexi.com/lco. Accessed July 28, 2022.
4. Lexi-Drugs. Hudson, OH: Lexicomp, 2019. http://online.lexi.com/. Accessed July 28, 2022.
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6. Lakraj AA, Moghimi N, Jabbari B. Sialorrhea: Anatomy, Pathophysiology and Treatment with Emphasis on the Role of Botulinum Toxins. *Toxins* 2013, 5, 1010-1031
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8. Garuti G, Rao F, Ribuffo V et al. Sialorrhea in patients with ALS: current treatment options. *Degener Neurol Neuromuscul Dis*. 2019; 9: 19–26.

POLICY Document for NAGLAZYME (galsulfase)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, lower cost site of care and overall, clinically appropriate use. This document provides specific information to each of the three sections of the overall policy.

Section 1: Site of Care
- Policy information specific to site of care (outpatient, hospital outpatient, home infusion)

Section 2: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 1: Site of Care

CareFirst Site of Care Criteria
Administration of Intravenous Naglazyme

POLICY

I. CRITERIA FOR APPROVAL FOR ADMINISTRATION IN OUTPATIENT HOSPITAL SETTING

This policy provides coverage for administration of Naglazyme in an outpatient hospital setting for up 54 days when a member is new to therapy or is reinitiating therapy after not being on therapy for at least 6 months.

This policy provides coverage for administration of Naglazyme in an outpatient hospital setting for a longer course of treatment when ANY of the following criteria are met:

A. The member has experienced an adverse reaction to the drug that did not respond to conventional interventions (eg, acetaminophen, steroids, diphenhydramine, fluids, other pre-medications or slowing of infusion rate) or a severe adverse event (anaphylaxis, anaphylactoid reactions, myocardial infarction, thromboembolism, or seizures) during or immediately after an infusion (up to 24 hours post infusion).
B. The member is medically unstable (eg respiratory, cardiovascular, or renal conditions).
C. The member has severe venous access issues that require the use of special interventions only available in the outpatient hospital setting.
D. The member has significant behavioral issues and/or physical or cognitive impairment that would impact the safety of the infusion therapy AND the patient does not have access to a caregiver.
E. The member is less than 14 years of age.

For situations where administration of Naglazyme does not meet the criteria for outpatient hospital infusion, coverage for Naglazyme is provided when administered in alternative sites such as; physician office, home infusion or ambulatory care.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the site of care prior authorization review (where applicable):

A. Medical records supporting the member has experienced an adverse reaction that did not respond to conventional interventions or a severe adverse event during or immediately after an infusion
B. Medical records supporting the member is medically unstable

C. Medical records supporting the member has severe venous access issues that requires specialized interventions only available in the outpatient hospital setting
D. Medical records supporting the member has behavioral issues and/or physical or cognitive impairment and no access to a caregiver

Section 2: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

NAGLAZYME (galsulfase)

POLICY

III. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Naglazyme is indicated for patients with mucopolysaccharidosis VI (MPS VI, Maroteaux-Lamy syndrome). Naglazyme has been shown to improve walking and stair-climbing capacity.

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

IV. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
A. Initial requests: N-acetylgalactosamine 4-sulfatase (arylsulfatase B) enzyme assay or genetic testing results supporting diagnosis.
B. Continuation requests: chart notes documenting a clinically positive response to therapy, which shall include improvement, stabilization, or slowing of disease progression.

V. CRITERIA FOR INITIAL APPROVAL

Mucopolysaccharidosis VI (MPS VI)
Authorization of 12 months may be granted for treatment of MPS VI when the diagnosis of MPS VI was confirmed by enzyme assay demonstrating a deficiency of N-acetylgalactosamine 4-sulfatase (arylsulfatase B) enzyme activity or by genetic testing.

VI. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for mucopolysaccharidosis VI (MPS VI, Maroteaux-Lamy syndrome) who have a clinically positive response to therapy, which shall include improvement, stabilization, or slowing of disease progression.

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POLICY Document for
NEULASTA (pegfilgrastim)
FULPHILA (pegfilgrastim-jmdb)
FYLNETRA (pegfilgrastim-pbbk)
NYVEPRIA (pegfilgrastim-apgf)
STIMUFEND (pegfilgrastim-fpgk)
UDENYCA (pegfilgrastim-cbqv)
ZIEXTENZO (pegfilgrastim-bmez)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, and overall, clinically appropriate use. This document provides specific information to both sections of the overall policy.

Section 1: Preferred Product
- Policy information specific to preferred medications

Section 2: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 3: Oncology Clinical Policy
- Policy information specific to regimen review per NCCN Guidelines.

Section 1: Preferred Product

EXCEPTIONS CRITERIA
Colony Stimulating Factors – Long Acting

PREFERRED PRODUCTS: FULPHILA, FYLNETRA, NYVEPRIA, UDENYCA, ZIEXTENZO

POLICY
This policy informs prescribers of preferred products and provides an exception process for targeted products through prior authorization.

I. PLAN DESIGN SUMMARY

This program applies to the long-acting colony stimulating factor products specified in this policy. Coverage for targeted products is provided based on clinical circumstances that would exclude the use of the preferred products and may be based on previous use of a product. The coverage review process will ascertain situations where a clinical exception can be made. This program applies to all members requesting treatment with a targeted product.

Each referral is reviewed based on all utilization management (UM) programs implemented for the client.

Table. Colony Stimulating Factors - Long Acting

	Product(s)
Preferred*	• **Fulphila** (pegfilgrastim-jmdb)

	• **Fylnetra** (pegfilgrastim-pbbk) • **Nyvepria** (pegfilgrastim-apgf) • **Udenyca** (pegfilgrastim-cbqv) • **Ziextenzo** (pegfilgrastim-bmez)
Targeted	• **Neulasta (including Onpro kit)** (pegfilgrastim)

*: Medications considered formulary or preferred on your plan may still require a clinical prior authorization review.

II. EXCEPTION CRITERIA

Coverage for the targeted product is provided when the member has had a documented intolerable adverse event to at least three of the preferred products and the adverse event was not an expected adverse event attributed to the active ingredient as described in the prescribing information (i.e., known adverse reaction for both the reference product and biosimilar products).

Section 2: Clinical Criteria

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.

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.

Section 3: Oncology Clinical Policy

PROGRAM DESCRIPTION

The National Comprehensive Care Network® (NCCN®) is an alliance of leading cancer centers devoted to patient care, research and education dedicated to improving the quality, effectiveness, and efficiency of cancer care so patients can live better lives.[1] It is comprised of oncology experts who convene regularly to establish the best treatments for patients. NCCN develops various resources for use by stakeholders in the health care delivery system. These resources include, but are not limited to, the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®), the NCCN Drugs & Biologics Compendium (NCCN Compendium®) and the NCCN Chemotherapy Order Templates (NCCN Templates®).

NCCN Templates® are based on NCCN Guidelines® and NCCN Compendium®. The NCCN Compendium lists the appropriate drugs and biologics as treatment options for specific cancers using U.S. Food and Drug Administration (FDA)-approved disease indications and specific NCCN panel recommendations. Each recommendation is supported by a level of evidence category.

NCCN Categories of Evidence and Consensus[2]

- Category 1: Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
- Category 2A: Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
- Category 2B: Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.
- Category 3: Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

POLICY

Policy for Regimen Prior Authorization
A regimen prior authorization allows submission of a single prior authorization request for all oncology drugs or biologics within an NCCN template that require prior authorization.

PROCEDURE

This policy provides coverage of a regimen review when all of the following criteria are met:
1. Regimen prior authorization reviews, based on NCCN templates, are initiated through the provider portal.
    - If the prior authorization request is submitted via phone or fax, each drug or biologic will need to be submitted and reviewed as a separate prior authorization request for review with drug-specific criteria.
2. The prior authorization review is requested for an oncology drug or biologic.
3. The member is eligible for regimen review.
4. The indication is for a cancer that is eligible for regimen review. Currently, the cancer types in scope for regimen review include the following:
    - Ampullary Adenocarcinoma
    - Anal Carcinoma
    - B-Cell Lymphomas
    - Basal Cell Skin Cancer
    - Biliary Tract Cancers
    - Bone Cancer
    - Breast Cancer
    - Bladder Cancer
    - Central Nervous System Cancers
    - Cervical Cancer
    - Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma
    - Chronic Myeloid leukemia
    - Colon Cancer
    - Dermatofibrosarcoma Protuberans
    - Esophageal Cancer
    - Gastric Cancer
    - Gastrointestinal Stromal Tumors
    - Gestational Trophoblastic Neoplasms
    - Hairy Cell Leukemia
    - Head and Neck Cancers
    - Hodgkin Lymphoma
    - Hepatocellular Carcinoma
    - Kaposi Sarcoma
    - Kidney Cancer
    - Melanoma: Cutaneous
    - Melanoma: Uveal
    - Merkel Cell Carcinoma
    - Mesothelioma: Peritoneal
    - Mesothelioma: Pleural
    - Myelodysplastic Syndromes
    - Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Gene Fusions
    - Myeloproliferative Neoplasms
    - Neuroendocrine and Adrenal Tumors
    - Non-Small Cell Lung Cancer
    - Occult Primary
    - Ovarian Cancer

- Pancreatic Cancer
- Penile Cancer
- Prostate Cancer
- Rectal Cancer
- Small Bowl Adenocarcinoma
- Small Cell Lung Cancer
- Soft Tissue Sarcoma
- Squamous Cell Skin Cancer
- Systemic Mastocytosis
- Systemic Light Chain Amyloidosis
- Testicular Cancer
- Thymomas and Thymic Carcinomas
- Thyroid Carcinoma
- Uterine Neoplasms
- Vulvar Cancer
- Waldenström Macroglobulinemia / Lymphoplasmacytic Lymphoma

In addition, the following criteria must be met for approval:

1. The requested regimen for the drug(s) or biologic(s) and indication is consistent with an NCCN recommendation with a level of evidence category of 1 or 2A.
2. The NCCN template must be accepted by the provider without modification.

Further review may be indicated when the above criteria are not met.

Authorizations may be granted for 12 months or as medically required, based on the member's condition and provider's assessment.

Supportive Care: Myeloid Growth Factor Therapy
Granulocyte colony stimulating factors are recommended for primary prophylaxis based on the febrile neutropenia risk of the chemotherapy regimen. Febrile neutropenia risk levels vary by NCCN Chemotherapy Order template and are listed at the top of the template. Regimens associated with a high or intermediate risk of febrile neutropenia may include a granulocyte colony stimulating factor as part of the prior authorization.

Continuation of Therapy
To submit a request for continuation of therapy, a new regimen prior authorization review must be requested. Upon template selection, the template must be modified to include the appropriate therapies being used for maintenance treatment. The regimen request will be submitted for further review.

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

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SECTION 3

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POLICY Document for NEUPOGEN (filgrastim)
GRANIX (tbo-filgrastim)
NIVESTYM (filgrastim-aafi)
RELEUKO (filgrastim-ayow)
ZARXIO (filgrastim-sndz)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, and overall, clinically appropriate use. This document provides specific information to both sections of the overall policy.

Section 1: Preferred Product
- Policy information specific to preferred medications

Section 2: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 3: Oncology Clinical Policy
- Policy information specific to regimen review per NCCN Guidelines.

Section 1: Preferred Product

EXCEPTIONS CRITERIA
Colony Stimulating Factors – Short Acting

PREFERRED PRODUCTS: NIVESTYM, RELEUKO AND ZARXIO

POLICY
This policy informs prescribers of preferred products and provides an exception process for targeted products through prior authorization.

I. PLAN DESIGN SUMMARY

This program applies to the short-acting colony stimulating factor products specified in this policy. Coverage for targeted products is provided based on clinical circumstances that would exclude the use of the preferred products and may be based on previous use of a product. The coverage review process will ascertain situations where a clinical exception can be made. This program applies to all members requesting treatment with Granix or Neupogen and for members who are new to treatment with Leukine for the first time.

Each referral is reviewed based on all utilization management (UM) programs implemented for the client.

Table. Colony Stimulating Factors – Short Acting

	Product(s)
Preferred*	• **Nivestym** (filgrastim-aafi) • **Releuko** (filgrastim-ayow) • **Zarxio** (filgrastim-sndz)
Targeted	• **Granix** (TBO-filgrastim)

	• **Leukine** (sargramostim) • **Neupogen** (filgrastim)

*: Medications considered formulary or preferred on your plan may still require a clinical prior authorization review.

II. EXCEPTION CRITERIA

A. Coverage for the targeted products, Neupogen or Granix, is provided when one of the following criteria is met:
   1. Member has had a documented intolerable adverse event to all of the preferred products and the adverse event was not an expected adverse event attributed to the active ingredient as described in the prescribing information (i.e., known adverse reaction for both the reference products and biosimilar products)
   2. Member has a documented latex allergy and the prescriber states that the member must use latex-free products (Neupogen vial, Granix pre-filled syringe, or Granix vial) and the member has had an intolerable adverse effect to Nivestym and Releuko.
   3. Neupogen or Granix are requested for doses less than 180 mcg and the member has had an intolerable adverse effect to Nivestym.

B. Coverage for the targeted product, Leukine, is provided when one of the following criteria is met:
   1. Member has had a documented inadequate response or an intolerable adverse event to one of the preferred products.
   2. Leukine is being requested for an indication that is not FDA-approved for the preferred product.
   3. Member is currently receiving treatment with Leukine, excluding when the requested targeted product is obtained as samples or via manufacturer's patient assistance programs.

Section 2: Clinical Criteria

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.

Section 3: Oncology Clinical Policy

PROGRAM DESCRIPTION

The National Comprehensive Care Network® (NCCN®) is an alliance of leading cancer centers devoted to patient care, research and education dedicated to improving the quality, effectiveness, and efficiency of cancer care so patients can live better lives.[1] It is comprised of oncology experts who convene regularly to establish the best treatments for patients. NCCN develops various resources for use by stakeholders in the health care delivery system. These resources include, but are not limited to, the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®), the NCCN Drugs & Biologics Compendium (NCCN Compendium®) and the NCCN Chemotherapy Order Templates (NCCN Templates®).

NCCN Templates® are based on NCCN Guidelines® and NCCN Compendium®. The NCCN Compendium lists the appropriate drugs and biologics as treatment options for specific cancers using U.S. Food and Drug Administration (FDA)-approved disease indications and specific NCCN panel recommendations. Each recommendation is supported by a level of evidence category.

NCCN Categories of Evidence and Consensus[2]

- Category 1: Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
- Category 2A: Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
- Category 2B: Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.
- Category 3: Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

POLICY

Policy for Regimen Prior Authorization
A regimen prior authorization allows submission of a single prior authorization request for all oncology drugs or biologics within an NCCN template that require prior authorization.

PROCEDURE

This policy provides coverage of a regimen review when all of the following criteria are met:
1. Regimen prior authorization reviews, based on NCCN templates, are initiated through the provider portal.
    - If the prior authorization request is submitted via phone or fax, each drug or biologic will need to be submitted and reviewed as a separate prior authorization request for review with drug-specific criteria.
2. The prior authorization review is requested for an oncology drug or biologic.
3. The member is eligible for regimen review.
4. The indication is for a cancer that is eligible for regimen review. Currently, the cancer types in scope for regimen review include the following:
    - Ampullary Adenocarcinoma
    - Anal Carcinoma
    - B-Cell Lymphomas
    - Basal Cell Skin Cancer
    - Biliary Tract Cancers
    - Bone Cancer
    - Breast Cancer
    - Bladder Cancer
    - Central Nervous System Cancers
    - Cervical Cancer
    - Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma
    - Chronic Myeloid leukemia
    - Colon Cancer
    - Dermatofibrosarcoma Protuberans
    - Esophageal Cancer
    - Gastric Cancer
    - Gastrointestinal Stromal Tumors
    - Gestational Trophoblastic Neoplasms
    - Hairy Cell Leukemia
    - Head and Neck Cancers
    - Hodgkin Lymphoma
    - Hepatocellular Carcinoma
    - Kaposi Sarcoma
    - Kidney Cancer
    - Melanoma: Cutaneous
    - Melanoma: Uveal
    - Merkel Cell Carcinoma
    - Mesothelioma: Peritoneal
    - Mesothelioma: Pleural
    - Myelodysplastic Syndromes
    - Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Gene Fusions
    - Myeloproliferative Neoplasms
    - Neuroendocrine and Adrenal Tumors
    - Non-Small Cell Lung Cancer
    - Occult Primary
    - Ovarian Cancer
    - Pancreatic Cancer
    - Penile Cancer
    - Prostate Cancer
    - Rectal Cancer
    - Small Bowl Adenocarcinoma
    - Small Cell Lung Cancer
    - Soft Tissue Sarcoma
    - Squamous Cell Skin Cancer
    - Systemic Mastocytosis

- Systemic Light Chain Amyloidosis
- Testicular Cancer
- Thymomas and Thymic Carcinomas
- Thyroid Carcinoma
- Uterine Neoplasms
- Vulvar Cancer
- Waldenström Macroglobulinemia / Lymphoplasmacytic Lymphoma

In addition, the following criteria must be met for approval:

1. The requested regimen for the drug(s) or biologic(s) and indication is consistent with an NCCN recommendation with a level of evidence category of 1 or 2A.
2. The NCCN template must be accepted by the provider without modification.

Further review may be indicated when the above criteria are not met.

Authorizations may be granted for 12 months or as medically required, based on the member's condition and provider's assessment.

Supportive Care: Myeloid Growth Factor Therapy
Granulocyte colony stimulating factors are recommended for primary prophylaxis based on the febrile neutropenia risk of the chemotherapy regimen. Febrile neutropenia risk levels vary by NCCN Chemotherapy Order template and are listed at the top of the template. Regimens associated with a high or intermediate risk of febrile neutropenia may include a granulocyte colony stimulating factor as part of the prior authorization.

Continuation of Therapy
To submit a request for continuation of therapy, a new regimen prior authorization review must be requested. Upon template selection, the template must be modified to include the appropriate therapies being used for maintenance treatment. The regimen request will be submitted for further review.

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

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POLICY Document for NEXVIAZYME (avalglucosidase alfa-ngpt)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, lower cost site of care and overall, clinically appropriate use. This document provides specific information to each of the three sections of the overall policy.

Section 1: Site of Care

- Policy information specific to site of care (outpatient, hospital outpatient, home infusion)

Section 2: Clinical Criteria

- Policy information specific to the clinical appropriateness for the medication

Section 1: Site of Care

CareFirst Site of Care Criteria
Administration of Intravenous Nexviazyme

\POLICY

I. CRITERIA FOR APPROVAL FOR ADMINISTRATION IN OUTPATIENT HOSPITAL SETTING

This policy provides coverage for administration of Nexviazyme in an outpatient hospital setting for up to 106 days when a member is new to therapy or is reinitiating therapy after not being on therapy for at least 6 months.

This policy provides coverage for administration of Nexviazyme in an outpatient hospital setting for a longer course of treatment when ANY of the following criteria are met:

A. The member has experienced an adverse reaction to the drug that did not respond to conventional interventions (eg, acetaminophen, steroids, diphenhydramine, fluids, other pre-medications or slowing of infusion rate) or a severe adverse event (anaphylaxis, anaphylactoid reactions, myocardial infarction, thromboembolism, or seizures) during or immediately after an infusion.
B. The member has developed laboratory confirmed anti-avalglucosidase alfa-ngpt antibodies which increases the risk for infusion related reactions
C. The member is medically unstable (eg respiratory, cardiovascular, or renal conditions).
D. The member has severe venous access issues that require the use of special interventions only available in the outpatient hospital setting.
E. The member has significant behavioral issues and/or physical or cognitive impairment that would impact the safety of the infusion therapy AND the patient does not have access to a caregiver.
F. The member is less than 14 years of age.

For situations where administration of Nexviazyme does not meet the criteria for outpatient hospital infusion, coverage for Nexviazyme is provided when administered in alternative sites such as; physician office, home infusion or ambulatory care.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the site of care prior authorization review (where applicable):

A. Medical records supporting the member has experienced an adverse reaction that did not respond to conventional interventions or a severe adverse event during or immediately after an infusion
B. Medical records supporting the member has developed anti-avalglucosidase alfa-ngpt antibodies
C. Medical records supporting the member is medically unstable
D. Medical records supporting the member has severe venous access issues that requires specialized interventions only available in the outpatient hospital setting
E. Medical records supporting the member has behavioral issues and/or physical or cognitive impairment and no access to a caregiver

Section 2: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

NEXVIAZYME (avalglucosidase alfa-ngpt)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Nexviazyme is indicated for the treatment of patients 1 year of age and older with late-onset Pompe disease (lysosomal acid alpha-glucosidase [GAA] 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: acid alpha-glucosidase enzyme assay or genetic testing results supporting diagnosis.
B. 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

Late-onset Pompe disease
Authorization of 12 months may be granted for treatment of late-onset Pompe disease when all of the following criteria are met:
A. Member is 1 year of age or older.
B. Diagnosis was confirmed by enzyme assay demonstrating a deficiency of acid alpha-glucosidase enzyme activity or by genetic testing.

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., improvement, stabilization, or slowing of disease progression for motor function, walking capacity, respiratory function, or muscle strength).

REFERENCES

SECTION 1

1. Nexviazyme [package insert]. Cambridge, MA: Genzyme Corporation; August 2021.

SECTION 2

1. Nexviazyme [package insert]. Cambridge, MA: Genzyme Corporation; August 2021.

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)
1947-A

SPECIALTY GUIDELINE MANAGEMENT

NOVOSEVEN RT (coagulation factor VIIa [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.

A. FDA-Approved Indications
   1. Hemophilia A or hemophilia B with inhibitors
   2. Congenital factor VII deficiency
   3. Glanzmann's thrombasthenia
   4. Acquired hemophilia

B. Compendial Uses
   1. Acquired von Willebrand syndrome
   2. Inhibitors to factor XI

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

II. PRESCRIBER SPECIALTIES

Must be prescribed by or in consultation with a hematologist.

III. CRITERIA FOR INITIAL APPROVAL

A. Congenital Factor VII Deficiency
Authorization of 12 months may be granted for treatment of congenital factor VII deficiency.

B. Hemophilia A with Inhibitors
Authorization of 12 months may be granted for treatment of hemophilia A with inhibitors (see Appendix) when the inhibitor titer is ≥ 5 Bethesda units per milliliter (BU/mL) or the member has a history of an inhibitor titer ≥ 5 BU.

C. Hemophilia B with Inhibitors
Authorization of 12 months may be granted for treatment of hemophilia B with inhibitors (see Appendix) when the inhibitor titer is ≥ 5 Bethesda units per milliliter (BU/mL) or the member has a history of an inhibitor titer ≥ 5 BU.

D. Glanzmann's Thrombasthenia
Authorization of 12 months may be granted for treatment of Glanzmann's thrombasthenia.

E. Acquired Hemophilia
Authorization of 12 months may be granted for treatment of acquired hemophilia.

F. Acquired von Willebrand Syndrome
Authorization of 12 months may be granted for treatment of acquired von Willebrand syndrome when other therapies failed to control the member's condition (e.g., desmopressin or factor VIII/von Willebrand factor).

G. Inhibitors to Factor XI
Authorization of 12 months may be granted for treatment of inhibitors to factor XI.

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 is experiencing benefit from therapy (e.g., reduced frequency or severity of bleeds).

V. APPENDIX

Appendix: Inhibitors - Bethesda Units (BU)
The presence of inhibitors is confirmed by a specific blood test called the Bethesda inhibitor assay.

- High-titer inhibitors:
  - $\geq$ 5 BU/mL
  - Inhibitors act strongly and quickly neutralize factor
- Low-titer inhibitors:
  - < 5 BU/mL
  - Inhibitors act weakly and slowly neutralize factor

VI. REFERENCES

1. NovoSeven RT [package insert]. Plainsboro, NJ: Novo Nordisk Inc.; July 2020.
2. National Institutes of Health. The diagnosis, evaluation, and management of von Willebrand disease. Bethesda, MD: US Dept of Health and Human Services, National Institutes of Health; 2007. NIH publication No. 08-5832
3. Tiede A, Rand J, Budde U, et al. How I treat the acquired von Willebrand syndrome. *Blood*. 2011;117(25):6777-85.

4. Federici AB, Budde U, Castaman G, Rand JH, Tiede A. Current diagnostic and therapeutic approaches to patients with acquired von Willebrand syndrome: a 2013 update. *Semin Thromb Hemost*. 2013;39(2):191-201.
5. O'Connell NM. Factor XI deficiency – from molecular genetics to clinical management. *Blood Coagul Fibrinolysis.* 2003;14(Suppl 1):S59-S64.
6. Salomon O, Zivelin A, Livnat T, Seligsohn U. Inhibitors to factor XI in patients with severe factor XI deficiency. *Semin Hematol*. 2006;43(1 Suppl 1):S10-S12.
7. 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.
8. 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 1, 2022.
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10. World Federation of Hemophilia. Platelet function disorders. http://www1.wfh.org/publication/files/pdf-1147.pdf. 2008. Accessed December 1, 2022.
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12. Duga S, Salomon O. Congenital factor XI deficiency: an update. *Semin Thromb Hemost*. 2013;39(6):621-631.

Reference number(s)
1927-A

SPECIALTY GUIDELINE MANAGEMENT

NPLATE (romiplostim)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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. Nplate is indicated for the treatment of thrombocytopenia in:
      a. Adult patients with immune thrombocytopenia (ITP) who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy.
      b. Pediatric patients 1 year of age and older with ITP for at least 6 months who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy.
   2. Nplate is indicated to increase survival in adults and in pediatric patients (including term neonates) acutely exposed to myelosuppressive doses of radiation (Hematopoietic Syndrome of Acute Radiation Syndrome [HSARS]).

B. Compendial Uses
   1. 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
   2. Chemotherapy-induced thrombocytopenia (CIT)

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. Immune thrombocytopenia: pretreatment and current platelet counts
B. Chemotherapy-induced thrombocytopenia (CIT): pretreatment and current platelet counts

III. EXCLUSIONS

Coverage will not be provided for members with the following exclusion: concomitant use of Nplate with other thrombopoietin receptor agonists (e.g., Promacta, Doptelet, Mulpleta) or with spleen tyrosine kinase inhibitors (e.g., Tavalisse)

IV. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with a hematologist or oncologist.

V. CRITERIA FOR INITIAL APPROVAL

A. Immune thrombocytopenia (ITP)

Authorization of 6 months may be granted for treatment of 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. Hematopoietic syndrome of acute radiation syndrome (HSARS)

Authorization of 1 month may be granted for treatment of hematopoietic syndrome of acute radiation syndrome (acute exposure to myelosuppressive doses of radiation).

C. Myelodysplastic Syndromes

Authorization of 12 months may be granted for treatment of myelodysplastic syndromes when both of the following criteria are met:

1. 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).
2. 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.

D. Chemotherapy-induced thrombocytopenia

Authorization of 6 months may be granted for treatment of chemotherapy-induced thrombocytopenia (CIT) when any of the following criteria are met:

1. The platelet count is less than $100x10^9$/L for at least 3-4 weeks following the last chemotherapy administration, or
2. Chemotherapy administration has been delayed related to thrombocytopenia

VI. CONTINUATION OF THERAPY

A. Immune thrombocytopenia (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 Nplate 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 Nplate dosing will be adjusted to achieve a platelet count sufficient to avoid clinically important bleeding.

B. Hematopoietic syndrome of acute radiation syndrome (HSARS)

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

C. 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).

D. Chemotherapy-induced thrombocytopenia
Authorization of 6 months may be granted for continued treatment of chemotherapy-induced thrombocytopenia (CIT) in members who experience benefit from therapy (e.g., increased platelet counts, decreased bleeding events, reduced need for platelet transfusions) to maintain a target platelet count goal of $100x10^9$/L – $200x10^9$/L.

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 member to trauma

VIII. REFERENCES

1. Nplate [package insert]. Thousand Oaks, CA: Amgen Inc.; February 2022.
2. The NCCN Drugs & Biologics Compendium® © 2020 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed June 15, 2021.
3. The NCCN Clinical Practice Guidelines in Oncology® Myelodysplastic Syndrome (Version 2.2020). © 2021 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed June 15, 2021.
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5. 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.
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POLICY Document for NUCALA (mepolizumab)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, lower cost site of care and overall, clinically appropriate use. This document provides specific information to each of the three sections of the overall policy.

Section 1: Preferred Product
- Policy information specific to preferred medications

Section 2: Site of Care
- Policy information specific to site of care (outpatient, hospital outpatient, home infusion)

Section 3: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 1: Preferred Product

EXCEPTIONS CRITERIA
ASTHMA

PREFERRED PRODUCTS: DUPIXENT, FASENRA, NUCALA, TEZSPIRE, XOLAIR

POLICY
This policy informs prescribers of preferred products and provides an exception process for targeted products through prior authorization.

I. PLAN DESIGN SUMMARY

This program applies to the asthma products specified in this policy. Coverage for targeted products is provided based on clinical circumstances that would exclude the use of the preferred product and may be based on previous use of a product. The coverage review process will ascertain situations where a clinical exception can be made. This program applies to all members requesting treatment with a targeted product.

Each referral is reviewed based on all utilization management (UM) programs implemented for the client.

Table. Asthma

	Product(s)
Preferred*	• **Dupixent** (dupilumab) • **Fasenra** (benralizumab) • **Nucala** (mepolizumab) • **Tezspire** (tezepelumab-ekko) • **Xolair** (omalizumab)
Targeted	• **Cinqair** (reslizumab)

*: Medications considered formulary or preferred on your plan may still require a clinical prior authorization review.

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II. EXCEPTION CRITERIA

This program applies to members requesting treatment for an indication that is FDA-approved for the preferred product.

Coverage for a targeted product is provided when the member has a documented inadequate response or intolerable adverse event with at least three of the preferred products.

Section 2: Site of Care

CareFirst Site of Care Criteria
Administration of Subcutaneous Nucala

POLICY

I. CRITERIA FOR APPROVAL FOR ADMINISTRATION IN OUTPATIENT HOSPITAL SETTING

This policy provides coverage for provider administered Nucala* in an outpatient hospital setting for up to 45 days when a member is new to therapy or is reinitiating therapy after not being on therapy for at least 6 months.

This policy provides coverage for administration of Nucala in an outpatient hospital setting for a longer course of treatment when ANY of the following criteria are met:

A. The member has experienced an adverse reaction to the drug that did not respond to conventional interventions (eg, acetaminophen, steroids, diphenhydramine, fluids or other pre-medications) or a severe adverse event (anaphylaxis, anaphylactoid reactions, myocardial infarction, thromboembolism, or seizures) during or immediately after administration.
B. The member is medically unstable (eg respiratory, cardiovascular, or renal conditions).
C. The member has significant behavioral issues and/or physical or cognitive impairment that would impact the safety of drug administration AND the patient does not have access to a caregiver.
D. The member is less than 14 years of age.

For situations where administration of Nucala does not meet the criteria for outpatient hospital administration, coverage for Nucala is provided when administered in alternative sites such as; physician office, home infusion or ambulatory care.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the site of care prior authorization review (where applicable):

A. Medical records supporting the member has experienced an adverse reaction that did not respond to conventional interventions or a severe adverse event during or immediately after administration
B. Medical records supporting the member is medically unstable
C. Medical records supporting the member has behavioral issues and/or physical or cognitive impairment and no access to a caregiver

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Section 3: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

NUCALA (mepolizumab)

POLICY

III. INDICATIONS

The indications below including FDA-approved indications and compendial 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. Nucala is indicated for add-on maintenance treatment of patients with severe asthma aged 6 years and older, and with an eosinophilic phenotype.
B. Nucala is indicated for the treatment of adult patients with eosinophilic granulomatosis with polyangiitis (EGPA).
C. Nucala is indicated for the treatment of adult and pediatric patients aged 12 years and older with hypereosinophilic syndrome (HES) for ≥6 months without an identifiable non-hematologic secondary cause.
D. Nucala is indicated for add-on maintenance treatment of adult patients 18 years and older with chronic rhinosinusitis with nasal polyps (CRSwNP).

Limitations of Use: Not for relief of acute bronchospasm or status asthmaticus

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

IV. DOCUMENTATION

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

A. Asthma:
    1. For initial requests:
        i. Member's chart or medical record showing pretreatment blood eosinophil count, dependance on systemic corticosteroids if 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.
B. EGPA:
    1. For initial requests: Member's chart or medical record showing pretreatment blood eosinophil count.
    2. For continuation requests: Chart notes or medical record documentation supporting improvement in EGPA control.
C. HES:
    1. For initial requests:
        i. FIP1L1-PDGFRA fusion gene test results.
        ii. Member's chart or medical record showing pretreatment blood eosinophil count.

2. For continuation requests: Chart notes or medical record documentation supporting improvement in HES control.

D. CRSwNP:
1. For initial requests:
    i. Member's chart or medical record showing nasal endoscopy, anterior rhinoscopy, or computed tomography details (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. For continuation requests: Chart notes or medical record documentation supporting positive clinical response.

V. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with one of the following:
A. Asthma: allergist/immunologist or pulmonologist
B. Chronic rhinosinusitis with nasal polyposis: allergist/immunologist or otolaryngologist

VI. CRITERIA FOR INITIAL APPROVAL

A. Asthma

Authorization of 6 months may be granted for treatment of asthma when all of the following criteria are met:
1. Member is 6 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; or
    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 Nucala.
6. Member will not use Nucala concomitantly with other biologics indicated for asthma (e.g., Cinqair, Dupixent, Fasenra, Tezspire, Xolair).

B. Eosinophilic granulomatosis with polyangiitis

Authorization of 12 months may be granted for treatment of eosinophilic granulomatosis with polyangiitis when all of the following criteria are met:
1. Member is 18 years of age or older.
2. Member has a history or the presence of an eosinophil count of more than 1000 cells per microliter or a blood eosinophil level of greater than 10%.

3. Member has at least two of the following disease characteristics of EGPA:
   i. Biopsy showing histopathological evidence of eosinophilic vasculitis, perivascular eosinophilic infiltration, or eosinophil-rich granulomatous inflammation
   ii. Neuropathy, mono or poly (motor deficit or nerve conduction abnormality)
   iii. Pulmonary infiltrates, non-fixed; sino-nasal abnormality
   iv. Cardiomyopathy (established by echocardiography or magnetic resonance imaging)
   v. Glomerulonephritis (hematuria, red cell casts, proteinuria)
   vi. Alveolar hemorrhage (by bronchoalveolar lavage)
   vii. Palpable purpura
   viii. Anti-neutrophil cytoplasmic anti-body (ANCA) positive (Myeloperoxidase or proteinease 3)
4. Member has had at least one relapse (requiring increase in oral corticosteroids dose, initiation/increased dose of immunosuppressive therapy or hospitalization) within 2 years prior to starting treatment with Nucala or has a refractory disease.

C. Hypereosinophilic syndrome (HES)

Authorization of 12 months may be granted for treatment of HES when all of the following criteria are met:

1. Member is 12 years of age or older.
2. Member does not have either of the following:
   i. HES secondary to a non-hematologic cause (e.g., drug hypersensitivity, parasitic helminth infection, [human immunodeficiency virus] HIV infection, non-hematologic malignancy)
   ii. FIP1L1-PDGFRA kinase-positive HES
3. Member has a history or presence of a blood eosinophil count of at least 1000 cells per microliter.
4. Member will not use Nucala as monotherapy.
5. Member has been on a stable dose of HES therapy (e.g., oral corticosteroid, immunosuppressive, and/or cytotoxic therapy).
6. Member has had HES for at least 6 months.
7. Member has experienced at least two HES flares within the past 12 months.

D. Chronic rhinosinusitis with nasal polyps

Authorization of 6 months may be granted for treatment of chronic rhinosinusitis with nasal polyps 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
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 Nucala, unless contraindicated or not tolerated.
6. Member will not use Nucala concomitantly with other biologics indicated for chronic rhinosinusitis with nasal polyps (e.g., Dupixent, Xolair).

VII. CONTINUATION OF THERAPY

A. Asthma

Authorization of 12 months may be granted for continuation of treatment of asthma when all of the following criteria are met:

1. Member is 6 years of age or older.
2. Asthma control has improved on Nucala 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
3. Member will continue to use maintenance asthma treatments (e.g., inhaled corticosteroid, additional controller) in combination with Nucala.
4. Member will not use Nucala concomitantly with other biologics indicated for asthma (e.g., Cinqair, Dupixent, Fasenra, Tezspire, Xolair).

B. Eosinophilic granulomatosis with polyangiitis

Authorization of 12 months may be granted for continuation of treatment of eosinophilic granulomatosis with polyangiitis when all of the following criteria are met:

1. Member is 18 years of age or older.
2. Member has beneficial response to treatment with Nucala as demonstrated by any of the following:
   i. A reduction in the frequency of relapses, or
   ii. A reduction in the daily oral corticosteroid dose, or
   iii. No active vasculitis

C. Hypereosinophilic syndrome (HES)

Authorization of 12 months may be granted for continuation of treatment of HES when all of the following criteria are met:

1. Member is 12 years of age or older.
2. Member has experienced a reduction in HES flares since starting treatment with Nucala.
3. Member will not use Nucala as monotherapy.

D. Chronic rhinosinusitis with nasal polyps

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 a positive clinical response to Nucala 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).
3. Member will not use Nucala concomitantly with other biologics indicated for chronic rhinosinusitis with nasal polyps (e.g., Dupixent, Xolair).

VIII. OTHER

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.

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5. Tezspire [package insert]. Thousand Oaks, CA: Amgen Inc.; December 2021.
6. Xolair [package insert]. South San Francisco, CA: Genentech, Inc.; July 2021.

SECTION 2

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Reference number(s)
4575-A

SPECIALTY GUIDELINE MANAGEMENT

NULIBRY (fosdenopterin)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Nulibry is cyclic pyranopterin monophosphate (cPMP) indicated to reduce the risk of mortality in patients with molybdenum cofactor deficiency (MoCD) Type A.

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: genetic testing results documenting a mutation in the molybdenum cofactor synthesis gene 1 *(MOSC1)*.
B. Continuation requests (where applicable):
    1. Genetic testing results documenting a mutation in the molybdenum cofactor synthesis gene 1 *(MOSC1)*.
    2. Chart notes or medical records documenting a benefit from therapy (e.g., improvement, stabilization, or slowing of disease progression for encephalopathy, seizure activity, improved or normalized uric acid, urinary S-sulfocysteine, and xanthine levels).

III. CRITERIA FOR INITIAL APPROVAL

Molybdenum cofactor deficiency (MoCD) Type A
A. Authorization 12 months may be granted when the diagnosis of MoCD Type A was confirmed by genetic testing documenting a mutation in the molybdenum cofactor synthesis gene 1 *(MOSC1).*

B. Authorization of 3 months may be granted when both of the following criteria are met:
    1. Member has a presumed diagnosis of MoCD Type A and genetic test results are pending.
    2. Member has clinical signs and symptoms associated with MoCD Type A (e.g., encephalopathy, intractable seizures, developmental delay, decreased uric acid levels, elevated urinary S-sulfocysteine and/or xanthine levels).

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for members with an indication listed in Section III when one of the following is met:

A. The member has received less than 12 months of therapy and has genetic testing results documenting a mutation in the molybdenum cofactor synthesis gene 1 *(MOSC1).*
B. Member has received 12 months of therapy or more and is experiencing benefit from therapy (e.g., improvement, stabilization, or slowing of disease progression for encephalopathy, seizure activity, improved or normalized uric acid, urinary S-sulfocysteine, and xanthine levels).

V. REFERENCES

1. Nulibry [package insert]. Boston, MA: Origin Biosciences, Inc.; February 2021.
2. Atwal PS, Scaglia F. Molybdenum cofactor deficiency. Mol Genet Metab. 2016;117(1):1-4.
3. Schwahn BC, Van Spronsen FJ, Belaidi AA, et al. Efficacy and safety of cyclic pyranopterin monophosphate substitution in severe molybdenum cofactor deficiency type A: a prospective cohort study. Lancet. 2015; 386: 1955-1963.
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5. ClinicalTrials.gov. Safety & efficacy study of ORGN001 (formerly ALXN1101) in pediatric patients with MoCD type A currently treated with rcPMP. Available at: https://clinicaltrials.gov/ct2/show/NCT02047461. Accessed: November 2, 2021.

Reference number(s)
1948-A

SPECIALTY GUIDELINE MANAGEMENT

OBIZUR (antihemophilic factor [recombinant], porcine sequence)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Obizur is indicated for the on-demand treatment and control of bleeding episodes in adults with acquired hemophilia A.

Limitations of Use:
A. Safety and efficacy of Obizur has not been established in patients with a baseline anti-porcine factor VIII inhibitor titer of greater than 20 BU.
B. Obizur is not indicated for the treatment of congenital hemophilia A or von Willebrand disease.

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

II. PRESCRIBER SPECIALTIES

Must be prescribed by or in consultation with a hematologist.

III. CRITERIA FOR INITIAL APPROVAL

Acquired hemophilia A
Authorization of 1 month may be granted for treatment of acquired hemophilia A.

IV. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

V. REFERENCES

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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)

POLICY Document for OCREVUS (ocrelizumab)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, lower cost site of care and overall, clinically appropriate use. This document provides specific information to each of the three sections of the overall policy.

Section 1: Site of Care

- Policy information specific to site of care (outpatient, hospital outpatient, home infusion)

Section 2: Clinical Criteria

- Policy information specific to the clinical appropriateness for the medication

Section 1: Site of Care

CareFirst Site of Care Criteria
Administration of Intravenous Ocrevus

POLICY

I. CRITERIA FOR APPROVAL FOR ADMINISTRATION IN OUTPATIENT HOSPITAL SETTING

This policy provides coverage for administration of Ocrevus in an outpatient hospital setting for 45 days when a member is new to therapy or is reinitiating therapy after not being on therapy for more than 6 months.

This policy provides coverage for administration of Ocrevus in an outpatient hospital setting for a longer course of treatment when ANY of the following criteria are met:

A. The member has experienced an adverse reaction that did not respond to conventional interventions (eg, acetaminophen, steroids, diphenhydramine, fluids, pre-medications, or slowing of infusion rate) or a severe adverse event (anaphylaxis, anaphylactoid reactions, myocardial infarction, thromboembolism, or seizures) during or immediately after an infusion.
B. The member is medically unstable (eg respiratory, cardiovascular, or renal conditions).
C. The member has severe venous access issues that require the use of special interventions only available in the outpatient hospital setting.
D. The member has significant behavioral issues and/or physical or cognitive impairment that would impact the safety of the infusion therapy AND the patient does not have access to a caregiver.
E. The member is less than 14 years of age.

For situations where administration of Ocrevus does not meet the criteria for outpatient hospital infusion, coverage for Ocrevus is provided when administered in alternative sites such as; physician office, home infusion or ambulatory care.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the site of care prior authorization review (where applicable):

A. Medical records supporting the member has experienced an adverse reaction that did not respond to conventional interventions or a severe adverse event during or immediately after an infusion
B. Medical records supporting the member is medically unstable

C. Medical records supporting the member has severe venous access issues that require specialized interventions only available in the outpatient hospital setting
D. Medical records supporting the member has behavioral issues and/or physical or cognitive impairment and no access to a caregiver

Section 2: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

OCREVUS (ocrelizumab)

POLICY

III. INDICATIONS

The indications below including FDA-approved indications and compendial 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. Ocrevus 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.
B. Ocrevus is indicated for the treatment of primary progressive MS, in adults.

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

IV. PRESCRIBER SPECIALTIES

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

V. 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. Primary Progressive Multiple Sclerosis
Authorization of 12 months may be granted to members for the treatment of primary progressive multiple sclerosis.

VI. CONTINUATION OF THERAPY

For all indications: Authorization of 12 months may be granted for members who are experiencing disease stability or improvement while receiving Ocrevus.

VII. OTHER

A. Members will not use Ocrevus 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.

REFERENCES

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2. Hauser SL, Bar-Or A, Comi G, et al. Ocrelizumab versus Interferon Beta-1a in Relapsing Multiple Sclerosis. N Engl J Med. 2017;376(3):221-234.
3. Montalban X, Hauser SL, Kappos L, et al. Ocrelizumab versus Placebo in Primary Progressive Multiple Sclerosis. N Engl J Med. 2017;376(3):209-220

SECTION 2

1. Ocrevus [package insert]. South San Francisco, CA: Genentech, Inc.; March 2023.
2. Clinical Consult: CVS Caremark Clinical Program Review. Focus on Multiple Sclerosis Clinical Programs. June 22, 2017.

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

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Reference number(s)
5904-A

SPECIALTY GUIDELINE MANAGEMENT

OMISIRGE (omidubicel-onlv)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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
OMISIRGE is a nicotinamide modified allogeneic hematopoietic progenitor cell therapy derived from cord blood indicated for use in adults and pediatric patients 12 years and older with hematologic malignancies who are planned for umbilical cord blood transplantation following myeloablative conditioning to reduce the time to neutrophil recovery and the incidence of infection.

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

II. CRITERIA FOR INITIAL APPROVAL

Umbilical Cord Blood Transplantation
Authorization of 3 months (one dose total) may be granted for members 12 years of age and older who will receive umbilical cord blood transplantation when all of the following criteria are met:
A. The member has a hematologic malignancy.
B. The requested medication is being used to reduce the time to neutrophil recovery and incidence of infection.
C. The member will receive myeloablative conditioning.

III. REFERENCES

1. Omisirge [package insert]. Jerusalem, Israel: Gamidia Cell Ltd.; April 2023.

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Reference number
2291-A

SPECIALTY GUIDELINE MANAGEMENT

ONCASPAR (pegaspargase)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Acute lymphoblastic leukemia (ALL):
1. Oncaspar is indicated as a component of a multi-agent chemotherapeutic regimen for the first line treatment of pediatric and adult patients with ALL.
2. Oncaspar is indicated as a component of a multi-agent chemotherapeutic regimen for the treatment of pediatric and adult patients with ALL and hypersensitivity to native forms of L-asparaginase.

B. Compendial Uses
1. Extranodal natural killer/T-cell lymphoma (ENKL)
2. Aggressive NK-cell leukemia (ANKL)
3. Lymphoblastic lymphoma (managed in the same manner as ALL)
4. Acute lymphoblastic leukemia (ALL) as a component of multi-agent chemotherapeutic regimen or central nervous system directed therapy as systemic therapy (IV/IM route)
5. Pediatric acute lymphoblastic leukemia (ALL) as a component of a multi-agent chemotherapeutic regimen
6. Hepatosplenic T-cell lymphoma

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

II. CRITERIA FOR INITIAL APPROVAL

A. Acute Lymphoblastic Leukemia (ALL) and Lymphoblastic Lymphoma (LL)
Authorization of 12 months may be granted for the treatment of ALL or LL when the requested medication is used in conjunction with multi-agent chemotherapy or as central nervous system directed therapy as systemic therapy.

B. Extranodal Natural Killer/T-cell Lymphoma (ENKL) / Aggressive NK-cell Leukemia (ANKL)
Authorization of 12 months may be granted for the treatment of ENKL or ANKL when the requested medication is used in conjunction with multi-agent chemotherapy.

C. Hepatosplenic T-cell Lymphoma
Authorization of 12 months may be granted for the treatment of hepatosplenic T-cell lymphoma as subsequent therapy when the requested medication is used in conjunction with multi-agent 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. Oncaspar [package insert]. Boston, MA: Servier Pharmaceuticals LLC; November 2021.
2. The NCCN Drugs & Biologics Compendium® ©2022 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed May 12, 2022.

POLICY Document for ONPATTRO (patisiran)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, lower cost site of care and overall, clinically appropriate use. This document provides specific information to each of the three sections of the overall policy.

Section 1: Site of Care
- Policy information specific to site of care (outpatient, hospital outpatient, home infusion)

Section 2: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 1: Site of Care

CareFirst Site of Care Criteria
Administration of Intravenous Onpattro

POLICY

I. CRITERIA FOR APPROVAL FOR ADMINISTRATION IN OUTPATIENT HOSPITAL SETTING

This policy provides coverage for administration of Onpattro in an outpatient hospital setting for up to 45 days when a member is new to therapy or is reinitiating therapy after not being on therapy for more than 6 months.

This policy provides coverage for administration of Onpattro in an outpatient hospital setting for a longer course of treatment when ANY of the following criteria are met:

A. The member has experienced an adverse reaction to the drug that did not respond to conventional interventions (eg, acetaminophen, steroids, diphenhydramine, fluids, other pre-medications or slowing of infusion rate) or a severe adverse event (anaphylaxis, anaphylactoid reactions, myocardial infarction, thromboembolism, or seizures) during or immediately after an infusion.
B. The member is medically unstable (eg respiratory, cardiovascular, or renal conditions).
C. The member has severe venous access issues that require the use of special interventions only available in the outpatient hospital setting.
D. The member has significant behavioral issues and/or physical or cognitive impairment that would impact the safety of the infusion therapy AND the patient does not have access to a caregiver.
E. The member is less than 14 years of age.

For situations where administration of Onpattro does not meet the criteria for outpatient hospital infusion, coverage for Onpattro is provided when administered in alternative sites such as; physician office, home infusion or ambulatory care.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the site of care prior authorization review (where applicable):

A. Medical records supporting the member has experienced an adverse reaction that did not respond to conventional interventions or a severe adverse event during or immediately after an infusion

B. Medical records supporting the member is medically unstable
C. Medical records supporting the member has severe venous access issues that requires specialized interventions only available in the outpatient hospital setting
D. Medical records supporting the member has behavioral issues and/or physical or cognitive impairment and no access to a caregiver

Section 2: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

ONPATTRO (patisiran)

POLICY

III. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Onpattro 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.

IV. 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

V. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with a neurologist, geneticist, or physician specializing in the treatment of amyloidosis.

VI. 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 inotersen (Tegsedi), tafamidis (Vyndaqel, Vyndamax) or vutrisiran (Amvuttra).

VII. 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 Onpattro 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.

REFERENCES

SECTION 1

1. Onpattro [package insert]. San Diego, CA: Alnylam Pharmaceuticals, Inc..; January 2023.

SECTION 2

1. Onpattro [package insert]. Cambridge, MA: Alnylam Pharmaceuticals, Inc.; May 2021.
2. Adams, et al. Patisiran, an RNAi Therapeutic, for Hereditary Transthyretin Amyloidosis. N Engl J Med. 2018 Jul 5; 379(1):11-21.
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.

POLICY Document for OPDUALAG
(nivolumab and relatlimab-rmbw)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, and overall, clinically appropriate use. This document provides specific information to both sections of the overall policy.

Section 1: Site of Care
- Policy information specific to site of care (outpatient, hospital outpatient, home infusion)

Section 2: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 1: Site of Care

CareFirst Site of Care Criteria
Administration of Intravenous Checkpoint Inhibitors
Bavencio, Imfinzi, Jemperli, Keytruda, Libtayo, Opdivo, Opdualag, Tecentriq, Yervoy and Zynyz

POLICY

I. CRITERIA FOR APPROVAL FOR ADMINISTRATION IN OUTPATIENT HOSPITAL SETTING

This policy provides coverage for administration of a checkpoint inhibitor in an outpatient hospital setting for the initial 6 months approval and up to 45 days for renewal of therapy.

This policy provides coverage for administration of a checkpoint inhibitor in an outpatient hospital setting for a longer course of treatment when ANY of the following criteria are met:

A. The member has experienced an adverse reaction that did not respond to conventional interventions (eg, acetaminophen, steroids, diphenhydramine, fluids, other pre-medications or slowing of infusion rate) or a severe adverse event (anaphylaxis, anaphylactoid reactions, myocardial infarction, thromboembolism, or seizures) during or immediately after an infusion or has experienced severe toxicity requiring continuous monitoring (e.g. Grade 2-4 bullous dermatitis, transaminitis, pneumonitis, Stevens-Johnson syndrome, acute pancreatitis, primary adrenal insufficiency aseptic meningitis, encephalitis, transverse myelitis, myocarditis, pericarditis, arrhythmias, impaired ventricular function, conduction abnormalities).
B. The member is medically unstable (eg respiratory, cardiovascular, or renal conditions).
C. The member has severe venous access issues that require the use of a special interventions only available in the outpatient hospital setting.
D. The member has significant behavioral issues and/or physical or cognitive impairment that would impact the safety of the infusion therapy AND the patient does not have access to a caregiver.
E. The member is receiving provider administered combination chemotherapy.
F. The member is less than 14 years of age.

For situations where administration of a checkpoint inhibitor does not meet the criteria for outpatient hospital infusion, coverage for a checkpoint inhibitor is provided when administered in alternative sites such as physician office, home infusion or ambulatory care.

POLICY Document for OPDIVO (nivolumab)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, and overall, clinically appropriate use. This document provides specific information to both sections of the overall policy.

Section 1: Site of Care
- Policy information specific to site of care (outpatient, hospital outpatient, home infusion)

Section 2: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 3: Oncology Clinical Policy
- Policy information specific to regimen review per NCCN Guidelines.

Section 1: Site of Care

CareFirst Site of Care Criteria
Administration of Intravenous Checkpoint Inhibitors
Bavencio, Imfinzi, Jemperli, Keytruda, Libtayo, Opdivo, Opdualag, Tecentriq, Yervoy and Zynyz

POLICY

I. CRITERIA FOR APPROVAL FOR ADMINISTRATION IN OUTPATIENT HOSPITAL SETTING

This policy provides coverage for administration of a checkpoint inhibitor in an outpatient hospital setting for the initial 6 months approval and up to 45 days for renewal of therapy.

This policy provides coverage for administration of a checkpoint inhibitor in an outpatient hospital setting for a longer course of treatment when ANY of the following criteria are met:

A. The member has experienced an adverse reaction that did not respond to conventional interventions (eg, acetaminophen, steroids, diphenhydramine, fluids, other pre-medications or slowing of infusion rate) or a severe adverse event (anaphylaxis, anaphylactoid reactions, myocardial infarction, thromboembolism, or seizures) during or immediately after an infusion or has experienced severe toxicity requiring continuous monitoring (e.g. Grade 2-4 bullous dermatitis, transaminitis, pneumonitis, Stevens-Johnson syndrome, acute pancreatitis, primary adrenal insufficiency aseptic meningitis, encephalitis, transverse myelitis, myocarditis, pericarditis, arrhythmias, impaired ventricular function, conduction abnormalities).
B. The member is medically unstable (eg respiratory, cardiovascular, or renal conditions).
C. The member has severe venous access issues that require the use of a special interventions only available in the outpatient hospital setting.
D. The member has significant behavioral issues and/or physical or cognitive impairment that would impact the safety of the infusion therapy AND the patient does not have access to a caregiver.
E. The member is receiving provider administered combination chemotherapy.
F. The member is less than 14 years of age.

For situations where administration of a checkpoint inhibitor does not meet the criteria for outpatient hospital infusion, coverage for a checkpoint inhibitor is provided when administered in alternative sites such as physician office, home infusion or ambulatory care.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the site of care prior authorization review (where applicable):

A. Medical records supporting the member has experienced an adverse reaction that did not respond to conventional interventions or a severe adverse event during or immediately after an infusion or a severe toxicity requiring continuous monitoring
B. Medical records supporting the member is medically unstable
C. Medical records supporting the member has severe venous access issues that require specialized interventions only available in the outpatient hospital setting
D. Medical records supporting the member has behavioral issues and/or physical or cognitive impairment and no access to a caregiver
E. Medical records supporting the member is receiving provider administered combination therapy.

Section 2: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

OPDIVO (nivolumab)

POLICY

III. INDICATIONS

The indications below including FDA-approved indications and compendial 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. Unresectable or Metastatic Melanoma
      Opdivo, as a single agent or in combination with ipilimumab, is indicated for the treatment of adult and pediatric patients 12 years and older with unresectable or metastatic melanoma.

   2. Adjuvant Treatment of Melanoma
      Opdivo is indicated for the adjuvant treatment of adult and pediatric patients 12 years and older with melanoma with involvement of lymph nodes or metastatic disease who have undergone complete resection.

   3. Metastatic Non-Small Cell Lung Cancer
      a. Opdivo, in combination with ipilimumab, is indicated for the first-line treatment of adult patients with metastatic non-small cell lung cancer (NSCLC) whose tumors express PD-L1 (≥1%) as determined by an FDA-approved test, with no EGFR or ALK genomic tumor aberrations.
      b. Opdivo, in combination with ipilimumab and 2 cycles of platinum-doublet chemotherapy, is indicated for the first-line treatment of adult patients with metastatic or recurrent NSCLC, with no EGFR or ALK genomic tumor aberrations.
      c. Opdivo is indicated for the treatment of adult patients with metastatic NSCLC with progression on or after platinum-based chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving Opdivo.

   4. Neoadjuvant Treatment of Resectable Non-Small Cell Lung Cancer
      Opdivo, in combination with platinum-doublet chemotherapy, is indicated as neoadjuvant treatment of adult patients with resectable (tumors ≥4 cm or node positive) non-small cell lung cancer (NSCLC).

   5. Malignant Pleural Mesothelioma
      Opdivo, in combination with ipilimumab, is indicated for the first-line treatment of adult patients with unresectable malignant pleural mesothelioma.

6. Advanced Renal Cell Carcinoma
   a. Opdivo as a single agent is indicated for the treatment of adult patients with advanced renal cell carcinoma (RCC) who have received prior anti-angiogenic therapy.
   b. Opdivo, in combination with ipilimumab, is indicated for the first-line treatment of adult patients with intermediate or poor risk advanced RCC.
   c. Opdivo, in combination with cabozantinib, is indicated for the first-line treatment of adult patients with advanced RCC.

7. Classical Hodgkin Lymphoma
   Opdivo is indicated for the treatment of adult patients with classical Hodgkin lymphoma (cHL) that has relapsed or progressed after:
   a. Autologous hematopoietic stem cell transplantation (HSCT) and brentuximab vedotin, or
   b. Three or more lines of systemic therapy that includes autologous HSCT.

8. Squamous Cell Carcinoma of the Head and Neck
   Opdivo is indicated for the treatment of adult patients with recurrent or metastatic squamous cell carcinoma of the head and neck (SCCHN) with disease progression on or after platinum-based therapy.

9. Urothelial Carcinoma
   a. Opdivo is indicated for the adjuvant treatment of adult patients with urothelial carcinoma (UC) who are at high risk of recurrence after undergoing radical resection of UC.
   b. Opdivo is indicated for the treatment of adult patients with locally advanced or metastatic urothelial carcinoma who:
      i. Have disease progression during or following platinum-containing chemotherapy
      ii. Have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy.

10. Microsatellite Instability-High or Mismatch Repair Deficient Metastatic Colorectal Cancer
    Opdivo, as a single agent or in combination with ipilimumab, is indicated for the treatment of adult and pediatric patients 12 years and older with microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) metastatic colorectal cancer (CRC) that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan.

11. Hepatocellular Carcinoma
    Opdivo, in combination with ipilimumab, is indicated for the treatment of adult patients with hepatocellular carcinoma (HCC) who have been previously treated with sorafenib.

12. Esophageal Carcinoma
    a. Opdivo is indicated for the adjuvant treatment of completely resected esophageal or gastroesophageal junction cancer with residual pathologic disease in adult patients who have received neoadjuvant chemoradiotherapy (CRT).
    b. Opdivo, in combination with fluoropyrimidine- and platinum-containing chemotherapy, is indicated for the first-line treatment of adult patients with unresectable advanced or metastatic esophageal squamous cell carcinoma (ESCC).
    c. Opdivo, in combination with ipilimumab, is indicated for the first-line treatment of adult patients with unresectable advanced or metastatic esophageal squamous cell carcinoma (ESCC).
    d. Opdivo is indicated for the treatment of adult patients with unresectable advanced, recurrent or metastatic esophageal squamous cell carcinoma (ESCC) after prior fluoropyrimidine- and platinum-based chemotherapy.

13. Gastric Cancer, Gastroesophageal Junction Cancer, Esophageal Adenocarcinoma
    Opdivo, in combination with fluoropyrimidine- and platinum-containing chemotherapy, is indicated for the treatment of adult patients with advanced or metastatic gastric cancer, gastroesophageal junction cancer, and esophageal adenocarcinoma.

B. Compendial Uses
   1. Cutaneous melanoma
   2. Non-small cell lung cancer
   3. Renal cell carcinoma
   4. Classical Hodgkin lymphoma
   5. Head and neck cancers
   6. Urothelial carcinoma
      a. Bladder cancer
      b. Primary carcinoma of the urethra
      c. Upper genitourinary tract tumors
      d. Urothelial carcinoma of the prostate
   7. Colorectal cancer, including appendiceal adenocarcinoma and anal adenocarcinoma
   8. Hepatocellular carcinoma
   9. Uveal Melanoma
   10. Anal Carcinoma
   11. Merkel Cell Carcinoma
   12. Central Nervous System (CNS) brain metastases
   13. Gestational trophoblastic neoplasia
   14. Malignant pleural mesothelioma
   15. Malignant peritoneal mesothelioma
   16. Small bowel adenocarcinoma
   17. Ampullary Adenocarcinoma
   18. Extranodal NK/T-cell lymphoma
   19. Endometrial Carcinoma
   20. Vulvar Cancer
   21. Gastric Cancer
   22. Esophageal/Esophagogastric Junction Cancers
   23. Small cell lung cancer
   24. Cervical Cancer
   25. Pediatric Diffuse High-Grade Gliomas
   26. Pediatric Primary Mediastinal Large B-cell Lymphoma
   27. Kaposi Sarcoma
   28. Bone Cancer
   29. Biliary Tract Cancers
      a. Cholangiocarcinoma
      b. Gallbladder Cancer
   30. Soft Tissue Sarcoma
      a. Extremity/body wall sarcoma
      b. Head/neck sarcoma
      c. Retroperitoneal/intra-abdominal sarcoma
      d. Rhabdomyosarcoma
      e. Angiosarcoma

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

IV. DOCUMENTATION

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

A. Documentation of laboratory report confirming MSI-H or mismatch repair deficient (dMMR) tumor status, where applicable.
B. Documentation of programmed death ligand 1 (PD-L1) tumor expression, where applicable.
C. Documentation of the presence of EGFR exon 19 deletions or exon 21 L858R mutations or ALK rearrangements, where applicable.

V. EXCLUSIONS

Coverage will not be provided for members who have experienced disease progression while on programmed death receptor-1 (PD-1) or programmed death ligand 1 (PD-L1) inhibitor therapy (other than when used as second-line or subsequent therapy for metastatic or unresectable melanoma in combination with ipilimumab following progression on single agent anti-PD-1 immunotherapy).

VI. CRITERIA FOR INITIAL APPROVAL

A. Cutaneous Melanoma

Authorization of 6 months may be granted for treatment of cutaneous melanoma in either of the following settings:

1. The requested medication will be used as a single agent or in combination with ipilimumab (4 doses of ipilimumab, followed by Opdivo as a single agent) for locally recurrent, unresectable, progressive or metastatic disease.
2. The requested medication will be used as a single agent or in combination with ipilimumab as adjuvant treatment of stage III or IV disease if no evidence of disease following metastasis-directed therapy (i.e., complete resection).

B. Non-Small Cell Lung Cancer (NSCLC)

1. Authorization of 6 months may be granted for treatment of recurrent, advanced or metastatic non-small cell lung cancer if either of the following criteria are met:
   a. There are no EGFR exon 19 deletions or exon 21 L858R mutations or ALK rearrangements (unless testing is not feasible due to insufficient tissue) and the requested medication will be used in a regimen containing ipilimumab.
   b. The requested medication will be used as single agent subsequent therapy.
2. Authorization of 3 months (for up to 3 cycles total) may be granted for neoadjuvant treatment of resectable non-small cell lung cancer (NSCLC) in combination with platinum-doublet chemotherapy.

C. Renal Cell Carcinoma

Authorization of 6 months may be granted for treatment of relapsed, advanced, or stage IV renal cell carcinoma, in any of the following settings:

1. The requested medication will be used as a single agent for clear cell histology as subsequent therapy.
2. The requested medication will be used as a single agent for non-clear cell histology.
3. The requested medication will be used in combination with ipilimumab (4 doses of ipilimumab, followed by Opdivo as a single agent) for disease with clear cell histology as:
   a. First-line therapy for poor or intermediate risk.
   b. First-line therapy for favorable risk.
   c. Subsequent therapy.
4. The requested medication will be used in combination with cabozantinib.

D. Classical Hodgkin Lymphoma (cHL)

Authorization of 6 months may be granted for treatment of classical Hodgkin lymphoma when either of the following criteria is met:

1. The requested medication will be used as palliative or subsequent therapy and the member meets any of the following criteria:
   a. Member has relapsed or progressed after high-dose therapy and autologous stem cell rescue (HDT/ASCR).
   b. Member has relapsed or refractory disease and is transplant-ineligible.
   c. Member has relapsed or refractory disease and was either heavily pretreated or there was a decrease in cardiac function.
   d. Member is post-allogeneic transplant

2. The requested medication will be used in combination with brentuximab vedotin or in combination with ICE (ifosfamide, carboplatin, etoposide) for relapsed or refractory disease.
3. The requested medication will be used as a single agent for disease refractory to at least three lines of prior therapy.

E. Head and Neck Cancers

Authorization of 6 months may be granted for treatment of head and neck cancers in members who meet either of the following criteria:

1. For unresectable, recurrent, persistent or metastatic disease.
2. For nasopharyngeal cancer in combination with cisplatin and gemcitabine for unresectable, recurrent, persistent or metastatic disease.

F. Urothelial Carcinoma – Bladder Cancer

Authorization of 6 months may be granted as a single agent for treatment of bladder cancer when any of the following conditions are met:

1. As subsequent therapy for locally advanced, recurrent, persistent, or metastatic disease.
2. As adjuvant therapy in members who are at high risk of recurrence after undergoing resection.

G. Urothelial Carcinoma – Primary Carcinoma of the Urethra

Authorization of 6 months may be granted as a single agent for treatment of primary carcinoma of the urethra when either of the following are met:

1. As subsequent therapy for recurrent, locally advanced, or metastatic disease.
2. As adjuvant therapy in members who are at high risk of recurrence after undergoing resection.

H. Urothelial Carcinoma – Upper Genitourinary Tract Tumors or Urothelial Carcinoma of the Prostate

Authorization of 6 months may be granted as a single agent for treatment of upper genitourinary (GU) tract tumors or urothelial carcinoma of the prostate when either of the following are met:

1. As subsequent therapy for locally advanced or metastatic disease.
2. As adjuvant therapy in members who are at high risk of recurrence after undergoing resection.

I. Colorectal Cancer

Authorization of 6 months may be granted for treatment of colorectal cancer, including appendiceal adenocarcinoma and anal adenocarcinoma, for microsatellite-instability high (MSI-H) or mismatch repair deficient (dMMR) tumors when used as a single agent or in combination with ipilimumab (4 doses of ipilimumab, followed by Opdivo as a single agent) for advanced, metastatic, unresectable, or inoperable disease.

J. Small Bowel Adenocarcinoma

Authorization of 6 months may be granted as a single agent or in combination with ipilimumab for treatment of advanced or metastatic small bowel adenocarcinoma for microsatellite-instability high (MSI-H) or mismatch repair deficient (dMMR) tumors.

K. Ampullary Adenocarcinoma

Authorization of 6 months may be granted in combination with ipilimumab for treatment of progressive, unresectable, or metastatic microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) ampullary adenocarcinoma.

L. Hepatocellular Carcinoma

Authorization of 6 months may be granted as a single agent or in combination with ipilimumab (4 doses of ipilimumab, followed by Opdivo as a single agent) for treatment of hepatocellular carcinoma.

M. Uveal Melanoma

Authorization of 6 months may be granted as a single agent or in combination with ipilimumab for treatment of uveal melanoma for distant metastatic disease.

N. Anal Carcinoma
Authorization of 6 months may be granted as a single agent for subsequent treatment of metastatic anal carcinoma.

O. Merkel Cell Carcinoma
Authorization of 6 months may be granted for treatment of Merkel cell carcinoma in either of the following settings:
1. Metastatic disease.
2. Neoadjuvant treatment of node positive disease.
3. Progressive, unresectable, recurrent, or stage IV disease when used in combination with ipilimumab.

P. CNS Brain Metastases
Authorization of 6 months may be granted for treatment of CNS brain metastases when either of the following criteria are met:
1. The requested medication will be used as a single agent or in combination with ipilimumab in members with melanoma.
2. The requested medication will be used as a single agent in members with PD-L1 positive non-small cell lung cancer.

Q. Gestational Trophoblastic Neoplasia
Authorization of 6 months may be granted as a single agent for treatment of gestational trophoblastic neoplasia for multiagent chemotherapy-resistant disease when either of the following criteria is met:
1. Member has recurrent or progressive intermediate trophoblastic tumor (placental site trophoblastic tumor or epithelioid trophoblastic tumor) following treatment with a platinum-based regimen.
2. Member has high-risk disease.

R. Malignant Pleural or Peritoneal Mesothelioma
Authorization of 6 months may be granted for the treatment of malignant pleural or peritoneal mesothelioma, including pericardial mesothelioma and tunica vaginalis testis mesothelioma, in either of the following settings:
1. The requested medication will be used as first line therapy in combination with ipilimumab.
2. The requested medication will be used as subsequent therapy as a single agent or in combination with ipilimumab.

S. Esophageal and Esophagogastric Junction Carcinoma
1. Authorization of 6 months may be granted for treatment of esophageal or esophagogastric junction carcinoma in any of the following settings:
   a. As first-line treatment of unresectable, advanced, recurrent or metastatic squamous cell carcinoma in combination with ipilimumab or fluoropyrimidine- and platinum-containing chemotherapy.
   b. As subsequent therapy for treatment of unresectable advanced, recurrent or metastatic squamous cell carcinoma.
   c. As treatment of adenocarcinoma in members who are not surgical candidates or have unresectable locally advanced, recurrent or metastatic disease when the requested medication will be used in combination with chemotherapy.
2. Authorization of 6 months may be granted for adjuvant treatment of completely resected esophageal or gastroesophageal junction cancer with residual pathologic disease.

T. Extranodal NK/T-Cell Lymphoma
Authorization of 6 months may be granted for treatment of relapsed or refractory extranodal NK/T-cell lymphoma.

U. Endometrial Carcinoma
Authorization of 6 months may be granted as a single agent for subsequent treatment of recurrent or metastatic microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) endometrial carcinoma.

V. Vulvar Cancer
Authorization of 6 months may be granted for treatment of HPV-related advanced, recurrent, or metastatic vulvar cancer as subsequent therapy as a single agent.

W. Gastric Cancer
Authorization of 6 months may be granted for treatment of gastric cancer in members who are not surgical candidates or have unresectable locally advanced, recurrent, or metastatic disease, when the requested medication will be used in combination with chemotherapy.

X. Small Cell Lung Cancer
Authorization of 6 months may be granted for subsequent treatment of relapsed or progressive small cell lung cancer as a single agent.

Y. Cervical Cancer
Authorization of 6 months may be granted for subsequent treatment of recurrent or metastatic cervical cancer as a single agent if PD-L1 positive (combined positive score [CPS] ≥1).

Z. Pediatric Diffuse High-Grade Gliomas
Authorization of 6 months may be granted for hypermutant tumor pediatric diffuse high-grade glioma as adjuvant treatment or for recurrent or progressive disease.

AA. Pediatric Primary Mediastinal Large B-Cell Lymphoma
Authorization of 6 months may be granted as a single agent or in combination with brentuximab vedotin for treatment of relapsed or refractory primary mediastinal large B-cell lymphoma.

BB. Kaposi Sarcoma
Authorization of 6 months may be granted in combination with ipilimumab for subsequent treatment of relapsed/refractory classic Kaposi Sarcoma.

CC. Bone Cancer
Authorization of 6 months may be granted in combination with ipilimumab for unresectable or metastatic disease when all of the following are met:
1. Disease has tumor mutation burden-high (TMB-H) [≥10 mutations/megabase (mut/Mb)] tumors
2. Disease has progressed following prior treatment and has no satisfactory alternative treatment options

DD. Biliary Tract Cancers (Cholangiocarcinoma and Gallbladder Cancer)
Authorization of 6 months may be granted as subsequent treatment in combination with ipilimumab for unresectable or resected gross residual (R2) disease, or metastatic disease that is tumor mutation burden-high (TMB-H).

EE. Soft Tissue Sarcoma
Authorization of 6 months may be granted for treatment of soft tissue sarcoma in the following settings:
1. The requested medication will be used as a single agent or in combination with ipilimumab for treatment of extremity/body wall sarcomas, head/neck sarcomas and retroperitoneal/intra-abdominal sarcomas and rhabdomyosarcoma.
2. The requested medication will be used in combination with ipilimumab for the treatment of angiosarcoma.

VII. CONTINUATION OF THERAPY

A. Adjuvant treatment of melanoma or urothelial carcinoma
Authorization of 6 months may be granted (up to 12 months total) for continued treatment in members requesting reauthorization for cutaneous melanoma or urothelial carcinoma who have not experienced disease recurrence or an unacceptable toxicity.

B. Non-small cell lung cancer or Malignant pleural mesothelioma
Authorization of 6 months may be granted (up to 24 months total when used in combination with ipilimumab) for continued treatment in members requesting reauthorization for non-small cell lung cancer or malignant pleural, including pericardial mesothelioma and tunica vaginalis testis mesothelioma subtypes, when there is no evidence of unacceptable toxicity or disease progression while on the current regimen. Neoadjuvant treatment of NSCLC will be approved for a total of 3 months of therapy.

C. Renal Cell Carcinoma
Authorization of 6 months may be granted (up to 24 months total when used in combination with cabozantinib) for continued treatment in members requesting reauthorization for renal cell carcinoma when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

D. Gastric Cancer, Esophageal Cancer, and Esophagogastric Junction Carcinoma
Authorization of 6 months may be granted for continued treatment in members requesting reauthorization for gastric cancer, esophageal cancer, and esophagogastric junction carcinoma when there is no evidence of unacceptable toxicity or disease progression while on the current regimen for the following durations of therapy:
1. Esophageal squamous cell carcinoma in combination with ipilimumab or chemotherapy for up to 24 months
2. Unresectable advanced, recurrent or metastatic esophageal squamous cell carcinoma as a single agent until disease progression or unacceptable toxicity
3. Adjuvant treatment of resected esophageal or esophagogastric junction cancer as a single agent for up to 12 months
4. Gastric cancer, esophagogastric junction cancer, and esophageal adenocarcinoma in combination with chemotherapy for up to 24 months

E. All other indications
Authorization of 6 months may be granted for continued treatment in members requesting reauthorization for all other indications listed in Section IV when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

Section 3: Oncology Clinical Policy

PROGRAM DESCRIPTION

The National Comprehensive Care Network® (NCCN®) is an alliance of leading cancer centers devoted to patient care, research and education dedicated to improving the quality, effectiveness, and efficiency of cancer care so patients can live better lives.[1] It is comprised of oncology experts who convene regularly to establish the best treatments for patients. NCCN develops various resources for use by stakeholders in the health care delivery system. These resources include, but are not limited to, the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®), the NCCN Drugs & Biologics Compendium (NCCN Compendium®) and the NCCN Chemotherapy Order Templates (NCCN Templates®).

NCCN Templates® are based on NCCN Guidelines® and NCCN Compendium®. The NCCN Compendium lists the appropriate drugs and biologics as treatment options for specific cancers using U.S. Food and Drug Administration (FDA)-approved disease indications and specific NCCN panel recommendations. Each recommendation is supported by a level of evidence category.

NCCN Categories of Evidence and Consensus[2]

• Category 1: Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
• Category 2A: Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
• Category 2B: Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.

• Category 3: Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

POLICY

Policy for Regimen Prior Authorization
A regimen prior authorization allows submission of a single prior authorization request for all oncology drugs or biologics within an NCCN template that require prior authorization.

PROCEDURE

This policy provides coverage of a regimen review when all of the following criteria are met:
1. Regimen prior authorization reviews, based on NCCN templates, are initiated through the provider portal.
   - If the prior authorization request is submitted via phone or fax, each drug or biologic will need to be submitted and reviewed as a separate prior authorization request for review with drug-specific criteria.
2. The prior authorization review is requested for an oncology drug or biologic.
3. The member is eligible for regimen review.
4. The indication is for a cancer that is eligible for regimen review. Currently, the cancer types in scope for regimen review include the following:
   - Ampullary Adenocarcinoma
   - Anal Carcinoma
   - B-Cell Lymphomas
   - Basal Cell Skin Cancer
   - Biliary Tract Cancers
   - Bone Cancer
   - Breast Cancer
   - Bladder Cancer
   - Central Nervous System Cancers
   - Cervical Cancer
   - Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma
   - Chronic Myeloid leukemia
   - Colon Cancer
   - Dermatofibrosarcoma Protuberans
   - Esophageal Cancer
   - Gastric Cancer
   - Gastrointestinal Stromal Tumors
   - Gestational Trophoblastic Neoplasms
   - Hairy Cell Leukemia
   - Head and Neck Cancers
   - Hodgkin Lymphoma
   - Hepatocellular Carcinoma
   - Kaposi Sarcoma
   - Kidney Cancer
   - Melanoma: Cutaneous
   - Melanoma: Uveal
   - Merkel Cell Carcinoma
   - Mesothelioma: Peritoneal
   - Mesothelioma: Pleural
   - Myelodysplastic Syndromes
   - Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Gene Fusions
   - Myeloproliferative Neoplasms
   - Neuroendocrine and Adrenal Tumors
   - Non-Small Cell Lung Cancer

- Occult Primary
- Ovarian Cancer
- Pancreatic Cancer
- Penile Cancer
- Prostate Cancer
- Rectal Cancer
- Small Bowl Adenocarcinoma
- Small Cell Lung Cancer
- Soft Tissue Sarcoma
- Squamous Cell Skin Cancer
- Systemic Mastocytosis
- Systemic Light Chain Amyloidosis
- Testicular Cancer
- Thymomas and Thymic Carcinomas
- Thyroid Carcinoma
- Uterine Neoplasms
- Vulvar Cancer
- Waldenström Macroglobulinemia / Lymphoplasmacytic Lymphoma

In addition, the following criteria must be met for approval:

1. The requested regimen for the drug(s) or biologic(s) and indication is consistent with an NCCN recommendation with a level of evidence category of 1 or 2A.
2. The NCCN template must be accepted by the provider without modification.

Further review may be indicated when the above criteria are not met.

Authorizations may be granted for 12 months or as medically required, based on the member's condition and provider's assessment.

Supportive Care: Myeloid Growth Factor Therapy
Granulocyte colony stimulating factors are recommended for primary prophylaxis based on the febrile neutropenia risk of the chemotherapy regimen. Febrile neutropenia risk levels vary by NCCN Chemotherapy Order template and are listed at the top of the template. Regimens associated with a high or intermediate risk of febrile neutropenia may include a granulocyte colony stimulating factor as part of the prior authorization.

Continuation of Therapy
To submit a request for continuation of therapy, a new regimen prior authorization review must be requested. Upon template selection, the template must be modified to include the appropriate therapies being used for maintenance treatment. The regimen request will be submitted for further review.

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

REFERENCES:

SECTION 1

1. Opdivo [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; February 2023.
2. Bavencio [package insert]. Rockland, MA: EMD Serono, Inc; July 2020.
3. Imfinzi [prescribing information]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; November 2022.
4. Jemperli [prescribing information]. Philadelphia, PA: GlaxoSmithKline LLC; February 2023.
5. Keytruda [prescribing information]. Rahway, NJ: Merck Sharp & Dome LLC.; April 2023.
6. Libtayo [prescribing information]. Tarrytown, NY: Regeneron Pharmaceuticals, Inc.; April 2023.
7. Tecentriq [package insert]. South San Francisco, CA: Genentech, Inc.; December 2022.
8. Yervoy [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; February 2023.

9. Opdualag [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; March 2022.
10. Zynyz [package insert]. Wilmington, DE: Incyte Corporation; March 2023.

SECTION 2

1. Opdivo [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; February 2023.
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SECTION 3

1. National Comprehensive Cancer Network. About NCCN website. https://www.nccn.org/home/about, accessed June 6, 2023.
2. National Comprehensive Cancer Network. NCCN Categories of Evidence and Consensus website, https://www.nccn.org/guidelines/guidelines-process/development-and-update-of-guidelines, accessed June 6, 2023.
3. National Comprehensive Cancer Network. NCCN Guidelines website. https://www.nccn.org/guidelines/category_1, accessed June 6, 2023. (Note: An account may be required.)
4. National Comprehensive Cancer Network. NCCN Drugs and Biologics Compendium website https://www.nccn.org/compendia-templates/compendia/drugs-and-biologics-compendia, accessed June 6, 2023. (Note: A subscription may be required.)
5. National Comprehensive Cancer Network. NCCN Chemotherapy Order Templates (NCCN Templates) website. https://www.nccn.org/compendia-templates/nccn-templates-main/browse-by-cancer-type, accessed June 6, 2023. (Note: A subscription may be required.)

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the site of care prior authorization review (where applicable):

A. Medical records supporting the member has experienced an adverse reaction that did not respond to conventional interventions or a severe adverse event during or immediately after an infusion or a severe toxicity requiring continuous monitoring
B. Medical records supporting the member is medically unstable
C. Medical records supporting the member has severe venous access issues that require specialized interventions only available in the outpatient hospital setting
D. Medical records supporting the member has behavioral issues and/or physical or cognitive impairment and no access to a caregiver
E. Medical records supporting the member is receiving provider administered combination therapy.

Section 2: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

OPDUALAG (nivolumab and relatlimab-rmbw)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Opdualag is indicated for the treatment of adult and pediatric patients 12 years of age or older with unresectable or metastatic melanoma.

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

II. CRITERIA FOR INITIAL APPROVAL

Melanoma
Authorization of 6 months may be granted for treatment of adult members and children, 12 years of age and older weighing at least 40kg, with unresectable or metastatic melanoma.

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 there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

REFERENCES:

SECTION 1

1. Opdivo [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; February 2023.
2. Bavencio [package insert]. Rockland, MA: EMD Serono, Inc; July 2020.
3. Imfinzi [prescribing information]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; November 2022.
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8. Yervoy [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; February 2023.

9. Opdualag [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; March 2022.
10. Zynyz [package insert]. Wilmington, DE: Incyte Corporation; March 2023.

SECTION 2

1. Opdualag [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; March 2022.

POLICY Document for OPDUALAG (nivolumab and relatlimab-rmbw)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, lower cost site of care and overall, clinically appropriate use. This document provides specific information to each of the three sections of the overall policy.

Section 1: Site of Care

- Policy information specific to site of care (outpatient, hospital outpatient, home infusion)

Section 2: Clinical Criteria

- Policy information specific to the clinical appropriateness for the medication

Section 1: Site of Care

CareFirst Site of Care Criteria
Administration of Intravenous Checkpoint Inhibitors
Bavencio, Imfinzi, Jemperli, Keytruda, Libtayo, Opdivo, Opdualag, Tecentriq, Yervoy and Zynyz

POLICY

I. CRITERIA FOR APPROVAL FOR ADMINISTRATION IN OUTPATIENT HOSPITAL SETTING

This policy provides coverage for administration of a checkpoint inhibitor in an outpatient hospital setting for the initial 6 months approval and up to 45 days for renewal of therapy.

This policy provides coverage for administration of a checkpoint inhibitor in an outpatient hospital setting for a longer course of treatment when ANY of the following criteria are met:

A. The member has experienced an adverse reaction that did not respond to conventional interventions (eg, acetaminophen, steroids, diphenhydramine, fluids, other pre-medications or slowing of infusion rate) or a severe adverse event (anaphylaxis, anaphylactoid reactions, myocardial infarction, thromboembolism, or seizures) during or immediately after an infusion or has experienced severe toxicity requiring continuous monitoring (e.g. Grade 2-4 bullous dermatitis, transaminitis, pneumonitis, Stevens-Johnson syndrome, acute pancreatitis, primary adrenal insufficiency aseptic meningitis, encephalitis, transverse myelitis, myocarditis, pericarditis, arrhythmias, impaired ventricular function, conduction abnormalities).
B. The member is medically unstable (eg respiratory, cardiovascular, or renal conditions).
C. The member has severe venous access issues that require the use of a special interventions only available in the outpatient hospital setting.
D. The member has significant behavioral issues and/or physical or cognitive impairment that would impact the safety of the infusion therapy AND the patient does not have access to a caregiver.
E. The member is receiving provider administered combination chemotherapy.
F. The member is less than 14 years of age.

For situations where administration of a checkpoint inhibitor does not meet the criteria for outpatient hospital infusion, coverage for a checkpoint inhibitor is provided when administered in alternative sites such as physician office, home infusion or ambulatory care.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the site of care prior authorization review (where applicable):

A. Medical records supporting the member has experienced an adverse reaction that did not respond to conventional interventions or a severe adverse event during or immediately after an infusion or a severe toxicity requiring continuous monitoring
B. Medical records supporting the member is medically unstable
C. Medical records supporting the member has severe venous access issues that require specialized interventions only available in the outpatient hospital setting
D. Medical records supporting the member has behavioral issues and/or physical or cognitive impairment and no access to a caregiver
E. Medical records supporting the member is receiving provider administered combination therapy.

Section 2: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

OPDUALAG (nivolumab and relatlimab-rmbw)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Opdualag is indicated for the treatment of adult and pediatric patients 12 years of age or older with unresectable or metastatic melanoma.

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

II. CRITERIA FOR INITIAL APPROVAL

Melanoma
Authorization of 6 months may be granted for treatment of adult members and children, 12 years of age and older weighing at least 40kg, with unresectable or metastatic melanoma.

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 there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

REFERENCES

SECTION 1

1. Opdivo [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; February 2023.
2. Bavencio [package insert]. Rockland, MA: EMD Serono, Inc; July 2020.
3. Imfinzi [prescribing information]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; June 2023.
4. Jemperli [prescribing information]. Philadelphia, PA: GlaxoSmithKline LLC; July 2023.
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7. Tecentriq [package insert]. South San Francisco, CA: Genentech, Inc.; December 2022.
8. Yervoy [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; February 2023.
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10. Zynyz [package insert]. Wilmington, DE: Incyte Corporation; March 2023.

SECTION 2

1. Opdualag [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; March 2022.

POLICY Document for ORENCIA (abatacept)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, lower cost site of care and overall, clinically appropriate use. This document provides specific information to each of the three sections of the overall policy.

Section 1: Preferred Product
- Policy information specific to preferred medications

Section 2: Site of Care
- Policy information specific to site of care (outpatient, hospital outpatient, home infusion)

Section 3: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 1: Preferred Product

EXCEPTIONS CRITERIA
AUTOIMMUNE CONDITIONS

PREFERRED PRODUCTS: ENTYVIO, ILUMYA, SIMPONI ARIA AND STELARA IV

POLICY
This policy informs prescribers of preferred products and provides an exception process for targeted products through prior authorization.

I. PLAN DESIGN SUMMARY

This program applies to the autoimmune drug products specified in this policy. Coverage for targeted products is provided based on clinical circumstances that would exclude the use of the preferred product and may be based on previous use of a product. The coverage review process will ascertain situations where a clinical exception can be made. This program applies to all members requesting treatment with Cimzia vial. For plaque psoriasis, this program applies to all members requesting treatment with a targeted product. For all other indications, this program applies to all members who are new to treatment with a targeted product for the first time.

Each referral is reviewed based on all utilization management (UM) programs implemented for the client.

Table. Drugs for autoimmune conditions

	Product(s)
Preferred*	• **Entyvio** (vedolizumab) • **Ilumya** (tildrakizumab-asmn) • **Simponi Aria** (golimumab, intravenous) • **Stelara IV** (ustekinumab)**
Targeted	• **Actemra** (tocilizumab) • **Cimzia** (certolizumab pegol) • **Orencia** (abatacept)

Abbreviation: IV = intravenous

*: Medications considered formulary or preferred on your plan may still require a clinical prior authorization review

**Stelara IV is indicated for a one-time induction dose for Crohn's disease and ulcerative colitis.

II. EXCEPTION CRITERIA

This program applies to members requesting treatment for an indication that is FDA-approved for the preferred products.

Coverage for a targeted product is provided when any of the following criteria is met:

A. For Cimzia, when any of the following criteria is met:
   1. For prefilled syringe requests, member is currently receiving treatment with Cimzia prefilled syringes excluding when the requested targeted product is obtained as samples or via manufacturer's patient assistance programs, unless the request is for plaque psoriasis.
   2. Member has a documented inadequate response or intolerable adverse event with all of the preferred products (Entyvio, Ilumya, Simponi Aria, and Stelara IV) where the product's indications overlap.
   3. Member is currently breastfeeding, pregnant or planning pregnancy.

B. For all other targeted products, when any of the following criteria is met:
   1. Member is currently receiving treatment with the requested targeted product, excluding when the requested targeted product is obtained as samples or via manufacturer's patient assistance programs.
   2. Member has a documented inadequate response or intolerable adverse event with all of the preferred products (Entyvio, Ilumya, Simponi Aria, and Stelara IV) where the product's indications overlap, unless there is a documented clinical reason to avoid TNF inhibitors (see Appendix).

III. Appendix: Clinical reasons to avoid TNF inhibitors

- History of demyelinating disorder
- History of congestive heart failure
- History of hepatitis B virus infection
- Autoantibody formation/lupus-like syndrome
- History or risk of lymphoma or other malignancy
- History of being a primary non-responder to a TNF inhibitor

Section 2: Site of Care

CareFirst Site of Care Criteria
Administration of Orencia

POLICY

I. CRITERIA FOR APPROVAL FOR ADMINISTRATION IN OUTPATIENT HOSPITAL SETTING

This policy provides coverage for administration of Orencia in an outpatient hospital setting for 3 months when a member is new to therapy or is reinitiating therapy after not being on therapy for more than 6 months.

This policy provides coverage for administration of Orencia in an outpatient hospital setting for a longer course of treatment when ANY of the following criteria are met:

A. The member has experienced an adverse reaction that did not respond to conventional interventions (eg, acetaminophen, steroids, diphenhydramine, fluids or other pre-medications) or a severe adverse event

(anaphylaxis, anaphylactoid reactions, myocardial infarction, thromboembolism, or seizures) during or immediately after an infusion.
B. The member is medically unstable (eg respiratory, cardiovascular, or renal conditions).
C. The member has severe venous access issues that require the use of special interventions only available in the outpatient hospital setting.
D. The member has significant behavioral issues and/or physical or cognitive impairment that would impact the safety of the infusion therapy AND the patient does not have access to a caregiver.
E. The member is less than 14 years of age.

For situations where administration of Orencia does not meet the criteria for outpatient hospital infusion, coverage for Orencia is provided when administered in alternative sites such as; physician office, home infusion or ambulatory care.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the site of care prior authorization review (where applicable):
A. Medical records supporting the member has experienced an adverse reaction that did not respond to conventional interventions or a severe adverse event during or immediately after an infusion
B. Medical records supporting the member is medically unstable
C. Medical records supporting the member has severe venous access issues that require specialized interventions only available in the outpatient hospital setting
D. Medical records supporting the member has behavioral issues and/or physical or cognitive impairment and no access to a caregiver

Section 3: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

ORENCIA (abatacept)

POLICY

III. INDICATIONS

The indications below including FDA-approved indications and compendial 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.

IV. 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. 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.

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.

V. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with one of the following:
A. Rheumatoid arthritis and articular juvenile idiopathic arthritis: rheumatologist
B. Psoriatic arthritis: rheumatologist or dermatologist
C. Prophylaxis of acute graft versus host disease (aGVHD), chronic GVHD, and immune checkpoint inhibitor-related toxicity: oncologist or hematologist

VI. 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 (JIA)

1. Authorization of 12 months may be granted for members 2 years of age and 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 and 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 member also meets one of the following:
      a. High-risk joints are involved (e.g., cervical spine, wrist, or hip).
      b. Has 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. Prophylaxis of acute graft versus host disease
Authorization of 1 month may be granted for prophylaxis of acute graft versus host disease in members 2 years of age and older 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.

VII. 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 (JIA)
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 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. 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.

VIII. 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.

IX. DOSAGE AND ADMINISTRATION

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

X. APPENDICES

Appendix A: Examples of Contraindications to Methotrexate or Leflunomide

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

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POLICY Document for ELOXATIN (oxaliplatin) oxaliplatin

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, and overall, clinically appropriate use. This document provides specific information to both sections of the overall policy.

Section 1: Clinical Criteria

- Policy information specific to the clinical appropriateness for the medication

Section 2: Oncology Clinical Policy

- Policy information specific to regimen review per NCCN Guidelines.

Section 1: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

ELOXATIN (oxaliplatin)
oxaliplatin

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Oxaliplatin, in combination with infusional fluorouracil and leucovorin, is indicated for:
1. Adjuvant treatment of stage III colon cancer in patients who have undergone complete resection of the primary tumor.
2. Treatment of advanced colorectal cancer.

B. Compendial Uses
1. Colon cancer
2. Rectal cancer
3. Esophageal or esophagogastric junction cancers
4. Gastric cancer
5. Hepatobiliary cancers
   a. Extrahepatic cholangiocarcinoma
   b. Intrahepatic cholangiocarcinoma
   c. Gallbladder cancer
6. Bladder cancer (including non-urothelial and urothelial cancer with variant histology)
7. Neuroendocrine and adrenal tumors
   a. Neuroendocrine tumors of the gastrointestinal tract, lung, and thymus
   b. Neuroendocrine tumors of the pancreas
   c. Well differentiated grade 3 neuroendocrine tumors
   d. Poorly differentiated/large or small cell disease/mixed neuroendocrine-non-neuroendocrine neoplasms
8. Occult primary tumors (cancer of unknown primary)

9. Ovarian cancer, fallopian tube cancer, and primary peritoneal cancer
    a. Epithelial ovarian cancer, fallopian tube cancer, and primary peritoneal cancer
    b. Carcinosarcoma (malignant mixed Müllerian tumors)
    c. Clear cell carcinoma of the ovary
    d. Mucinous carcinoma of the ovary
    e. Grade 1 endometrioid carcinoma
    f. Low-grade serous carcinoma/ovarian borderline epithelial tumors (low malignant potential)
    g. Malignant germ cell tumors
10. Pancreatic adenocarcinoma
11. Testicular cancer
12. Chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL)
13. Anal carcinoma
14. B-Cell lymphomas
    a. Follicular lymphoma (grade 1-2)
    b. Histologic Transformation of Indolent Lymphomas to Diffuse Large B-Cell Lymphoma
    c. Mantle Cell Lymphoma
    d. Diffuse Large B-Cell Lymphoma
    e. High-Grade B-Cell Lymphomas
    f. AIDS-Related B-Cell Lymphomas
    g. Post-Transplant Lymphoproliferative Disorders
15. Primary cutaneous lymphomas
    a. Mycosis fungoides/Sezary syndrome
    b. Primary cutaneous CD30+ T-Cell lymphoproliferative disorders
16. T-Cell lymphomas
    a. Peripheral T-Cell lymphomas
    b. Adult T-Cell leukemia/lymphoma
    c. Extranodal NK/T-Cell lymphoma
    d. Hepatosplenic T-Cell lymphoma
    e. Breast Implant-Associated Anaplastic Large Cell Lymphoma (ALCL)
17. Classic Hodgkin lymphoma
18. Small bowel adenocarcinoma
19. Ampullary adenocarcinoma

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

II. CRITERIA FOR INITIAL APPROVAL

A. Colorectal Cancer
Authorization of 6 months may be granted for treatment of colorectal cancer (including appendiceal adenocarcinoma, anal adenocarcinoma, and colon and rectal cancers).

B. Pancreatic Adenocarcinoma
Authorization of 6 months may be granted for treatment of pancreatic adenocarcinoma.

C. Esophageal and Esophagogastric Junction Cancers
Authorization of 6 months may be granted for treatment of esophageal and esophagogastric junction cancers.

D. Gastric Cancer
Authorization of 6 months may be granted for treatment of gastric cancer.

E. Hepatobiliary Cancers
Authorization of 6 months may be granted for treatment of hepatobiliary cancers (including intrahepatic and extrahepatic cholangiocarcinoma and gallbladder cancer).

F. Neuroendocrine and Adrenal Tumors
Authorization of 6 months may be granted for treatment of neuroendocrine and adrenal tumors (including neuroendocrine tumors of the gastrointestinal tract, lung, and thymus, neuroendocrine tumors of the pancreas, well differentiated grade 3 neuroendocrine tumors and poorly differentiated/large or small cell disease/mixed neuroendocrine-non-neuroendocrine neoplasms).

G. Occult Primary Tumors (cancer of unknown primary)
Authorization for 6 months may be granted for treatment of occult primary tumors.

H. Ovarian Cancer, Fallopian Tube Cancer, and Primary Peritoneal Cancer
Authorization of 6 months may be granted for treatment of epithelial ovarian cancer, fallopian tube cancer, primary peritoneal cancer, carcinosarcoma (malignant mixed Müllerian tumors), clear cell carcinoma of the ovary, mucinous carcinoma of the ovary, grade 1 endometrioid carcinoma, low-grade serous carcinoma/ovarian borderline epithelial tumors (low malignant potential), and malignant germ cell tumors.

I. Testicular Cancer
Authorization of 6 months may be granted for treatment of testicular cancer.

J. Bladder Cancer
Authorization of 6 months may be granted for treatment of bladder cancer (including non-urothelial and urothelial cancer with variant histology).

K. Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (CLL/SLL)
Authorization of 6 months may be granted for treatment of CLL/SLL.

L. Anal Carcinoma
Authorization of 6 months may be granted for treatment of metastatic anal cancer.

M. B-Cell Lymphomas
Authorization of 6 months may be granted for treatment of B-Cell lymphomas (including follicular lymphoma [grade 1-2], histologic transformation of indolent lymphomas to diffuse large B-Cell lymphoma, mantle cell lymphoma, diffuse large B-Cell lymphoma, high-grade B-Cell lymphomas, AIDS-Related B-Cell lymphomas, and post-transplant lymphoproliferative disorders).

N. Primary Cutaneous Lymphomas
Authorization of 6 months may be granted for treatment of primary cutaneous lymphomas (including mycosis fungoides/Sezary syndrome and primary cutaneous CD30+ T-Cell lymphoproliferative disorders).

O. T-Cell Lymphomas
Authorization of 6 months may be granted for treatment of T-Cell lymphomas (including peripheral T-Cell lymphomas, adult T-Cell leukemia/lymphoma, hepatosplenic T-Cell lymphoma, extranodal NK/T-Cell lymphoma, and breast implant-associated ALCL).

P. Classic Hodgkin Lymphoma
Authorization of 6 months may be granted for treatment of classic Hodgkin lymphoma.

Q. Small Bowel Adenocarcinoma
Authorization of 6 months may be granted for treatment of small bowel adenocarcinoma.

R. Ampullary Adenocarcinoma
Authorization of 6 months may be granted for treatment of ampullary adenocarcinoma.

III. CONTINUATION OF THERAPY

Authorization of 6 months may be granted for continued treatment in members requesting reauthorization for an indication in Section II when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

Section 2: Oncology Clinical Policy

PROGRAM DESCRIPTION

The National Comprehensive Care Network® (NCCN®) is an alliance of leading cancer centers devoted to patient care, research and education dedicated to improving the quality, effectiveness, and efficiency of cancer care so patients can live better lives.[1] It is comprised of oncology experts who convene regularly to establish the best treatments for patients. NCCN develops various resources for use by stakeholders in the health care delivery system. These resources include, but are not limited to, the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®), the NCCN Drugs & Biologics Compendium (NCCN Compendium®) and the NCCN Chemotherapy Order Templates (NCCN Templates®).

NCCN Templates® are based on NCCN Guidelines® and NCCN Compendium®. The NCCN Compendium lists the appropriate drugs and biologics as treatment options for specific cancers using U.S. Food and Drug Administration (FDA)-approved disease indications and specific NCCN panel recommendations. Each recommendation is supported by a level of evidence category.

NCCN Categories of Evidence and Consensus[2]

- Category 1: Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
- Category 2A: Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
- Category 2B: Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.
- Category 3: Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

POLICY

Policy for Regimen Prior Authorization

A regimen prior authorization allows submission of a single prior authorization request for all oncology drugs or biologics within an NCCN template that require prior authorization.

PROCEDURE

This policy provides coverage of a regimen review when all of the following criteria are met:

1. Regimen prior authorization reviews, based on NCCN templates, are initiated through the provider portal.
   - If the prior authorization request is submitted via phone or fax, each drug or biologic will need to be submitted and reviewed as a separate prior authorization request for review with drug-specific criteria.
2. The prior authorization review is requested for an oncology drug or biologic.
3. The member is eligible for regimen review.
4. The indication is for a cancer that is eligible for regimen review. Currently, the cancer types in scope for regimen review include the following:
   - Ampullary Adenocarcinoma
   - Anal Carcinoma
   - B-Cell Lymphomas
   - Basal Cell Skin Cancer

- Biliary Tract Cancers
- Bone Cancer
- Breast Cancer
- Bladder Cancer
- Central Nervous System Cancers
- Cervical Cancer
- Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma
- Chronic Myeloid leukemia
- Colon Cancer
- Dermatofibrosarcoma Protuberans
- Esophageal Cancer
- Gastric Cancer
- Gastrointestinal Stromal Tumors
- Gestational Trophoblastic Neoplasms
- Hairy Cell Leukemia
- Head and Neck Cancers
- Hodgkin Lymphoma
- Hepatocellular Carcinoma
- Kaposi Sarcoma
- Kidney Cancer
- Melanoma: Cutaneous
- Melanoma: Uveal
- Merkel Cell Carcinoma
- Mesothelioma: Peritoneal
- Mesothelioma: Pleural
- Myelodysplastic Syndromes
- Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Gene Fusions
- Myeloproliferative Neoplasms
- Neuroendocrine and Adrenal Tumors
- Non-Small Cell Lung Cancer
- Occult Primary
- Ovarian Cancer
- Pancreatic Cancer
- Penile Cancer
- Prostate Cancer
- Rectal Cancer
- Small Bowl Adenocarcinoma
- Small Cell Lung Cancer
- Soft Tissue Sarcoma
- Squamous Cell Skin Cancer
- Systemic Mastocytosis
- Systemic Light Chain Amyloidosis
- Testicular Cancer
- Thymomas and Thymic Carcinomas
- Thyroid Carcinoma
- Uterine Neoplasms
- Vulvar Cancer
- Waldenström Macroglobulinemia / Lymphoplasmacytic Lymphoma

In addition, the following criteria must be met for approval:

1. The requested regimen for the drug(s) or biologic(s) and indication is consistent with an NCCN recommendation with a level of evidence category of 1 or 2A.
2. The NCCN template must be accepted by the provider without modification.

Further review may be indicated when the above criteria are not met.

Authorizations may be granted for 12 months or as medically required, based on the member's condition and provider's assessment.

Supportive Care: Myeloid Growth Factor Therapy
Granulocyte colony stimulating factors are recommended for primary prophylaxis based on the febrile neutropenia risk of the chemotherapy regimen. Febrile neutropenia risk levels vary by NCCN Chemotherapy Order template and are listed at the top of the template. Regimens associated with a high or intermediate risk of febrile neutropenia may include a granulocyte colony stimulating factor as part of the prior authorization.

Continuation of Therapy
To submit a request for continuation of therapy, a new regimen prior authorization review must be requested. Upon template selection, the template must be modified to include the appropriate therapies being used for maintenance treatment. The regimen request will be submitted for further review.

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

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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.

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POLICY Document for OXLUMO (lumasiran)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, lower cost site of care and overall, clinically appropriate use. This document provides specific information to each of the three sections of the overall policy.

Section 1: Site of Care

- Policy information specific to site of care (outpatient, hospital outpatient, home infusion)

Section 2: Clinical Criteria

- Policy information specific to the clinical appropriateness for the medication

Section 1: Site of Care

CareFirst Site of Care Criteria
Administration of Subcutaneous Oxlumo

POLICY

I. CRITERIA FOR APPROVAL FOR ADMINISTRATION IN OUTPATIENT HOSPITAL SETTING

This policy provides coverage for administration of Oxlumo in an outpatient hospital setting for up to 60 days when a member is new to therapy or is reinitiating therapy after not being on therapy for at least 6 months.

This policy provides coverage for administration of Oxlumo in an outpatient hospital setting for a longer course of treatment when ANY of the following criteria are met:

A. The member has experienced an adverse reaction that did not respond to conventional interventions (eg, acetaminophen, steroids, diphenhydramine, fluids or other pre-medications) or a severe adverse event (anaphylaxis, anaphylactoid reactions, myocardial infarction, thromboembolism, or seizures) during or immediately after administration.
B. The member is medically unstable (eg respiratory, cardiovascular, or renal conditions).
C. The member has significant behavioral issues and/or physical or cognitive impairment that would impact the safety of therapy AND the patient does not have access to a caregiver.
D. The member is less than 14 years of age.

For situations where administration of Oxlumo does not meet the criteria for outpatient hospital administration, coverage for Oxlumo is provided when given in alternative sites such as; physician office, home, or ambulatory care.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the site of care prior authorization review (where applicable):

A. Medical records supporting the member has experienced an adverse reaction that did not respond to conventional interventions or a severe adverse event during or immediately after administration
B. Medical records supporting the member is medically unstable
C. Medical records supporting the member has behavioral issues and/or physical or cognitive impairment and no access to a caregiver

CVS/caremark

Section 2: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

OXLUMO (lumasiran)

POLICY

III. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Oxlumo is indicated for the treatment of primary hyperoxaluria type 1 (PH1) to lower urinary and plasma oxalate levels in pediatric and adult patients.

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

IV. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: Molecular genetic tests showing a mutation in the alanine:glyoxylate aminotransferase (AGXT) gene or liver enzyme analysis demonstrating absent or significantly reduced alanine:glyoxylate aminotransferase (AGT) activity.

V. CRITERIA FOR INITIAL APPROVAL

Primary hyperoxaluria type 1 (PH1)
Authorization of 12 months may be granted for treatment of primary hyperoxaluria type 1 (PH1) when the member has a documented diagnosis of primary hyperoxaluria type 1 (PH1) confirmed by either:
A. Molecular genetic test showing a mutation in the alanine:glyoxylate aminotransferase (AGXT) gene.
B. Liver enzyme analysis demonstrating absent or significantly reduced alanine:glyoxulate aminotransferase (AGT) activity.

VI. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for members who meet all initial authorization criteria and the member's urinary and/or plasma oxalate has decreased or normalized since initiation of therapy.

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POLICY Document for PADCEV (enfortumab vedotin-ejfv)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication. This document provides specific information to each section of the overall policy.

Section 1: Clinical Criteria
Policy information specific to the clinical appropriateness for the medication
Section 2: Oncology Clinical Policy
Policy information specific to regimen review per NCCN Guidelines.

Section 1: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

PADCEV (enfortumab vedotin-ejfv)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Padcev (enfortumab vedotin-ejfv) is indicated for the treatment of adult patients with locally advanced or metastatic urothelial cancer who have previously received a programmed death receptor-1 (PD-1) or programmed death-ligand 1 (PD-L1) inhibitor, and a platinum-containing chemotherapy or are ineligible for cisplatin-containing chemotherapy and have previously received one or more prior lines of therapy.

B. Compendial Uses
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. CRITERIA FOR INITIAL APPROVAL

A. Urothelial Carcinoma – Bladder Cancer
Authorization of 12 months may be granted for treatment of bladder cancer as a single agent when used as subsequent therapy following platinum-containing chemotherapy and prior treatment with a programmed death receptor-1 (PD-1) or programmed death-ligand 1 (PD-L1) inhibitor or when used as subsequent therapy for members who are ineligible for cisplatin-containing chemotherapy 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 treatment of locally advanced, recurrent, or metastatic primary carcinoma of the urethra as a single agent when used as subsequent therapy following platinum-containing chemotherapy and prior treatment with a programmed death receptor-1 (PD-1) or programmed death-ligand 1 (PD-L1) inhibitor or when used as subsequent therapy for members who are ineligible for cisplatin-containing chemotherapy.

C. Urothelial Carcinoma – Upper Genitourinary Tract Tumors or Urothelial Carcinoma of the Prostate
Authorization of 12 months may be granted for treatment of locally advanced or metastatic upper genitourinary tract tumors or urothelial carcinoma of the prostate as a single agent when used as subsequent therapy following platinum-containing chemotherapy and prior treatment with a programmed death receptor-1 (PD-1) or programmed death-ligand 1 (PD-L1) inhibitor or when used as subsequent therapy for members who are ineligible for cisplatin containing 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.

Section 2: Oncology Clinical Policy

Oncology Clinical Policy

Program Description

The National Comprehensive Care Network® (NCCN®) is an alliance of leading cancer centers devoted to patient care, research and education dedicated to improving the quality, effectiveness and efficiency of cancer care so patients can live better lives.[1] It is comprised of oncology experts who convene regularly to establish the best treatments for patients. NCCN develops various resources for use by stakeholders in the health care delivery system. These resources include, but are not limited to, the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®), the NCCN Drugs & Biologics Compendium (NCCN Compendium®) and the NCCN Chemotherapy Order Templates (NCCN Templates®).

NCCN templates are based on NCCN Clinical Practice Guidelines and NCCN Compendium. The NCCN Compendium lists the appropriate drugs and biologics for specific cancers using U.S. Food and Drug Administration (FDA)-approved disease indications and specific NCCN panel recommendations. Each recommendation is supported by a level of evidence category.

NCCN Categories of Evidence and Consensus[2]

Category 1: Based on high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2A: Based on lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2B: Based on lower-level evidence, there is NCCN consensus that the intervention is appropriate.
Category 3: Based any level of evidence, there is major NCCN disagreement that the intervention is

appropriate.

Policy for Regimen Prior Authorization

A regimen prior authorization allows submission of a single prior authorization request for all oncology drugs or biologics within an NCCN template that require prior authorization.

This policy provides coverage of a regimen review when *all* of the following criteria are met:

a. Regimen prior authorization reviews, based on NCCN templates, are initiated through the provider portal: https://provider.carefirst.com/providers/home.page
b. If the prior authorization request is submitted via phone or fax, each drug or biologic will need to be submitted and reviewed as a separate prior authorization request for review with drug-specific criteria.
c. The prior authorization review is requested for an oncology drug or biologic that requires prior authorization on the medical benefit.
d. The indication is for a cancer that is eligible for regimen review. Currently, the cancer types in scope for regimen review include breast, lung, colon and rectal cancer.
e. The member is eligible for regimen review.

In addition, the following criteria must be met for approval:

a. The requested regimen for the drug(s) or biologic(s) and indication is consistent with an NCCN recommendation with a level of evidence category of 1 or 2A.
b. The NCCN template must be accepted by the provider without modification. Authorizations may be granted for 12 months. Further review may be indicated where the above criteria are not met.

Continuation of Therapy

To submit a request for continuation of therapy, a new regimen prior authorization review must be requested. Upon template selection, the template must be modified to include the appropriate therapies being used for maintenance treatment. The regimen request will be submitted for further review.

Dosage and Administration

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

REFERENCES

SECTION 1

1. Padcev [package insert]. Northbrook, IL: Astellas Pharma US, Inc.; May 2022.
2. The NCCN Drugs & Biologics Compendium® © 2022 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed July 6, 2022.

SECTION 2

1. National Comprehensive Cancer Network. About NCCN website. https://www.nccn.org/about/default.aspx, accessed September 16, 2019.
2. National Comprehensive Cancer Network. NCCN Categories of Evidence and Consensus website. https://www.nccn.org/professionals/physician_gls/categories_of_consensus.aspx, accessed September 16, 2019.
3. National Comprehensive Cancer Network. NCCN Guidelines website. http://www.nccn.org/professionals/physician_gls/f_guidelines.asp, accessed September 16, 2019. (Note: An account may be required.)

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5. National Comprehensive Cancer Network. NCCN Chemotherapy Order Templates (NCCN Templates) website. https://www.nccn.org/professionals/OrderTemplates/Default.aspx, accessed September 16, 2019. (Note: A subscription may be required.)

POLICY Document for PADCEV (enfortumab vedotin-ejfv)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, and overall, clinically appropriate use. This document provides specific information to both sections of the overall policy.

Section 1: Clinical Criteria

- Policy information specific to the clinical appropriateness for the medication

Section 2: Oncology Clinical Policy

- Policy information specific to regimen review per NCCN Guidelines.

Section 1: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

PADCEV (enfortumab vedotin-ejfv)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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. Padcev (enfortumab vedotin-ejfv), as a single agent, is indicated for the treatment of adult patients with locally advanced or metastatic urothelial cancer who have previously received a programmed death receptor-1 (PD-1) or programmed death-ligand 1 (PD-L1) inhibitor, and a platinum-containing chemotherapy or are ineligible for cisplatin-containing chemotherapy and have previously received one or more prior lines of therapy.
2. Padcev, in combination with pembrolizumab, is indicated for the treatment of adult patients with locally advanced or metastatic urothelial cancer (mUC) who are not eligible for cisplatin-containing chemotherapy.

B. Compendial Uses
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. CRITERIA FOR INITIAL APPROVAL

Urothelial Carcinoma

A. Authorization of 12 months may be granted for treatment of urothelial carcinoma as a single agent when used as subsequent therapy following platinum-containing chemotherapy and prior treatment with a programmed death receptor-1 (PD-1) or programmed death-ligand 1 (PD-L1) inhibitor or when used as subsequent therapy for members who are ineligible for cisplatin-containing chemotherapy for any of the following subtypes:
   1. Urothelial carcinoma of the bladder in any of the following settings:
      a. 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)
      b. Locally advanced or metastatic disease
      c. Metastatic or local recurrence post-cystectomy
      d. Muscle invasive local recurrence or persistent disease in a preserved bladder
   2. Primary carcinoma of the urethra with locally advanced, recurrent or metastatic disease.
   3. Urothelial carcinoma of the upper genitourinary tract or urothelial carcinoma of the prostate with locally advanced or metastatic disease.

B. Authorization of 12 months may be granted for treatment of locally advanced or metastatic urothelial carcinoma in combination with pembrolizumab for members who are ineligible for cisplatin-containing 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.

Section 2: Oncology Clinical Policy

PROGRAM DESCRIPTION

The National Comprehensive Care Network® (NCCN®) is an alliance of leading cancer centers devoted to patient care, research and education dedicated to improving the quality, effectiveness, and efficiency of cancer care so patients can live better lives.[1] It is comprised of oncology experts who convene regularly to establish the best treatments for patients. NCCN develops various resources for use by stakeholders in the health care delivery system. These resources include, but are not limited to, the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®), the NCCN Drugs & Biologics Compendium (NCCN Compendium®) and the NCCN Chemotherapy Order Templates (NCCN Templates®).

NCCN Templates® are based on NCCN Guidelines® and NCCN Compendium®. The NCCN Compendium lists the appropriate drugs and biologics as treatment options for specific cancers using U.S. Food and Drug Administration (FDA)-approved disease indications and specific NCCN panel recommendations. Each recommendation is supported by a level of evidence category.

NCCN Categories of Evidence and Consensus[2]

- Category 1: Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
- Category 2A: Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
- Category 2B: Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.
- Category 3: Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

POLICY

Policy for Regimen Prior Authorization
A regimen prior authorization allows submission of a single prior authorization request for all oncology drugs or biologics within an NCCN template that require prior authorization.

PROCEDURE

This policy provides coverage of a regimen review when all of the following criteria are met:
1. Regimen prior authorization reviews, based on NCCN templates, are initiated through the provider portal.
    - If the prior authorization request is submitted via phone or fax, each drug or biologic will need to be submitted and reviewed as a separate prior authorization request for review with drug-specific criteria.
2. The prior authorization review is requested for an oncology drug or biologic.
3. The member is eligible for regimen review.
4. The indication is for a cancer that is eligible for regimen review. Currently, the cancer types in scope for regimen review include the following:
    - Ampullary Adenocarcinoma
    - Anal Carcinoma
    - B-Cell Lymphomas
    - Basal Cell Skin Cancer
    - Biliary Tract Cancers
    - Bone Cancer
    - Breast Cancer
    - Bladder Cancer
    - Central Nervous System Cancers
    - Cervical Cancer
    - Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma
    - Chronic Myeloid leukemia
    - Colon Cancer
    - Dermatofibrosarcoma Protuberans
    - Esophageal Cancer
    - Gastric Cancer
    - Gastrointestinal Stromal Tumors
    - Gestational Trophoblastic Neoplasms
    - Hairy Cell Leukemia
    - Head and Neck Cancers
    - Hodgkin Lymphoma
    - Hepatocellular Carcinoma
    - Kaposi Sarcoma
    - Kidney Cancer
    - Melanoma: Cutaneous
    - Melanoma: Uveal
    - Merkel Cell Carcinoma
    - Mesothelioma: Peritoneal
    - Mesothelioma: Pleural
    - Myelodysplastic Syndromes
    - Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Gene Fusions
    - Myeloproliferative Neoplasms
    - Neuroendocrine and Adrenal Tumors
    - Non-Small Cell Lung Cancer
    - Occult Primary
    - Ovarian Cancer
    - Pancreatic Cancer

- Penile Cancer
- Prostate Cancer
- Rectal Cancer
- Small Bowl Adenocarcinoma
- Small Cell Lung Cancer
- Soft Tissue Sarcoma
- Squamous Cell Skin Cancer
- Systemic Mastocytosis
- Systemic Light Chain Amyloidosis
- Testicular Cancer
- Thymomas and Thymic Carcinomas
- Thyroid Carcinoma
- Uterine Neoplasms
- Vulvar Cancer
- Waldenström Macroglobulinemia / Lymphoplasmacytic Lymphoma

In addition, the following criteria must be met for approval:

1. The requested regimen for the drug(s) or biologic(s) and indication is consistent with an NCCN recommendation with a level of evidence category of 1 or 2A.
2. The NCCN template must be accepted by the provider without modification.

Further review may be indicated when the above criteria are not met.

Authorizations may be granted for 12 months or as medically required, based on the member's condition and provider's assessment.

Supportive Care: Myeloid Growth Factor Therapy
Granulocyte colony stimulating factors are recommended for primary prophylaxis based on the febrile neutropenia risk of the chemotherapy regimen. Febrile neutropenia risk levels vary by NCCN Chemotherapy Order template and are listed at the top of the template. Regimens associated with a high or intermediate risk of febrile neutropenia may include a granulocyte colony stimulating factor as part of the prior authorization.

Continuation of Therapy
To submit a request for continuation of therapy, a new regimen prior authorization review must be requested. Upon template selection, the template must be modified to include the appropriate therapies being used for maintenance treatment. The regimen request will be submitted for further review.

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

REFERENCES:

SECTION 1

1. Padcev [package insert]. Northbrook, IL: Astellas Pharma US, Inc.; April 2023.
2. The NCCN Drugs & Biologics Compendium® © 2022 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed July 6, 2022.

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5. National Comprehensive Cancer Network. NCCN Chemotherapy Order Templates (NCCN Templates) website. https://www.nccn.org/compendia-templates/nccn-templates-main/browse-by-cancer-type, accessed June 6, 2023. (Note: A subscription may be required.)

Reference number(s)
2222-A

SPECIALTY GUIDELINE MANAGEMENT

PARSABIV (etelcalcetide)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Secondary hyperparathyroidism (HPT) in adult patients with chronic kidney disease (CKD) on hemodialysis.

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

II. CRITERIA FOR INITIAL APPROVAL

Secondary hyperparathyroidism with CKD on hemodialysis
Authorization of 12 months may be granted for treatment of secondary hyperparathyroidism in a member with chronic kidney disease on hemodialysis who has a serum calcium level (corrected for albumin) greater than or equal to 8.3 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 III when the member is experiencing benefit from therapy as evidenced by a decrease in intact parathyroid hormone (iPTH) levels from pretreatment baseline.

IV. APPENDIX

Corrected calcium = measured total calcium + 0.8(4.0 – serum albumin)

V. REFERENCES

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2. Micromedex Solutions [database online]. Truven Health Analytics, Inc. Ann Arbor, MI. Available at: www.micromedexsolutions.com. Accessed October 11, 2022.
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POLICY Document for
ALIMTA (pemetrexed)
PEMFEXY (pemetrexed)
pemetrexed

The overall objective of this policy is to support the appropriate and cost-effective use of the medication. This document provides specific information to each section of the overall policy.

Section 1: Clinical Criteria
Policy information specific to the clinical appropriateness for the medication
Section 2: Oncology Clinical Policy
Policy information specific to regimen review per NCCN Guidelines.

Section 1: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

ALIMTA (pemetrexed)
PEMFEXY (pemetrexed)
pemetrexed

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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-squamous non-small cell lung cancer (NSCLC)
   a. Alimta is indicated in combination with pembrolizumab and platinum chemotherapy, for the initial treatment of patients with metastatic non-squamous NSCLC, with no EFGR or ALK genomic tumor aberrations.
   b. Alimta/Pemfexy is indicated in combination with cisplatin for the initial treatment of patients with locally advanced or metastatic, non-squamous, non-small cell lung cancer (NSCLC).
   c. Alimta/Pemfexy is indicated as a single agent for the maintenance treatment of patients with locally advanced or metastatic, non-squamous NSCLC whose disease has not progressed after four cycles of platinum-based first-line chemotherapy.
   d. Alimta/Pemfexy is indicated as a single agent for the treatment of patients with recurrent, metastatic non-squamous, NSCLC after prior chemotherapy.

   Limitations of use: Alimta/Pemfexy is not indicated for the treatment of patients with squamous cell, non-small cell lung cancer (NSCLC).

2. Mesothelioma

Alimta/Pemfexy is indicated, in combination with cisplatin, for the initial treatment of patients with malignant pleural mesothelioma whose disease is unresectable or who are otherwise not candidates for curative surgery.

B. Compendial Uses
1. Bladder cancer
2. Malignant pleural mesothelioma
3. Malignant peritoneal mesothelioma
4. Pericardial mesothelioma
5. Tunica vaginalis testis mesothelioma
6. Nonsquamous non-small cell lung cancer (NSCLC)
7. Ovarian cancer, fallopian tube cancer, and primary peritoneal cancer: 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), and mucinous carcinoma of the ovary
8. Primary central nervous system (CNS) lymphoma
9. Thymomas and thymic carcinomas
10. Cervical cancer

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

II. EXCLUSIONS

Coverage will not be provided for members with squamous cell NSCLC.

III. CRITERIA FOR INITIAL APPROVAL

A. Bladder Cancer
Authorization of 6 months may be granted for treatment of locally advanced, metastatic, or relapsed transitional cell urothelium cancer, as second-line treatment.

B. Malignant Pleural or Peritoneal Mesothelioma
Authorization of 6 months may be granted for treatment of malignant pleural or peritoneal mesothelioma, including pericardial mesothelioma and tunica vaginalis testis mesothelioma, when any of the following criteria are met:
1. The requested medication will be used as a single agent or in combination with cisplatin or carboplatin; or
2. The requested medication will be used in combination with bevacizumab and either cisplatin or carboplatin.

C. Non-Small Cell Lung Cancer (Non-Squamous Histology)
Authorization of 6 months may be granted for treatment of non-squamous non-small cell lung cancer.

D. Ovarian Cancer, Fallopian Tube Cancer, and Primary Peritoneal Cancer
Authorization of 6 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 serious carcinoma/ovarian borderline epithelial tumor (low malignant potential), or mucinous carcinoma of the ovary, as single agent therapy.

E. Primary Central Nervous System (CNS) Lymphoma

Authorization of 6 months may be granted for treatment of primary CNS lymphoma, as a single agent.

F. Thymomas and Thymic Carcinomas
Authorization of 6 months may be granted for treatment of thymoma or thymic carcinoma, as a single agent.

G. Cervical Cancer
Authorization of 6 months may be granted for treatment of persistent or recurrent cervical cancer.

IV. CONTINUATION OF THERAPY

Authorization of 6 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.

Section 2: Oncology Clinical Policy

Oncology Clinical Policy

Program Description
The National Comprehensive Care Network® (NCCN®) is an alliance of leading cancer centers devoted to patient care, research and education dedicated to improving the quality, effectiveness and efficiency of cancer care so patients can live better lives.[1] It is comprised of oncology experts who convene regularly to establish the best treatments for patients. NCCN develops various resources for use by stakeholders in the health care delivery system. These resources include, but are not limited to, the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®), the NCCN Drugs & Biologics Compendium (NCCN Compendium®) and the NCCN Chemotherapy Order Templates (NCCN Templates®).

NCCN templates are based on NCCN Clinical Practice Guidelines and NCCN Compendium. The NCCN Compendium lists the appropriate drugs and biologics for specific cancers using U.S. Food and Drug Administration (FDA)-approved disease indications and specific NCCN panel recommendations. Each recommendation is supported by a level of evidence category.

NCCN Categories of Evidence and Consensus[2]
Category 1: Based on high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2A: Based on lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2B: Based on lower-level evidence, there is NCCN consensus that the intervention is appropriate.
Category 3: Based any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

Policy for Regimen Prior Authorization
A regimen prior authorization allows submission of a single prior authorization request for all oncology drugs or biologics within an NCCN template that require prior authorization.

This policy provides coverage of a regimen review when *all* of the following criteria are met:
a. Regimen prior authorization reviews, based on NCCN templates, are initiated through the provider portal: https://provider.carefirst.com/providers/home.page
b. If the prior authorization request is submitted via phone or fax, each drug or biologic will need to be submitted and reviewed as a separate prior authorization request for review with drug-specific criteria.

c. The prior authorization review is requested for an oncology drug or biologic that requires prior authorization on the medical benefit.
d. The indication is for a cancer that is eligible for regimen review. Currently, the cancer types in scope for regimen review include breast, lung, colon and rectal cancer.
e. The member is eligible for regimen review.

In addition, the following criteria must be met for approval:
a. The requested regimen for the drug(s) or biologic(s) and indication is consistent with an NCCN recommendation with a level of evidence category of 1 or 2A.
b. The NCCN template must be accepted by the provider without modification. Authorizations may be granted for 12 months. Further review may be indicated where the above criteria are not met.

Continuation of Therapy

To submit a request for continuation of therapy, a new regimen prior authorization review must be requested. Upon template selection, the template must be modified to include the appropriate therapies being used for maintenance treatment. The regimen request will be submitted for further review.

Dosage and Administration

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

REFERENCES

SECTION 1

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2. Pemfexy [package insert]. Woodcliff Lake, NJ: Eagle Pharmaceuticals, Inc.; June 2020.
3. Pemetrexed disodium [package insert]. Princeton, NJ: Dr. Reddy's Laboratories Inc.; July 2019.
4. The NCCN Drugs & Biologics Compendium® © 2022 National Comprehensive Cancer Network, Inc. Available at: https://www.nccn.org. Accessed July 19, 2022.
5. Lexicomp [database online]. Hudson, OH: Lexi-Comp, Inc.; https://online.lexi.com/lco/action/index/dataset/complete_ashp [available with subscription]. Accessed July 19, 2022.

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2. National Comprehensive Cancer Network. NCCN Categories of Evidence and Consensus website. https://www.nccn.org/professionals/physician_gls/categories_of_consensus.aspx, accessed September 16, 2019.
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5. National Comprehensive Cancer Network. NCCN Chemotherapy Order Templates (NCCN Templates) website. https://www.nccn.org/professionals/OrderTemplates/Default.aspx, accessed September 16, 2019. (Note: A subscription may be required.)

Reference number(s)
4576-A

SPECIALTY GUIDELINE MANAGEMENT

PEPAXTO (melphalan flufenamide)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Pepaxto 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 lines of therapy and whose disease is refractory to at least one proteasome inhibitor, one immunomodulatory agent and one CD38-directed monoclonal antibody.

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 treatment of multiple myeloma in combination with dexamethasone when all of the following are met:
1. The member has received at least four prior lines of therapy.
2. The disease is refractory to at least one proteasome inhibitor.
3. The disease is refractory to at least one immunomodulatory agent.
4. The disease is refractory to at least one anti-CD38 monoclonal antibody.

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. Pepaxto [package insert]. Waltham, MA: Oncopeptides Inc.; February 2021.

POLICY Document for PERJETA (pertuzumab)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, and overall, clinically appropriate use. This document provides specific information to both sections of the overall policy.

Section 1: Clinical Criteria

- Policy information specific to the clinical appropriateness for the medication

Section 2: Oncology Clinical Policy

- Policy information specific to regimen review per NCCN Guidelines.

Section 1: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

PERJETA (pertuzumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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. Metastatic breast cancer
   In combination with trastuzumab and docetaxel for the treatment of patients with human epidermal growth factor receptor 2 (HER2)-positive metastatic breast cancer who have not received prior anti-HER2 therapy or chemotherapy for metastatic disease.

2. Neoadjuvant treatment of breast cancer
   In combination with trastuzumab and chemotherapy as neoadjuvant treatment of patients with HER2-positive, locally advanced, inflammatory, or early stage breast cancer (either greater than 2 cm in diameter or node positive) as part of a complete treatment regimen for early breast cancer.

3. Adjuvant treatment of breast cancer
   In combination with trastuzumab and chemotherapy as adjuvant treatment of patients with HER2-positive early breast cancer at high risk of recurrence.

B. Compendial Uses

1. Treatment of recurrent or stage IV (M1) human epidermal growth factor receptor 2 (HER2)-positive breast cancer
2. Adjuvant treatment of locally advanced HER2-positive breast cancer
3. HER2-amplified and RAS and BRAF wild-type colorectal cancer (including appendiceal adenocarcinoma and anal adenocarcinoma) in combination with trastuzumab
4. HER2-positive recurrent salivary gland tumors
5. HER2-positive hepatobiliary cancers

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: human epidermal growth factor receptor 2 (HER2) status, RAS mutation status (where applicable), BRAF mutation status (where applicable)

III. CRITERIA FOR INITIAL APPROVAL

A. **Breast Cancer**
1. Authorization of 12 months may be granted for pre-operative (neoadjuvant) therapy of HER2-positive breast cancer in combination with trastuzumab and chemotherapy for locally advanced, inflammatory or early stage breast cancer (either greater than 2 cm in diameter or node positive).
2. Authorization of 12 months may be granted for adjuvant therapy of HER2-positive breast cancer that is either node-positive or at high risk for recurrence in combination with trastuzumab and chemotherapy.
3. Authorizations of 12 months may be granted for the treatment of recurrent or metastatic HER2-positive breast cancer or HER2-positive breast cancer with no response to preoperative systemic therapy in combination with trastuzumab.

B. **Colorectal Cancer**
Authorization of 12 months may be granted for treatment of colorectal cancer, including appendiceal adenocarcinoma and anal adenocarcinoma, with HER2-amplified and RAS and BRAF wild-type disease not previously treated with HER2 inhibitor in combination with trastuzumab when either of the following are met:
1. Member is not appropriate for intensive therapy
2. Perjeta will be used as subsequent therapy for progression of advanced or metastatic disease

C. **Salivary Gland Tumor**
Authorization of 12 months may be granted for treatment of recurrent HER2-positive salivary gland tumors in combination with trastuzumab.

D. **Hepatobiliary Cancers**
Authorization of 12 months may be granted for subsequent treatment of unresectable or metastatic HER2-positive hepatobiliary cancers (including intrahepatic and extrahepatic cholangiocarcinoma and gallbladder cancer) when used in combination with trastuzumab.

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. Adjuvant and neoadjuvant treatment of breast cancer will be approved for a total of 12 months of therapy.

Section 2: Oncology Clinical Policy

PROGRAM DESCRIPTION

The National Comprehensive Care Network® (NCCN®) is an alliance of leading cancer centers devoted to patient care, research and education dedicated to improving the quality, effectiveness, and efficiency of cancer care so patients can live better lives.[1] It is comprised of oncology experts who convene regularly to establish the best treatments for patients. NCCN develops various resources for use by stakeholders in the health care delivery system.

These resources include, but are not limited to, the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®), the NCCN Drugs & Biologics Compendium (NCCN Compendium®) and the NCCN Chemotherapy Order Templates (NCCN Templates®).

NCCN Templates® are based on NCCN Guidelines® and NCCN Compendium®. The NCCN Compendium lists the appropriate drugs and biologics as treatment options for specific cancers using U.S. Food and Drug Administration (FDA)-approved disease indications and specific NCCN panel recommendations. Each recommendation is supported by a level of evidence category.

NCCN Categories of Evidence and Consensus[2]

- Category 1: Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
- Category 2A: Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
- Category 2B: Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.
- Category 3: Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

POLICY

Policy for Regimen Prior Authorization
A regimen prior authorization allows submission of a single prior authorization request for all oncology drugs or biologics within an NCCN template that require prior authorization.

PROCEDURE

This policy provides coverage of a regimen review when all of the following criteria are met:
1. Regimen prior authorization reviews, based on NCCN templates, are initiated through the provider portal.
   - If the prior authorization request is submitted via phone or fax, each drug or biologic will need to be submitted and reviewed as a separate prior authorization request for review with drug-specific criteria.
2. The prior authorization review is requested for an oncology drug or biologic.
3. The member is eligible for regimen review.
4. The indication is for a cancer that is eligible for regimen review. Currently, the cancer types in scope for regimen review include the following:
   - Ampullary Adenocarcinoma
   - Anal Carcinoma
   - B-Cell Lymphomas
   - Basal Cell Skin Cancer
   - Biliary Tract Cancers
   - Bone Cancer
   - Breast Cancer
   - Bladder Cancer
   - Central Nervous System Cancers
   - Cervical Cancer
   - Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma
   - Chronic Myeloid leukemia
   - Colon Cancer
   - Dermatofibrosarcoma Protuberans
   - Esophageal Cancer
   - Gastric Cancer
   - Gastrointestinal Stromal Tumors
   - Gestational Trophoblastic Neoplasms
   - Hairy Cell Leukemia

- Head and Neck Cancers
- Hodgkin Lymphoma
- Hepatocellular Carcinoma
- Kaposi Sarcoma
- Kidney Cancer
- Melanoma: Cutaneous
- Melanoma: Uveal
- Merkel Cell Carcinoma
- Mesothelioma: Peritoneal
- Mesothelioma: Pleural
- Myelodysplastic Syndromes
- Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Gene Fusions
- Myeloproliferative Neoplasms
- Neuroendocrine and Adrenal Tumors
- Non-Small Cell Lung Cancer
- Occult Primary
- Ovarian Cancer
- Pancreatic Cancer
- Penile Cancer
- Prostate Cancer
- Rectal Cancer
- Small Bowl Adenocarcinoma
- Small Cell Lung Cancer
- Soft Tissue Sarcoma
- Squamous Cell Skin Cancer
- Systemic Mastocytosis
- Systemic Light Chain Amyloidosis
- Testicular Cancer
- Thymomas and Thymic Carcinomas
- Thyroid Carcinoma
- Uterine Neoplasms
- Vulvar Cancer
- Waldenström Macroglobulinemia / Lymphoplasmacytic Lymphoma

In addition, the following criteria must be met for approval:

1. The requested regimen for the drug(s) or biologic(s) and indication is consistent with an NCCN recommendation with a level of evidence category of 1 or 2A.
2. The NCCN template must be accepted by the provider without modification.

Further review may be indicated when the above criteria are not met.

Authorizations may be granted for 12 months or as medically required, based on the member's condition and provider's assessment.

Supportive Care: Myeloid Growth Factor Therapy

Granulocyte colony stimulating factors are recommended for primary prophylaxis based on the febrile neutropenia risk of the chemotherapy regimen. Febrile neutropenia risk levels vary by NCCN Chemotherapy Order template and are listed at the top of the template. Regimens associated with a high or intermediate risk of febrile neutropenia may include a granulocyte colony stimulating factor as part of the prior authorization.

Continuation of Therapy

To submit a request for continuation of therapy, a new regimen prior authorization review must be requested. Upon template selection, the template must be modified to include the appropriate therapies being used for maintenance treatment. The regimen request will be submitted for further review.

Dosage and Administration

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

REFERENCES:

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1. Perjeta [package insert]. South San Francisco, CA: Genentech, Inc.; February 2021.
2. The NCCN Drugs & Biologics Compendium® © 2022 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed December 9, 2022.
3. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Breast Cancer. Version 4.2022. https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed December 9, 2022.
4. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Anal Carcinoma. Version 2.2022. https://www.nccn.org/professionals/physician_gls/pdf/anal.pdf Accessed December 9, 2022.

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1. National Comprehensive Cancer Network. About NCCN website. https://www.nccn.org/home/about, accessed June 6, 2023.
2. National Comprehensive Cancer Network. NCCN Categories of Evidence and Consensus website, https://www.nccn.org/guidelines/guidelines-process/development-and-update-of-guidelines, accessed June 6, 2023.
3. National Comprehensive Cancer Network. NCCN Guidelines website. https://www.nccn.org/guidelines/category_1, accessed June 6, 2023. (Note: An account may be required.)
4. National Comprehensive Cancer Network. NCCN Drugs and Biologics Compendium website https://www.nccn.org/compendia-templates/compendia/drugs-and-biologics-compendia, accessed June 6, 2023. (Note: A subscription may be required.)
5. National Comprehensive Cancer Network. NCCN Chemotherapy Order Templates (NCCN Templates) website. https://www.nccn.org/compendia-templates/nccn-templates-main/browse-by-cancer-type, accessed June 6, 2023. (Note: A subscription may be required.)

Reference number(s)
3986-A

SPECIALTY GUIDELINE MANAGEMENT

PHESGO (pertuzumab, trastuzumab, and hyaluronidase-zzxf)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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. Neoadjuvant treatment of breast cancer
   For use in combination with chemotherapy for the neoadjuvant treatment of adult patients with HER2-positive, locally advanced, inflammatory, or early stage breast cancer (either greater than 2 cm in diameter or node positive) as part of a complete treatment regimen for early breast cancer.

2. Adjuvant treatment of breast cancer
   For use in combination with chemotherapy for the adjuvant treatment of adult patients with HER2-positive early breast cancer at high risk of recurrence.

3. Metastatic breast cancer (MBC)
   For use in combination with docetaxel for the treatment of adult patients with HER2-positive metastatic breast cancer who have not received prior anti-HER2 therapy or chemotherapy for metastatic disease.

B. Compendial Uses
HER2-positive breast cancer: May be substituted anywhere that the combination of intravenous pertuzumab and intravenous trastuzumab are given as part of systemic 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: human epidermal growth factor receptor 2 (HER2) status

III. CRITERIA FOR INITIAL APPROVAL

Breast Cancer

1. Authorization of 12 months may be granted for pre-operative (neoadjuvant) treatment of HER2-positive breast cancer in combination with chemotherapy for locally advanced, inflammatory, or early stage breast cancer (either greater than 2 cm in diameter or node positive).
2. Authorization of 12 months may be granted for adjuvant treatment of HER2-positive breast cancer that is either node-positive or at high risk for recurrence in combination with chemotherapy.
3. Authorization of 12 months may be granted for the treatment of HER2-positive recurrent 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 listed in Section III when there is no evidence of unacceptable toxicity or disease progression while on the current regimen. Adjuvant and neoadjuvant treatment of breast cancer will be approved for a total of 12 months of therapy.

V. REFERENCES

1. Phesgo [package insert]. South San Francisco, CA: Genentech, Inc; June 2020.
2. The NCCN Drugs & Biologics Compendium® © 2021 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed December 8, 2021.
3. Von Minckwitz, G. *et al*. Adjuvant Pertuzumab and Trastuzumab in Early HER2-Positive Breast Cancer. *N. Engl. J. Med.* **377**, 122–131 (2017). Available at: https://www.nejm.org/doi/full/10.1056/nejmoa1703643

Reference number
1860-A

SPECIALTY GUIDELINE MANAGEMENT

MOZOBIL (plerixafor)
plerixafor

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Mozobil is indicated in combination with granulocyte-colony stimulating factor (G-CSF) to mobilize hematopoietic stem cells (HSCs) to the peripheral blood for collection and subsequent autologous transplantation in patients with non-Hodgkin's lymphoma or multiple myeloma.

B. Compendial Use
Hematopoietic cell transplantation

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

II. CRITERIA FOR INITIAL APPROVAL

Hematopoietic Stem Cell Mobilization
Authorization of 6 months may be granted when all of the following criteria are met:
A. The requested medication will be used to mobilize hematopoietic stem cells for collection prior to transplantation.
B. The requested medication will be administered after the member has received a G-CSF (e.g., filgrastim) or chemo-mobilization.
C. The requested medication will not be used beyond 4 consecutive days or after completion of stem cell harvest/apheresis.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

1. Mozobil [package insert]. Cambridge, MA: Genzyme Corporation; August 2020.
2. Plerixafor [package insert]. Bridgewater, NJ: Amneal Pharmaceuticals LLC; May 2023.
3. The NCCN Drugs & Biologics Compendium® © 2023 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed January 5, 2023.
4. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Hematopoietic Cell Transplantation (HCT) Version 2.2022. https://www.nccn.org/professionals/physician_gls/pdf/hct.pdf Accessed January 5, 2023.

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Reference number(s)
3095-A

SPECIALTY GUIDELINE MANAGEMENT

POLIVY (polatuzumab vedotin-piiq)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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. Polivy in combination with bendamustine and a rituximab product is indicated for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL), not otherwise specified, after at least two prior therapies.
2. Polivy in combination with a rituximab product, cyclophosphamide, doxorubicin, and prednisone (R-CHP) for the treatment of adult patients who have previously untreated diffuse large B-cell lymphoma (DLBCL), not otherwise specified (NOS) or high-grade B-cell lymphoma (HGBL) and who have an International Prognostic Index score of 2 or greater.

B. Compendial Uses
B-Cell Lymphomas
1. High-grade B-cell lymphomas (HGBLs)
2. Monomorphic post-transplant lymphoproliferative disorders (B-cell type)
3. Human Immunodeficiency Virus (HIV) Related B-Cell Lymphomas (HIV-related diffuse large B-cell lymphoma, primary effusion lymphoma, HIV-related plasmablastic lymphoma, and human herpesvirus-8 (HHV8)-positive diffuse large B-cell lymphoma)
4. Histologic transformation of indolent lymphomas to diffuse large B-cell lymphoma
5. Follicular lymphoma
6. Diffuse large B-cell lymphoma (DLBCL)

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

II. CRITERIA FOR INITIAL APPROVAL

B-Cell Lymphomas
Authorization of 6 months (up to 6 cycles) may be granted for treatment of B-cell lymphomas with any of the following subtypes:
A. Diffuse Large B-cell Lymphoma (DLBCL) when any of the following criteria are met:
1. The requested drug is used as subsequent treatment as a single agent, or in combination with bendamustine with or without rituximab for relapsed or refractory disease when the member is not a candidate for transplant, or the requested medication will be used as a bridging option until CAR T-cell product is available.

2. The requested drug will be used as first line therapy for stage II-IV disease in combination with a rituximab product, cyclophosphamide, doxorubicin, and prednisone (R-CHP) in members who have an International Prognostic Index score of 2 or greater (low intermediate-high).

B. High-grade B-cell lymphomas (HGBLs) (also referred to as “double-hit” or “triple-hit” lymphomas) when any of the following criteria are met:
   1. The requested drug is used as subsequent treatment as a single agent, or in combination with bendamustine with or without rituximab, and member is not a candidate for transplant or the requested medication will be used as a bridging option until CAR T-cell product is available.
   2. The requested drug will be used as first line therapy in combination with a rituximab product, cyclophosphamide, doxorubicin, and prednisone (R-CHP) and member has an International Prognostic Index score of 2 or greater.

C. Monomorphic post-transplant lymphoproliferative disorders (B-cell type) when all the following criteria are met:
   1. The requested drug is used as subsequent treatment as a single agent, or in combination with bendamustine with or without rituximab, and
   2. Member is not a candidate for transplant or the requested medication will be used as a bridging option until CAR T-cell product is available.

D. Human Immunodeficiency Virus (HIV) -related B-cell lymphomas (HIV-related diffuse large B-cell lymphoma, primary effusion lymphoma, HIV-related plasmablastic lymphoma, and human herpesvirus-8 (HHV8)-positive diffuse large B-cell lymphoma) when all of the following criteria are met:
   1. The requested drug is used as subsequent treatment as a single agent, or in combination with bendamustine with or without rituximab, and
   2. Member is not a candidate for transplant or the requested medication will be used as a bridging option until CAR T-cell product is available.

E. Histologic transformation of indolent lymphomas to diffuse large B-cell lymphoma (DLBCL) when all of the following criteria are met:
   1. The requested drug is used as subsequent treatment as a single agent, or in combination with bendamustine with or without rituximab, and
   2. Member is not a candidate for transplant

F. Follicular lymphoma when the requested drug is used as subsequent treatment as a single agent, or in combination with bendamustine with or without rituximab.

III. CONTINUATION OF THERAPY

Authorization up to 6 months (6 cycles total) 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 and who have not received 6 or more cycles of the requested drug.

IV. REFERENCES

1. Polivy [package insert]. South San Francisco, CA: Genentech, Inc.; April 2023.
2. The NCCN Drugs & Biologics Compendium® © 2023 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed April 4, 2023.
3. Micromedex Solutions [database online]. Truven Health Analytics, Greenwood Village, Colorado, USA. Available at: http://www.micromedexsolutions.com/. Accessed April 4, 2023.
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5. Clinical Consult: CVS Caremark Clinical Programs Review. Focus on Hematology – Oncology Clinical Programs. July 2022.

Reference number(s)
5324-A

SPECIALTY GUIDELINE MANAGEMENT

PLUVICTO (lutetium Lu 177 vipivotide tetraxetan)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Pluvicto is indicated for the treatment of adult patients with prostate-specific membrane antigen (PSMA)-positive metastatic castration-resistant prostate cancer (mCRPC) who have been treated with androgen receptor (AR) pathway inhibition and taxane-based chemotherapy.

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:
Prostate-specific membrane antigen (PSMA) status.

III. CRITERIA FOR INITIAL APPROVAL

Prostate Cancer
Authorization of 6 months (up to 6 total doses) may be granted for treatment of prostate cancer when all of the following criteria are met:
1. The member has metastatic castration-resistant prostate cancer.
2. The member has been treated with androgen receptor (AR) pathway inhibition (e.g., abiraterone) and taxane-based chemotherapy (e.g., docetaxel).
3. The disease is prostate-specific membrane antigen (PSMA)-positive.

IV. CONTINUATION OF THERAPY

Authorization of 6 months (up to 6 total doses) 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. Pluvicto [package insert]. Millburn, NJ: Advanced Accelerator Applications USA, Inc.; March 2022.

Reference number(s)
2652-A

SPECIALTY GUIDELINE MANAGEMENT

POTELIGEO (mogamulizumab-kpkc)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Poteligeo is indicated for the treatment of adult patients with relapsed or refractory mycosis fungoides (MF) or Sézary syndrome (SS) after at least one prior systemic therapy.

B. Compendial Uses
1. Mycosis fungoides (MF) or Sézary syndrome (SS)
2. Adult T-cell leukemia/lymphoma (ATLL)

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

II. CRITERIA FOR INITIAL APPROVAL

A. Mycosis fungoides (MF) or Sézary syndrome (SS)
Authorization of 12 months may be granted for treatment of mycosis fungoides (MF) or Sézary syndrome (SS).

B. Adult T-cell leukemia/lymphoma (ATLL)
Authorization of 12 months may be granted for treatment of ATLL when used as a single-agent second line or subsequent therapy for acute or lymphoma subtypes.

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. Poteligo [package insert]. Bedminster, NJ: Kyowa Kirin, Inc.; July 2021.
2. The NCCN Drugs & Biologics Compendium® © 2022 National Comprehensive Cancer Network, Inc. Available at: https://www.nccn.org. Accessed January 4, 2022.

POLICY Document for PROLEUKIN (aldesleukin)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication. This document provides specific information to each section of the overall policy.

Section 1: Clinical Criteria
Policy information specific to the clinical appropriateness for the medication
Section 2: Oncology Clinical Policy
Policy information specific to regimen review per NCCN Guidelines.

Section 1: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

PROLEUKIN (aldesleukin)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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. Proleukin is indicated for the treatment of adults with metastatic renal cell carcinoma (metastatic RCC).
2. Proleukin is indicated for the treatment of adults with metastatic melanoma.

B. Compendial Uses
1. Unresectable cutaneous melanoma
2. Chronic graft-versus-host disease (GVHD)
3. Neuroblastoma

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

II. CRITERIA FOR INITIAL APPROVAL

A. Renal Cell Carcinoma
Authorization of 6 months may be granted for treatment of metastatic renal cell carcinoma.

B. Cutaneous Melanoma
Authorization of 6 months may be granted as high-dose single-agent subsequent therapy for metastatic or unresectable disease.

C. Chronic graft-versus-host disease (GVHD)

Authorization of 6 months may be granted for treatment of chronic graft-versus host-disease (GVHD) as additional therapy in conjunction with systemic corticosteroids following no response to first-line therapy options.

D. Neuroblastoma
Authorization of 6 months may be granted for the treatment of neuroblastoma.

III. CONTINUATION OF THERAPY

A. Renal Cell Carcinoma or Cutaneous Melanoma
Authorization of 6 months may be granted for continued treatment in members requesting reauthorization for renal cell carcinoma or cutaneous melanoma when all of the following criteria are met:
1. The member must be evaluated for response approximately 4 weeks after completion of a course of therapy and again immediately prior to the scheduled start of the next treatment course,
2. Additional courses of treatment should be given only if there is some tumor shrinkage following the last course,
3. Retreatment is not contraindicated,
4. Each treatment course should be separated by a rest period of at least 7 weeks from the date of hospital discharge.

B. Chronic graft-versus-host disease (GVHD)
Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for chronic graft-versus-host disease (GVHD) who have improvement in symptoms and no unacceptable toxicity.

C. Neuroblastoma
Authorization of 6 months may be granted for continued treatment in members requesting reauthorization for neuroblastoma when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

Section 2: Oncology Clinical Policy

Oncology Clinical Policy

Program Description

The National Comprehensive Care Network® (NCCN®) is an alliance of leading cancer centers devoted to patient care, research and education dedicated to improving the quality, effectiveness and efficiency of cancer care so patients can live better lives.[1] It is comprised of oncology experts who convene regularly to establish the best treatments for patients. NCCN develops various resources for use by stakeholders in the health care delivery system. These resources include, but are not limited to, the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®), the NCCN Drugs & Biologics Compendium (NCCN Compendium®) and the NCCN Chemotherapy Order Templates (NCCN Templates®).

NCCN templates are based on NCCN Clinical Practice Guidelines and NCCN Compendium. The NCCN Compendium lists the appropriate drugs and biologics for specific cancers using U.S. Food and Drug Administration (FDA)-approved disease indications and specific NCCN panel recommendations. Each recommendation is supported by a level of evidence category.

NCCN Categories of Evidence and Consensus[2]
Category 1: Based on high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.

Category 2A: Based on lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2B: Based on lower-level evidence, there is NCCN consensus that the intervention is appropriate.
Category 3: Based any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

Policy for Regimen Prior Authorization

A regimen prior authorization allows submission of a single prior authorization request for all oncology drugs or biologics within an NCCN template that require prior authorization.

This policy provides coverage of a regimen review when *all* of the following criteria are met:
a. Regimen prior authorization reviews, based on NCCN templates, are initiated through the provider portal: https://provider.carefirst.com/providers/home.page
b. If the prior authorization request is submitted via phone or fax, each drug or biologic will need to be submitted and reviewed as a separate prior authorization request for review with drug-specific criteria.
2. The prior authorization review is requested for an oncology drug or biologic that requires prior authorization on the medical benefit.
3. The indication is for a cancer that is eligible for regimen review. Currently, the cancer types in scope for regimen review include breast, lung, colon and rectal cancer.
4. The member is eligible for regimen review.

In addition, the following criteria must be met for approval:
1. The requested regimen for the drug(s) or biologic(s) and indication is consistent with an NCCN recommendation with a level of evidence category of 1 or 2A.
2. The NCCN template must be accepted by the provider without modification. Authorizations may be granted for 12 months. Further review may be indicated where the above criteria are not met.

Continuation of Therapy

To submit a request for continuation of therapy, a new regimen prior authorization review must be requested. Upon template selection, the template must be modified to include the appropriate therapies being used for maintenance treatment. The regimen request will be submitted for further review.

Dosage and Administration

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

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1. Proleukin [package insert]. Yardley, PA: Clinigen, Inc.; September 2019.
2. The NCCN Drugs & Biologic Compendium 2022 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed May 3, 2022.
3. Pistoia V, Bianchi G, Borgonovo G, Raffaghello L. Cytokines in neuroblastoma: From pathogenesis to treatment. Immunotherapy. 2011;3(7):895-907.
4. Russell HV, Shohet JM, Nuchtern JG. Treatment and prognosis of neuroblastoma. UpToDate [online serial]. Waltham, MA: UpToDate; reviewed September 2012.
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2. National Comprehensive Cancer Network. NCCN Categories of Evidence and Consensus website. https://www.nccn.org/professionals/physician_gls/categories_of_consensus.aspx, accessed September 16, 2019.
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4. National Comprehensive Cancer Network. NCCN Drugs and Biologics Compendium® website. http://www.nccn.org/professionals/drug_compendium/content/contents.asp, accessed September 16, 2019. (Note: A subscription may be required.)
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9891A FNL3 Oncology Clinical Policy.docx

Reference number(s)
2026-A

SPECIALTY GUIDELINE MANAGEMENT

PROLIA (denosumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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 postmenopausal women 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
2. Treatment to increase bone mass 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
3. Treatment of men and women with glucocorticoid-induced osteoporosis at high risk for fracture who are either initiating or continuing systemic glucocorticoids in a daily dosage equivalent to 7.5 mg or greater of prednisone and expected to remain on glucocorticoids for at least 6 months
4. Treatment to increase bone mass in men at high risk for fracture receiving androgen deprivation therapy (ADT) for non-metastatic prostate cancer
5. Treatment to increase bone mass in women at high risk for fracture receiving adjuvant aromatase inhibitor therapy for breast cancer

B. Compendial Uses
1. Prevention or treatment of osteoporosis during androgen deprivation therapy for prostate cancer in patients with high fracture risk
2. Consider in postmenopausal (natural or induced) patients receiving adjuvant aromatase inhibition therapy along with calcium and vitamin D supplementation to maintain or improve bone mineral density and reduce risk of fractures

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 Sections III.A, III.B, and III.C.

III. CRITERIA FOR INITIAL APPROVAL

A. Postmenopausal osteoporosis
Authorization 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], teriparatide [Forteo, Bonsity], 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. Osteoporosis in men

Authorization 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:
   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 12 months may be granted to members with glucocorticoid-induced osteoporosis when ALL of the following criteria are met:

1. Member is currently receiving or will be initiating glucocorticoid therapy at an equivalent prednisone dose of ≥ 2.5 mg/day for ≥ 3 months.
2. 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)
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)

D. Breast cancer

Authorization of 12 months may be granted to members who are receiving adjuvant aromatase inhibition therapy for breast cancer.

E. Prostate cancer

Authorization of 12 months may be granted to members who are receiving androgen deprivation therapy for prostate cancer.

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. 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.

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3. Bisphosphonates. *Drug Facts and Comparisons.* Facts & Comparisons [database online]. St. Louis, MO: Wolters Kluwer Health Inc; September 1, 2022. Accessed October 5, 2022.
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POLICY Document for PROLEUKIN (aldesleukin)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, and overall, clinically appropriate use. This document provides specific information to both sections of the overall policy.

Section 1: Clinical Criteria

- Policy information specific to the clinical appropriateness for the medication

Section 2: Oncology Clinical Policy

- Policy information specific to regimen review per NCCN Guidelines.

Section 1: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

PROLEUKIN (aldesleukin)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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. Proleukin is indicated for the treatment of adults with metastatic renal cell carcinoma (metastatic RCC).
2. Proleukin is indicated for the treatment of adults with metastatic melanoma.

B. Compendial Uses
1. Unresectable cutaneous melanoma
2. Chronic graft-versus-host disease (GVHD)
3. Neuroblastoma

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

II. CRITERIA FOR INITIAL APPROVAL

A. Renal Cell Carcinoma
Authorization of 6 months may be granted for treatment of metastatic renal cell carcinoma with clear cell histology.

B. Cutaneous Melanoma
Authorization of 6 months may be granted as high-dose single-agent subsequent therapy for metastatic or unresectable disease.

C. Chronic graft-versus-host disease (GVHD)

Authorization of 6 months may be granted for treatment of chronic graft-versus host-disease (GVHD) as additional therapy in conjunction with systemic corticosteroids following no response to first-line therapy options.

D. Neuroblastoma
Authorization of 6 months may be granted for the treatment of neuroblastoma.

III. CONTINUATION OF THERAPY

A. Renal Cell Carcinoma or Cutaneous Melanoma
Authorization of 6 months may be granted for continued treatment in members requesting reauthorization for renal cell carcinoma or cutaneous melanoma when all of the following criteria are met:
1. The member must be evaluated for response approximately 4 weeks after completion of a course of therapy and again immediately prior to the scheduled start of the next treatment course,
2. Additional courses of treatment should be given only if there is some tumor shrinkage following the last course,
3. Retreatment is not contraindicated,
4. Each treatment course should be separated by a rest period of at least 7 weeks from the date of hospital discharge.

B. Chronic graft-versus-host disease (GVHD)
Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for chronic graft-versus-host disease (GVHD) who have improvement in symptoms and no unacceptable toxicity.

C. Neuroblastoma
Authorization of 6 months may be granted for continued treatment in members requesting reauthorization for neuroblastoma when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

Section 2: Oncology Clinical Policy

PROGRAM DESCRIPTION

The National Comprehensive Care Network® (NCCN®) is an alliance of leading cancer centers devoted to patient care, research and education dedicated to improving the quality, effectiveness, and efficiency of cancer care so patients can live better lives.[1] It is comprised of oncology experts who convene regularly to establish the best treatments for patients. NCCN develops various resources for use by stakeholders in the health care delivery system. These resources include, but are not limited to, the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®), the NCCN Drugs & Biologics Compendium (NCCN Compendium®) and the NCCN Chemotherapy Order Templates (NCCN Templates®).

NCCN Templates® are based on NCCN Guidelines® and NCCN Compendium®. The NCCN Compendium lists the appropriate drugs and biologics as treatment options for specific cancers using U.S. Food and Drug Administration (FDA)-approved disease indications and specific NCCN panel recommendations. Each recommendation is supported by a level of evidence category.

NCCN Categories of Evidence and Consensus[2]
- Category 1: Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
- Category 2A: Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.

• Category 2B: Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.
• Category 3: Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

POLICY

Policy for Regimen Prior Authorization
A regimen prior authorization allows submission of a single prior authorization request for all oncology drugs or biologics within an NCCN template that require prior authorization.

PROCEDURE

This policy provides coverage of a regimen review when all of the following criteria are met:
1. Regimen prior authorization reviews, based on NCCN templates, are initiated through the provider portal.
    - If the prior authorization request is submitted via phone or fax, each drug or biologic will need to be submitted and reviewed as a separate prior authorization request for review with drug-specific criteria.
2. The prior authorization review is requested for an oncology drug or biologic.
3. The member is eligible for regimen review.
4. The indication is for a cancer that is eligible for regimen review. Currently, the cancer types in scope for regimen review include the following:
    - Ampullary Adenocarcinoma
    - Anal Carcinoma
    - B-Cell Lymphomas
    - Basal Cell Skin Cancer
    - Biliary Tract Cancers
    - Bone Cancer
    - Breast Cancer
    - Bladder Cancer
    - Central Nervous System Cancers
    - Cervical Cancer
    - Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma
    - Chronic Myeloid leukemia
    - Colon Cancer
    - Dermatofibrosarcoma Protuberans
    - Esophageal Cancer
    - Gastric Cancer
    - Gastrointestinal Stromal Tumors
    - Gestational Trophoblastic Neoplasms
    - Hairy Cell Leukemia
    - Head and Neck Cancers
    - Hodgkin Lymphoma
    - Hepatocellular Carcinoma
    - Kaposi Sarcoma
    - Kidney Cancer
    - Melanoma: Cutaneous
    - Melanoma: Uveal
    - Merkel Cell Carcinoma
    - Mesothelioma: Peritoneal
    - Mesothelioma: Pleural
    - Myelodysplastic Syndromes
    - Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Gene Fusions
    - Myeloproliferative Neoplasms
    - Neuroendocrine and Adrenal Tumors

- Non-Small Cell Lung Cancer
- Occult Primary
- Ovarian Cancer
- Pancreatic Cancer
- Penile Cancer
- Prostate Cancer
- Rectal Cancer
- Small Bowl Adenocarcinoma
- Small Cell Lung Cancer
- Soft Tissue Sarcoma
- Squamous Cell Skin Cancer
- Systemic Mastocytosis
- Systemic Light Chain Amyloidosis
- Testicular Cancer
- Thymomas and Thymic Carcinomas
- Thyroid Carcinoma
- Uterine Neoplasms
- Vulvar Cancer
- Waldenström Macroglobulinemia / Lymphoplasmacytic Lymphoma

In addition, the following criteria must be met for approval:

1. The requested regimen for the drug(s) or biologic(s) and indication is consistent with an NCCN recommendation with a level of evidence category of 1 or 2A.
2. The NCCN template must be accepted by the provider without modification.

Further review may be indicated when the above criteria are not met.

Authorizations may be granted for 12 months or as medically required, based on the member's condition and provider's assessment.

Supportive Care: Myeloid Growth Factor Therapy
Granulocyte colony stimulating factors are recommended for primary prophylaxis based on the febrile neutropenia risk of the chemotherapy regimen. Febrile neutropenia risk levels vary by NCCN Chemotherapy Order template and are listed at the top of the template. Regimens associated with a high or intermediate risk of febrile neutropenia may include a granulocyte colony stimulating factor as part of the prior authorization.

Continuation of Therapy
To submit a request for continuation of therapy, a new regimen prior authorization review must be requested. Upon template selection, the template must be modified to include the appropriate therapies being used for maintenance treatment. The regimen request will be submitted for further review.

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

REFERENCES:

SECTION 1

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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.

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.
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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.
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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
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 CRITERIA

Members will not use Rebif concomitantly with other disease modifying multiple sclerosis agents (Note: Ampyra and Nuedexta are not disease modifying).

VI. REFERENCES

1. Rebif [package insert]. Rockland, MA; EMD Serono Inc.; November 2021.
2. 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 31, 2022.
3. Clinical Pharmacology. [database online.] Tampa, FL: Gold Standard, Inc.; https://www.clinicalkey.com/pharmacology [available with subscription]. Accessed March 31, 2022.

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.
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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

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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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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.
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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. Histiocytic Neoplasms:
   a. Erdheim-Chester Disease (ECD)
   b. Langerhans Cell Histiocytosis (LCH)
   c. Rosai-Dorfman Disease
3. Neoadjuvant therapy for RET-fusion positive anaplastic thyroid carcinoma

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 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 anaplastic thyroid cancer with a *RET* gene fusion when used as single agent neoadjuvant therapy.

D. Thyroid Cancer
Authorization of 12 months may be granted for treatment of members 12 years of age and older with advanced or metastatic radioactive iodine-refractory (if radioactive iodine is appropriate) thyroid cancer whose tumors have a *RET* gene fusion.

E. Solid Tumors
Authorization of 12 months may be granted for treatment of members with 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.

F. 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)

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. Retevmo [package insert]. Indianapolis, IN: Lilly USA, LLC; September 2022.
2. The NCCN Drugs & Biologics Compendium® © 2022 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed March 15, 2022.

Reference number(s)
2983-A

SPECIALTY GUIDELINE MANAGEMENT

RIASTAP (fibrinogen concentrate [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
RiaSTAP is indicated for the treatment of acute bleeding episodes in pediatric and adult patients with congenital fibrinogen deficiency, including afibrinogenemia and hypofibrinogenemia.

Limitation of use:
RiaSTAP is not indicated for dysfibrinogenemia.

B. Compendial Uses
1. Perioperative management of bleeding in afibrinogenemia
2. Prophylaxis to reduce the frequency of bleeding episodes in afibrinogenemia

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 prophylaxis to reduce the frequency of bleeding episodes in afibrinogenemia, justification from the medical records.

III. CRITERIA FOR INITIAL APPROVAL

Congenital Fibrinogen Deficiency
A. Authorization of 1 month may be granted for treatment of acute bleeding episodes in members with a diagnosis of congenital fibrinogen deficiency, including afibrinogenemia and hypofibrinogenemia.
B. Authorization of 1 month may be granted for perioperative management of bleeding in members with a diagnosis of afibrinogenemia.
C. Authorization of 12 months may be granted for prophylaxis to reduce the frequency of bleeding episodes in members with afibrinogenemia (with justification from the medical records).

IV. CONTINUATION OF THERAPY

A. Prophylaxis to reduce the frequency of bleeding episodes in afibrinogenemia

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for prophylaxis to reduce the frequency of bleeding episodes in afibrinogenemia when the member is experiencing benefit from therapy (e.g., reduced frequency of bleeding episodes).

B. All other indications
All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

V. REFERENCES

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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.
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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

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. Atopic dermatitis
   1. For initial requests:
      i. Chart notes or medical records showing affected areas and affected body surface area

ii. Chart notes, medical record documentation, or claims history of prerequisite therapies, including response to therapy. If therapy is not advisable, documentation of why therapy is not advisable.

2. For 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.

D. Ulcerative colitis (UC)
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 or remission.

E. Ankylosing spondylitis (AS) and axial spondyloarthritis
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.

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., Xeljanz, 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 the member has experienced an inadequate response or intolerance to at least one TNF inhibitor.

C. Moderate-to-severe atopic dermatitis
Authorization of 4 months may be granted for treatment of moderate-to-severe atopic dermatitis 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 has had an inadequate response to treatment with a topical corticosteroid or topical calcineurin inhibitor, or topical corticosteroids and topical calcineurin inhibitors are not advisable for the member.
3. Member has had an inadequate response to treatment with other systemic drug products, including biologics, or use of these therapies is not advisable for the member.
4. Member is 12 years of age or older.

D. Moderately to severely active ulcerative colitis (UC)
1. Authorization of 12 months may be granted for 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., Xeljanz) indicated for moderately to severely active ulcerative colitis.

E. Active ankylosing spondylitis (AS) and axial spondyloarthritis

1. Authorization of 12 months may be granted for treatment of active ankylosing spondylitis or active 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 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 axial spondyloarthritis.

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

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. Moderate-to-severe atopic dermatitis

Authorization of 12 months may be granted for members 12 years of age or older who are using the requested medication for moderate-to-severe atopic dermatitis and who achieve or maintain 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. 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 ankylosing spondylitis (AS) and 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 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)

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 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 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.

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POLICY Document for
REMICADE (infliximab)
AVSOLA (infliximab-axxq)
INFLECTRA (infliximab-dyyb)
RENFLEXIS (infliximab-abda)
infliximab

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, lower cost site of care and overall, clinically appropriate use. This document provides specific information to each of the three sections of the overall policy.

Section 1: Preferred Product
- Policy information specific to preferred medications

Section 2: Site of Care
- Policy information specific to site of care (outpatient, hospital outpatient, home infusion)

Section 3: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 1: Preferred Product

EXCEPTIONS CRITERIA
INFLIXIMAB
PREFERRED PRODUCTS: AVSOLA, INFLECTRA AND RENFLEXIS

POLICY
This policy informs prescribers of preferred products and provides an exception process for targeted products through prior authorization.

I. PLAN DESIGN SUMMARY

This program applies to the infliximab products specified in this policy. Coverage for targeted products is provided based on clinical circumstances that would exclude the use of the preferred product and may be based on previous use of a product. The coverage review process will ascertain situations where a clinical exception can be made. This program applies to all members requesting treatment with a targeted product.

Each referral is reviewed based on all utilization management (UM) programs implemented for the client.

Table. Infliximab products

	Product(s)
Preferred*	• **Avsola** (infliximab-axxq) • **Inflectra** (infliximab-dyyb) • **Renflexis** (infliximab-abda)
Targeted	• infliximab • **Remicade** (infliximab)

*: Medications considered formulary or preferred on your plan may still require a clinical prior authorization review.

II. EXCEPTION CRITERIA

Coverage for the targeted product is provided when the member has a documented intolerable adverse event to all of the preferred products, and the adverse event was not an expected adverse event attributed to the active ingredient as described in the prescribing information (i.e., known adverse reaction for both the reference product and biosimilar products).

Section 2: Site of Care

CareFirst Site of Care Criteria
Administration of Intravenous Infliximab
Avsola, Inflectra, Remicade, Renflexis, infliximab (unbranded)

POLICY

I. CRITERIA FOR APPROVAL FOR ADMINISTRATION IN OUTPATIENT HOSPITAL SETTING

This policy provides coverage for administration of infliximab in an outpatient hospital setting 3 months when ANY of the following criteria are met:

A. The member is new to infliximab therapy or is reinitiating therapy after not being on therapy for at least 6 months
B. The member is switching to an infliximab product that he/she has not received before.
C. The member has experienced a gap in therapy of greater than 2 infusions.

This policy provides coverage for administration of infliximab in an outpatient hospital setting for a longer course of treatment when ANY of the following criteria are met:

A. The member has experienced an adverse reaction that did not respond to conventional interventions (eg, acetaminophen, steroids, diphenhydramine, fluids, other pre-medications or slowing of infusion rate) or a severe adverse event (anaphylaxis, anaphylactoid reactions, myocardial infarction, thromboembolism, or seizures) during or immediately after an infusion.
B. The member has developed antibodies to infliximab which increases the risk for infusion related reactions.
C. The member is medically unstable (eg respiratory, cardiovascular, or renal conditions).
D. The member has severe venous access issues that require the use of a special interventions only available in the outpatient hospital setting.
E. The member has significant behavioral issues and/or physical or cognitive impairment that would impact the safety of the infusion therapy AND the patient does not have access to a caregiver.
F. The member is less than 14 years of age.

For situations where administration of infliximab does not meet the criteria for outpatient hospital infusion, coverage for infliximab is provided when administered in alternative sites such as; physician office, home infusion or ambulatory care.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the site of care prior authorization review (where applicable):

A. Medical records supporting the member has experienced an adverse reaction that did not respond to conventional interventions or a severe adverse event during or immediately after an infusion
B. Medical records supporting the member has developed antibodies to infliximab
C. Medical records supporting the member is medically unstable

D. Medical records supporting the member has severe venous access issues that require specialized interventions only available in the outpatient hospital setting
E. Medical records supporting the member has behavioral issues and/or physical or cognitive impairment and no access to a caregiver

Section 3: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

REMICADE (infliximab)
AVSOLA (infliximab-axxq)
INFLECTRA (infliximab-dyyb)
RENFLEXIS (infliximab-abda)
infliximab

POLICY

III. INDICATIONS

The indications below including FDA-approved indications and compendial 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 Crohn's disease (CD) and fistulizing CD who have had an inadequate response to conventional therapy
2. Pediatric patients 6 years of age and older with moderately to severely active Crohn's disease who have had an inadequate response to conventional therapy
3. Moderately to severely active ulcerative colitis (UC) in patients 6 years of age or older who have had an inadequate response to conventional therapy
4. Adult patients with moderately to severely active rheumatoid arthritis (RA), in combination with methotrexate
5. Adult patients with active ankylosing spondylitis (AS)
6. Adult patients with active psoriatic arthritis (PsA)
7. Adult patients with chronic severe plaque psoriasis (PsO) who are candidates for systemic therapy and when other systemic therapies are medically less appropriate

B. Compendial Uses
1. Non-radiographic axial spondyloarthritis
2. Behcet's disease
3. Hidradenitis suppurativa
4. Pyoderma gangrenosum
5. Sarcoidosis
6. Takayasu's arteritis
7. Uveitis
8. Reactive arthritis
9. Immune checkpoint inhibitor toxicity
10. Acute graft versus host disease
11. Moderate to severe plaque psoriasis

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

IV. DOCUMENTATION

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

A. Crohn's disease (CD) and ulcerative colitis (UC)
Continuation requests: Chart notes or medical record documentation supporting positive clinical response to therapy or remission.

B. 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.

C. Ankylosing spondylitis (AS), non-radiographic axial spondyloarthritis (nr-axSpA), psoriatic arthritis (PsA), reactive arthritis, hidradenitis suppurativa, and uveitis
   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. 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.

E. Behcet's disease (initial requests only)
Chart notes, medical record documentation, or claims history supporting previous medications tried, including response to therapy (if applicable).

F. Pyoderma gangrenosum, sarcoidosis, Takayasu's arteritis, immune checkpoint inhibitor toxicity, and acute graft versus host disease (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.

V. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with one of the following:
A. Crohn's disease and ulcerative colitis: gastroenterologist
B. Rheumatoid arthritis, ankylosing spondylitis, non-radiographic axial spondyloarthritis, Behcet's disease, Takayasu's arteritis, and reactive arthritis: rheumatologist
C. Psoriatic arthritis and hidradenitis suppurativa:[60] rheumatologist or dermatologist
D. Plaque psoriasis and pyoderma gangrenosum: dermatologist
E. Sarcoidosis: dermatologist or pulmonologist
F. Uveitis: ophthalmologist or rheumatologist
G. Immune checkpoint inhibitor toxicity and acute graft versus host disease: oncologist or hematologist

VI. CRITERIA FOR INITIAL APPROVAL

A. 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.

B. Ulcerative colitis (UC)
Authorization of 12 months may be granted for members 6 years of age or older for treatment of moderately to severely active UC.

C. 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).

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. 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.

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 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).

G. 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).

H. Hidradenitis suppurativa

1. Authorization of 12 months may be granted for members who have previously received a biologic indicated for 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 an oral antibiotic for at least 90 days.
ii. Member has an intolerance or contraindication to oral antibiotics.

I. 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).

J. Sarcoidosis

Authorization of 12 months may be granted for treatment of sarcoidosis in members when either of the following criteria is met:
1. Member has experienced an inadequate response to corticosteroids or immunosuppressive therapy.
2. Member has an intolerance or contraindication to corticosteroids and immunosuppressive therapy.

K. Takayasu's arteritis

Authorization of 12 months may be granted for treatment of refractory Takayasu's arteritis when either of the following criteria is met:
1. Member has experienced an inadequate response to corticosteroids or immunosuppressive therapy (e.g., methotrexate, azathioprine, or mycophenolate mofetil).
2. Member has an intolerance or contraindication to corticosteroids and immunosuppressive therapy (e.g., methotrexate, azathioprine, or mycophenolate mofetil).

L. Uveitis

1. Authorization of 12 months may be granted for members who have previous received a biologic indicated for uveitis.

2. Authorization of 12 months may be granted for treatment of uveitis when either of the following criteria is met:
   i. Member has experienced an inadequate response to corticosteroids or immunosuppressive therapy (e.g., methotrexate, azathioprine, or mycophenolate mofetil).
   ii. Member has an intolerance or contraindication to corticosteroids and immunosuppressive therapy (e.g., methotrexate, azathioprine, or mycophenolate mofetil).

M. 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 either of the following criteria is met:
   i. Member has experienced an inadequate response to at least a 3-month trial of one of the following despite adequate dosing or maximally tolerated dose:
      a. Sulfasalazine (i.e., titrated to 1000 mg twice daily)
      b. Methotrexate (i.e., titrated to at least 15 mg/week)
   ii. Member has an intolerance or contraindication to methotrexate (see Appendix) and sulfasalazine (e.g., porphyria, intestinal or urinary obstruction).

N. Immune checkpoint inhibitor toxicity

1. Authorization of 6 months may be granted for treatment of immune checkpoint inhibitor toxicity when either of the following criteria is met:
   i. Member has experienced an inadequate response, intolerance, or contraindication to corticosteroids.
   ii. Member has moderate or severe diarrhea or colitis.

2. Authorization of 12 months may be granted for treatment of immune checkpoint inhibitor toxicity when the member has severe inflammatory arthritis and has experienced an inadequate response, intolerance, or contraindication to corticosteroids.

O. 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.

VII. CONTINUATION OF THERAPY

A. 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)

B. Ulcerative colitis (UC)

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 ulcerative colitis 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 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)

C. 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.

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. 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

F. 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)

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. Uveitis

Authorization of 12 months may be granted for all members (including new members) who are using the requested medication for uveitis 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 recurrence compared to baseline
2. Zero anterior chamber inflammation or reduction in anterior chamber inflammation compared to baseline
3. Decreased reliance on topical corticosteroids

I. 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, pain).

J. Immune checkpoint inhibitor toxicity and acute graft versus host disease

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.

VIII. 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.

IX. DOSAGE AND ADMINISTRATION

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

X. 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(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

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Reference number(s)
6062-A

SPECIALTY GUIDELINE MANAGEMENT

ROCTAVIAN (valoctocogene roxaparvovec-rvox)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Roctavian is indicated for the treatment of adults with severe hemophilia A (congenital factor VIII deficiency with factor VIII activity < 1 IU/dL) without antibodies to adeno-associated virus serotype 5 (AAV5) 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:
Chart notes, medical records, or lab results documenting all of the following:
A. Severe factor VIII deficiency (factor VIII activity < 1 IU/dL).
B. Absence of pre-existing antibodies to the adeno-associated virus serotype 5 (AAV5) capsid.
C. Absence of factor VIII inhibitor confirmed by a Bethesda assay (lab test results required).

III. PRESCRIBER SPECIALTIES

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

IV. CRITERIA FOR INITIAL APPROVAL

Hemophilia A
Authorization of 3 months for one dose total may be granted for treatment of severe hemophilia A when all of the following criteria are met:
A. Member must be 18 years of age or older.
B. Member has severe disease with factor VIII activity levels less than or equal to 1 IU/dL.
C. Absence of pre-existing antibodies to AAV5 was confirmed by an FDA-approved test (e.g., AAV5 DetectCDx™).
D. Member does not have prior or active factor VIII inhibitors (inhibitor titer must be less than 0.6 Bethesda Units [BU]).
E. Member has not received treatment with the requested medication previously.

V. REFERENCES

1. Roctavian [package insert]. Novato, CA: BioMarin Pharmaceutical Inc.; June 2023.

POLICY Document for ROLVEDON (eflapegrastim-xnst)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, and overall, clinically appropriate use. This document provides specific information to both sections of the overall policy.

Section 1: Clinical Criteria

- Policy information specific to the clinical appropriateness for the medication

Section 2: Oncology Clinical Policy

- Policy information specific to regimen review per NCCN Guidelines.

Section 1: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

ROLVEDON (eflapegrastim-xnst)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Rolvedon is indicated to decrease the incidence of infection, as manifested by febrile neutropenia, in adult patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with clinically significant incidence of febrile neutropenia.

b. Compendial Uses
1. Stem cell transplantation-related indications
2. Prophylaxis for chemotherapy-induced febrile neutropenia in patients with solid tumors
3. Hematopoietic 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):

a. The requested medication will not be used in combination with other colony stimulating factors within any chemotherapy cycle.
b. The member will not be receiving chemotherapy and radiation therapy at the same time.
c. The requested medication will not be administered with weekly chemotherapy regimens.
d. 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:

a. Stem cell transplantation-related indications
b. Hematopoietic Acute Radiation Syndrome
    Treatment for radiation-induced myelosuppression following a radiological/nuclear incident
c. 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. VelP (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.

Section 2: Oncology Clinical Policy

PROGRAM DESCRIPTION

The National Comprehensive Care Network® (NCCN®) is an alliance of leading cancer centers devoted to patient care, research and education dedicated to improving the quality, effectiveness, and efficiency of cancer care so patients can live better lives.[1] It is comprised of oncology experts who convene regularly to establish the best treatments for patients. NCCN develops various resources for use by stakeholders in the health care delivery system. These resources include, but are not limited to, the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®), the NCCN Drugs & Biologics Compendium (NCCN Compendium®) and the NCCN Chemotherapy Order Templates (NCCN Templates®).

NCCN Templates® are based on NCCN Guidelines® and NCCN Compendium®. The NCCN Compendium lists the appropriate drugs and biologics as treatment options for specific cancers using U.S. Food and Drug Administration (FDA)-approved disease indications and specific NCCN panel recommendations. Each recommendation is supported by a level of evidence category.

NCCN Categories of Evidence and Consensus[2]

- Category 1: Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
- Category 2A: Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
- Category 2B: Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.
- Category 3: Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

POLICY

Policy for Regimen Prior Authorization
A regimen prior authorization allows submission of a single prior authorization request for all oncology drugs or biologics within an NCCN template that require prior authorization.

PROCEDURE

This policy provides coverage of a regimen review when all of the following criteria are met:
1. Regimen prior authorization reviews, based on NCCN templates, are initiated through the provider portal.
    - If the prior authorization request is submitted via phone or fax, each drug or biologic will need to be submitted and reviewed as a separate prior authorization request for review with drug-specific criteria.
2. The prior authorization review is requested for an oncology drug or biologic.
3. The member is eligible for regimen review.
4. The indication is for a cancer that is eligible for regimen review. Currently, the cancer types in scope for regimen review include the following:
    - Ampullary Adenocarcinoma
    - Anal Carcinoma
    - B-Cell Lymphomas
    - Basal Cell Skin Cancer
    - Biliary Tract Cancers
    - Bone Cancer
    - Breast Cancer
    - Bladder Cancer
    - Central Nervous System Cancers
    - Cervical Cancer
    - Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma
    - Chronic Myeloid leukemia
    - Colon Cancer
    - Dermatofibrosarcoma Protuberans
    - Esophageal Cancer
    - Gastric Cancer
    - Gastrointestinal Stromal Tumors
    - Gestational Trophoblastic Neoplasms
    - Hairy Cell Leukemia
    - Head and Neck Cancers
    - Hodgkin Lymphoma
    - Hepatocellular Carcinoma
    - Kaposi Sarcoma
    - Kidney Cancer
    - Melanoma: Cutaneous
    - Melanoma: Uveal
    - Merkel Cell Carcinoma
    - Mesothelioma: Peritoneal
    - Mesothelioma: Pleural
    - Myelodysplastic Syndromes
    - Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Gene Fusions
    - Myeloproliferative Neoplasms
    - Neuroendocrine and Adrenal Tumors
    - Non-Small Cell Lung Cancer
    - Occult Primary
    - Ovarian Cancer
    - Pancreatic Cancer
    - Penile Cancer

- Prostate Cancer
- Rectal Cancer
- Small Bowl Adenocarcinoma
- Small Cell Lung Cancer
- Soft Tissue Sarcoma
- Squamous Cell Skin Cancer
- Systemic Mastocytosis
- Systemic Light Chain Amyloidosis
- Testicular Cancer
- Thymomas and Thymic Carcinomas
- Thyroid Carcinoma
- Uterine Neoplasms
- Vulvar Cancer
- Waldenström Macroglobulinemia / Lymphoplasmacytic Lymphoma

In addition, the following criteria must be met for approval:

1. The requested regimen for the drug(s) or biologic(s) and indication is consistent with an NCCN recommendation with a level of evidence category of 1 or 2A.
2. The NCCN template must be accepted by the provider without modification.

Further review may be indicated when the above criteria are not met.

Authorizations may be granted for 12 months or as medically required, based on the member's condition and provider's assessment.

Supportive Care: Myeloid Growth Factor Therapy
Granulocyte colony stimulating factors are recommended for primary prophylaxis based on the febrile neutropenia risk of the chemotherapy regimen. Febrile neutropenia risk levels vary by NCCN Chemotherapy Order template and are listed at the top of the template. Regimens associated with a high or intermediate risk of febrile neutropenia may include a granulocyte colony stimulating factor as part of the prior authorization.

Continuation of Therapy
To submit a request for continuation of therapy, a new regimen prior authorization review must be requested. Upon template selection, the template must be modified to include the appropriate therapies being used for maintenance treatment. The regimen request will be submitted for further review.

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

REFERENCES:

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2. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Hematopoietic Growth Factors. Version 1.2022. https://www.nccn.org/professionals/physician_gls/pdf/growthfactors.pdf Accessed September 22, 2022.
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4. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Hematopoietic Cell Transplantation. Version 2.2022. https://www.nccn.org/professionals/physician_gls/pdf/hct.pdf Accessed September 22, 2022.

5. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Hairy Cell Leukemia. Version 1.2023. https://www.nccn.org/professionals/physician_gls/pdf/hairy_cell.pdf Accessed September 22, 2022.
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7. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Wilms Tumor (Nephroblastoma). Version 1.2022. https://www.nccn.org/professionals/physician_gls/pdf/wilms_tumor.pdf Accessed September 22, 2022.

SECTION 2

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2. National Comprehensive Cancer Network. NCCN Categories of Evidence and Consensus website, https://www.nccn.org/guidelines/guidelines-process/development-and-update-of-guidelines, accessed June 6, 2023.
3. National Comprehensive Cancer Network. NCCN Guidelines website. https://www.nccn.org/guidelines/category_1, accessed June 6, 2023. (Note: An account may be required.)
4. National Comprehensive Cancer Network. NCCN Drugs and Biologics Compendium website https://www.nccn.org/compendia-templates/compendia/drugs-and-biologics-compendia, accessed June 6, 2023. (Note: A subscription may be required.)
5. National Comprehensive Cancer Network. NCCN Chemotherapy Order Templates (NCCN Templates) website. https://www.nccn.org/compendia-templates/nccn-templates-main/browse-by-cancer-type, accessed June 6, 2023. (Note: A subscription may be required.)

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.

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.

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.

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® © 2022 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed June 30, 2022.

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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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)
4781-A

SPECIALTY GUIDELINE MANAGEMENT

RYPLAZIM (plasminogen, human-tvmh)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Ryplazim is plasma-derived human plasminogen indicated for the treatment of patients with plasminogen deficiency type 1 (hypoplasminogenemia).

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 a baseline plasminogen activity level and a history of lesions and symptoms consistent with diagnosis.
B. Continuation Requests: Medical records (e.g., chart notes, lab reports) documenting disease stability or improvement.

III. CRITERIA FOR INITIAL APPROVAL

Plasminogen deficiency type 1 (hypoplasminogenemia)
Authorization of 12 months may be granted for treatment of plasminogen deficiency type 1 (hypoplasminogenemia) when all of the following criteria are met:
A. Member has a baseline plasminogen activity level of 45% or less.
B. Member has a documented history of lesions and symptoms consistent with a diagnosis of plasminogen deficiency type 1 (e.g., ligneous conjunctivitis, ligneous gingivitis or gingival overgrowth, vision abnormalities, respiratory distress and/or obstruction, abnormal wound healing).

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for members with an indication listed in Section III who are experiencing benefit from therapy as evidenced by disease stability or disease improvement (e.g., improvement in lesion number and/or size, absence of new lesion development, improvement in respiratory function, increased quality of life).

V. REFERENCES

1. Ryplazim [package insert]. Fort Lee, NJ: Prometic Biotherapeutics Inc.; November 2021.

2. Shapiro AD, Nakar C, Parker JM, et al. Plasminogen replacement therapy for the treatment of children and adults with congenital plasminogen deficiency. *Blood*. 2018;131(12):1301-1310.
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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.
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Reference number(s)
3643-A

SPECIALTY GUIDELINE MANAGEMENT

SARCLISA (isatuximab-irfc)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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 multiple myeloma, in combination with pomalidomide and dexamethasone, for adult patients who have received at least two prior therapies including lenalidomide and a proteasome inhibitor.
2. Treatment of relapsed or refractory multiple myeloma, in combination with carfilzomib and dexamethasone, for adult patients who have received one to three prior lines of therapy.

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 treatment of multiple myeloma in either of the following settings:

1. The requested medication will be used in combination with pomalidomide and dexamethasone and the member has previously received at least two prior therapies for multiple myeloma, including lenalidomide and a proteasome inhibitor
2. The requested medication will be used in combination with carfilzomib and dexamethasone and the member has previously received at least one prior line of therapy for multiple myeloma

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. Sarclisa [package insert]. Bridgewater, NJ: sanofi-aventis U.S. LLC; July 2022.
2. The NCCN Drugs & Biologics Compendium® © 2022 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed October 4, 2022.

CVS/caremark

POLICY Document for Subcutaneous Immune Globulin (SCIG):

Hizentra®, HyQvia®, Cutaquig®, Cuvitru™ and Xembify®

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, lower cost site of care and overall, clinically appropriate use. This document provides specific information to each of the three sections of the overall policy.

Section 1: Site of Care

- Policy information specific to site of care (outpatient, hospital outpatient, home infusion)

Section 2: Clinical Criteria

- Policy information specific to the clinical appropriateness for the medication

Section 1: Site of Care

CareFirst Site of Care Criteria
Administration of Subcutaneous Immune Globulins
Cutaquig, Cuvitru, Hizentra, HyQvia, Xembify

POLICY

I. CRITERIA FOR APPROVAL FOR ADMINISTRATION IN OUTPATIENT HOSPITAL SETTING

This policy provides coverage for administration of subcutaneous Ig products in an outpatient hospital setting for up to 45 days when a member is new to therapy or reinitiating therapy after not being on therapy for at least 6 months.

This policy provides coverage for administration of subcutaneous Ig products in an outpatient hospital setting for a longer course of treatment when ANY of the following criteria are met:

A. The member has experienced an adverse reaction that did not respond to conventional interventions (eg, acetaminophen, steroids, diphenhydramine, fluids or other pre-medications) or a severe adverse event (anaphylaxis, anaphylactoid reactions, myocardial infarction, thromboembolism, or seizures) during or immediately after administration.
B. The member has developed anti-IgA antibodies which increases the risk for hypersensitivity and anaphylactic reactions.
C. The member is medically unstable (eg respiratory, cardiovascular, or renal conditions).
D. The member has significant behavioral issues and/or physical or cognitive impairment that would impact the safety of drug administration AND the patient does not have access to a caregiver.
E. The member is less than 14 years of age.

For situations where administration of subcutaneous Ig products does not meet the criteria for outpatient hospital infusion, coverage for subcutaneous Ig products is provided when administered in alternative sites such as; physician office, home infusion or ambulatory care.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the site of care prior authorization review (where applicable):

A. Medical records supporting the member has experienced an adverse reaction that did not respond to conventional interventions or a severe adverse event during or immediately after an administration
B. Medical records supporting the member has developed anti-IgA antibodies
C. Medical records supporting the member is medically unstable
D. Medical records supporting the member has behavioral issues and/or physical or cognitive impairment and no access to a caregiver

Section 2: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

Subcutaneous Immune Globulin (SCIG):
Hizentra®, HyQvia®, Cutaquig®, Cuvitru™ and Xembify®

POLICY

III. INDICATIONS

The indications below including FDA-approved indications and compendial 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. Cutaquig (Immune Globulin Subcutaneous [Human] - hipp, 16.5% Solution)
Cutaquig is indicated as replacement therapy for primary humoral immunodeficiency (PI) in adults and pediatric patients 2 years of age and older.
2. Cuvitru (Immune Globulin Subcutaneous [Human], 20% Solution)
Cuvitru is indicated as replacement therapy for primary humoral immunodeficiency in adult and pediatric patients two years of age and older.
3. Hizentra (Immune Globulin Subcutaneous [Human], 20% Liquid)
   a. Hizentra is indicated as replacement therapy for primary humoral immunodeficiency in adults and pediatric patients 2 years of age and older.
   b. Hizentra is indicated for the treatment of adult patients with chronic inflammatory demyelinating polyneuropathy (CIDP) as maintenance therapy to prevent relapse of neuromuscular disability and impairment.
   Limitations of Use:
   Hizentra maintenance therapy in CIDP has been systematically studied for 6 months and for a further 12 months in a follow-up study. Maintenance therapy beyond these periods should be individualized based upon the patient's response and need for continued therapy.
4. HyQvia (Immune Globulin Infusion 10% [Human] with Recombinant Human Hyaluronidase)
HyQvia is indicated for the treatment of primary immunodeficiency in adults.
Limitation of Use: Safety and efficacy of chronic use of recombinant human hyaluronidase in HyQvia have not been established in conditions other than primary immunodeficiency.
5. Xembify (Immune Globulin Subcutaneous [Human} – klhw, 20% Solution)
Xembify is indicated for treatment of primary humoral immunodeficiency (PI) in patients 2 years of age and older.

B. Compendial Uses
1. Idiopathic thrombocytopenic purpura (ITP)
2. Multifocal motor neuropathy
3. Kawasaki syndrome
4. B-cell chronic lymphocytic leukemia (CLL)

5. Prophylaxis of bacterial infections in pediatric human immunodeficiency virus (HIV) infection
6. Bone marrow transplant (BMT)/hematopoietic stem cell transplant (HSCT)
7. Dermatomyositis
8. Polymyositis
9. Myasthenia gravis
10. Guillain-Barré syndrome
11. Lambert-Eaton myasthenic syndrome
12. Fetal/neonatal alloimmune thrombocytopenia
13. Parvovirus B19-induced pure red cell aplasia
14. Stiff-person syndrome
15. Management of immune checkpoint inhibitor-related toxicities
16. Acquired red cell aplasia
17. Acute disseminated encephalomyelitis
18. Autoimmune mucocutaneous blistering diseases
19. Autoimmune hemolytic anemia
20. Autoimmune neutropenia
21. Birdshot retinochoroidopathy
22. BK virus associated nephropathy
23. Churg-Strauss Syndrome
24. Enteroviral meningoencephalitis
25. Hematophagocytic lymphohistiocytosis (HLH) or macrophage activation syndrome (MAS)
26. Hemolytic disease of newborn
27. HIV-associated thrombocytopenia
28. Hyperimmunoblobulinemia E Syndrome
29. Hypogammaglobulinemia from chimeric antigen receptor T (CAR-T) therapy
30. Multiple myeloma
31. Neonatal hemochromatosis, prophylaxis
32. Opsoclonus-myoclonus
33. Paraneoplastic opsonus-myoclonus ataxia associated with neuroblastoma
34. Post-transfusion purpura
35. Rasmussen encephalitis
36. Renal transplantation from a live donor with ABO incompatibility or positive cross match
37. Secondary immunosuppression associated with major surgery, hematological malignancy, major burns, and collagen-vascular diseases
38. Solid organ transplantation, for allosensitized members
39. Toxic epidermal necrolysis and Stevens-Johnson syndrome
40. Toxic shock syndrome
41. Systemic lupus erythematosus (SLE)
42. Toxic necrotizing fasciitis due to group A streptococcus
43. Measles (Rubeola) prophylaxis
44. Tetanus treatment and prophylaxis
45. Varicella prophylaxis

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

IV. DOCUMENTATION

The following information is necessary to initiate the prior authorization review:

A. Primary immunodeficiency
   1. Diagnostic test results
      a. Copy of laboratory report with serum immunoglobulin levels: IgG, IgA, IgM, and IgG subclasses

b. Vaccine response to pneumococcal polysaccharide vaccine (post-vaccination *Streptococcus pneumoniae* antibody titers)
c. Pertinent genetic or molecular testing in members with a known genetic disorder
d. Copy of laboratory report with lymphocyte subset enumeration by flow cytometry

2. IgG trough level for those continuing with IG therapy

B. Myasthenia gravis
1. Clinical records describing standard treatments tried and failed

C. Secondary hypogammaglobulinemia (CLL, HIV, BMT/HSCT recipient)
1. Copy of laboratory report with pre-treatment serum IgG level

D. Chronic inflammatory demyelinating polyneuropathy (CIDP) and multifocal motor neuropathy (MMN)
1. Pre-treatment electrodiagnostic studies (electromyography [EMG] or nerve conduction studies [NCS])

E. Dermatomyositis and polymyositis
1. Clinical records describing standard treatments tried and failed

F. Lambert-Eaton Myasthenic Syndrome (LEMS)
1. Neurophysiology studies (e.g., electromyography)
2. A positive anti- P/Q type voltage-gated calcium channel antibody test

G. Idiopathic thrombocytopenic purpura
1. Laboratory report with pre-treatment/current platelet count
2. Chronic/persistent ITP: copy of medical records supporting trial and failure with corticosteroid or anti-D therapy (unless contraindicated)

H. Parvovirus B19-indicated Pure Red Cell Aplasia (PRCA)
1. Copy of test result confirming presence of parvovirus B19

I. Stiff-person syndrome
1. Anti-glutamic acid decarboxylase (GAD) antibody testing results
2. Clinical records describing standard treatments tried and failed

J. Toxic shock syndrome or toxic necrotizing fasciitis due to group A streptococcus
1. Documented presence of fasciitis (toxic necrotizing fasciitis due to group A streptococcus only)
2. Microbiological data (culture or Gram stain)

V. CRITERIA FOR INITIAL APPROVAL

A. Primary Immunodeficiency

Initial authorization of 6 months may be granted for members with any of the following diagnoses:

1. Severe combined immunodeficiency (SCID) or congenital agammaglobulinemia (eg, X-linked or autosomal recessive agammaglobulinemia)
   a. Diagnosis confirmed by genetic or molecular testing, or
   b. Pretreatment IgG level < 200 mg/dL, or
   c. Absence or very low number of T cells (CD3 T cells < 300/microliter) or the presence of maternal T cells in the circulation (SCID only)

2. Wiskott-Aldrich syndrome, DiGeorge syndrome, or ataxia-telangiectasia (or other non-SCID combined immunodeficiency)
   a. Diagnosis confirmed by genetic or molecular testing (if applicable), and
   b. History of recurrent bacterial infections (eg, pneumonia, otitis media, sinusitis, sepsis, gastrointestinal), and
   c. Impaired antibody response to pneumococcal polysaccharide vaccine (see Appendix A)

3. Common variable immunodeficiency (CVID)
   a. Age 2 years or older, and
   b. Other causes of immune deficiency have been excluded (eg, drug induced, genetic disorders, infectious diseases such as HIV, malignancy), and
   c. Pretreatment IgG level < 500 mg/dL or ≥ 2 SD below the mean for age, and
   d. History of recurrent bacterial infections, and
   e. Impaired antibody response to pneumococcal polysaccharide vaccine (see Appendix A)

4. Hypogammaglobulinemia (unspecified), IgG subclass deficiency, selective IgA deficiency, selective IgM deficiency, or specific antibody deficiency
   a. History of recurrent bacterial infections, and
   b. Impaired antibody response to pneumococcal polysaccharide vaccine (see Appendix A), and
   c. Any of the following pre-treatment laboratory findings:
      i. Hypogammaglobulinemia: IgG < 500 mg/dL or ≥ 2 SD below the mean for age
      ii. Selective IgA deficiency: IgA level < 7 mg/dL with normal IgG and IgM levels
      iii. Selective IgM deficiency: IgM level < 30 mg/dL with normal IgG and IgA levels
      iv. IgG subclass deficiency: IgG1, IgG2, or IgG3 ≥ 2 SD below mean for age assessed on at least 2 occasions; normal IgG (total) and IgM levels, normal/low IgA levels
      v. Specific antibody deficiency: normal IgG, IgA and IgM levels
5. Other predominant antibody deficiency disorders must meet a., b., and c.i. in section 4. above.
6. Other combined immunodeficiency must meet criteria in section 2. above.

Re-authorization of 6 months may be granted when the following criteria are met:
1. A reduction in the frequency of bacterial infections has been demonstrated since initiation of IG therapy, AND
2. IgG trough levels are monitored at least yearly and maintained at or above the lower range of normal for age (when applicable for indication), OR
3. The prescriber will re-evaluate the dose of IG and consider a dose adjustment (when appropriate).

B. Myasthenia Gravis
1. Authorization of 1 month may be granted to members who are prescribed IG for worsening weakness, acute exacerbation, or in preparation for surgery.
   a. Worsening weakness includes an increase in any of the following symptoms: diplopia, ptosis, blurred vision, difficulty speaking (dysarthria), difficulty swallowing (dysphagia), difficulty chewing, impaired respiratory status, fatigue, and limb weakness. Acute exacerbations include more severe swallowing difficulties and/or respiratory failure
   b. Pre-operative management (eg, prior to thymectomy)
2. Authorization of 6 months may be granted to members with refractory myasthenia gravis who have tried and failed 2 or more of standard therapies (eg, corticosteroids, azathioprine, cyclosporine, mycophenolate mofetil, rituximab).

C. Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)
1. Initial authorization of 3 months may be granted when the following criteria are met:
   a. Disease course is progressive or relapsing/remitting for 2 months or longer
   b. Moderate to severe functional disability
   c. The diagnosis was confirmed by electrodiagnostic studies
2. Re-authorization of 6 months may be granted when the following criteria are met:
   a. Significant improvement in disability and maintenance of improvement since initiation of IG therapy
   b. IG is being used at the lowest effective dose and frequency

D. Dermatomyositis or Polymyositis
1. Initial authorization of 3 months may be granted when the following criteria are met:
   a. Member has at least 4 of the following:
      i. Proximal muscle weakness (upper or lower extremity and trunk)
      ii. Elevated serum creatine kinase (CK) or aldolase level
      iii. Muscle pain on grasping or spontaneous pain
      iv. Myogenic changes on EMG (short-duration, polyphasic motor unit potentials with spontaneous fibrillation potentials)
      v. Positive for anti-synthetase antibodies (e.g., anti-Jo-1, also called histadyl tRNA synthetase)

vi. Non-destructive arthritis or arthralgias
vii. Systemic inflammatory signs (fever: more than 37°C at axilla, elevated serum CRP level or accelerated ESR of more than 20 mm/h by the Westergren method)
viii. Pathological findings compatible with inflammatory myositis (inflammatory infiltration of skeletal evidence of active regeneration may be seen), and

b. Standard first-line treatments (corticosteroids) and second-line treatments (immunosuppressants) have been tried but were unsuccessful or not tolerated, or
c. Member is unable to receive standard first-line and second-line therapy because of a contraindication or other clinical reason.

2. Re-authorization of 6 months may be granted when the following criterion is met:
   a. Significant improvement in disability and maintenance of improvement since initiation of IG therapy

E. Idiopathic Thrombocytopenic Purpura ITP/(Immune Thrombocytopenia)

1. Newly diagnosed ITP (diagnosed within the past 3 months) or initial therapy: authorization of 1 month may be granted when the following criteria are met
   a. Children (< 18 years of age)
      i. Significant bleeding symptoms (mucosal bleeding or other moderate/severe bleeding) or
      ii. High risk for bleeding* (see Appendix B), or
      iii. Rapid increase in platelets is required* (eg, surgery or procedure)
   b. Adults (≥ 18 years of age)
      i. Platelet count < 30,000/mcL, or
      ii. Platelet count < 50,000/mcL and significant bleeding symptoms, high risk for bleeding or rapid increase in platelets is required*, and
      iii. Corticosteroid therapy is contraindicated and IG will be used alone or IG will be used in combination with corticosteroid therapy
2. Chronic/persistent ITP (≥ 3 months from diagnosis) or ITP unresponsive to first-line therapy: authorization of 6 months may be granted when the following criteria are met:
   a. Platelet count < 30,000/mcL, or
   b. Platelet count < 50,000/mcL and significant bleeding symptoms, high risk for bleeding* or rapid increase in platelets is required*, and
   c. Relapse after previous response to IG or inadequate response/intolerance/contraindication to corticosteroid or anti-D therapy
3. Adults with refractory ITP after splenectomy: authorization of 6 months may be granted when either of the following criteria is met:
   a. Platelet count < 30,000/mcL, or
   b. Significant bleeding symptoms
4. ITP in pregnant women: authorization through delivery may be granted to pregnant women with ITP.

* The member's risk factor(s) for bleeding (see Appendix B) or reason requiring a rapid increase in platelets must be provided.

F. B-cell Chronic Lymphocytic Leukemia (CLL)

1. Initial authorization of 6 months may be granted when all of the following criteria are met:
   a. IG is prescribed for prophylaxis of bacterial infections.
   b. Member has a history of recurrent sinopulmonary infections requiring intravenous antibiotics or hospitalization.
   c. Member has a pretreatment serum IgG level <500 mg/dL.
2. Re-authorization of 6 months may be granted when a reduction in the frequency of bacterial infections has been demonstrated since initiation of IG therapy.

G. Prophylaxis of Bacterial Infections in HIV-Infected Pediatric Patients

1. Initial authorization of 6 months may be granted to pediatric members with HIV infection when any of the following criteria are met:
   a. IG is prescribed for primary prophylaxis of bacterial infections and pretreatment serum IgG < 400 mg/dL, or
   b. IG is prescribed for secondary prophylaxis of bacterial infections for members with a history of recurrent bacterial infections (> 2 serious bacterial infections in a 1-year period), or
   c. Member has failed to form antibodies to common antigens, such as measles, pneumococcal, and/or Haemophilus influenzae type b vaccine, or
   d. Member lives in an area where measles is highly prevalent and who have not developed an antibody response after two doses of measles, mumps, and rubella virus vaccine live, or
   e. Member has been exposed to measles and request is for a single dose, or
   f. Member has chronic bronchiectasis that is suboptimally responsive to antimicrobial and pulmonary therapy
2. Re-authorization of 6 months may be granted when a reduction in the frequency of bacterial infections has been demonstrated since initiation of IG therapy.

H. Bone marrow transplant/hemopoietic stem cell transplant (BMT/HSCT)

1. Initial authorization of 6 months may be granted to members who are BMT/HSCT recipients when the following criteria are met:
   a. Therapy will be used to prevent the risk of acute graft-versus-host disease, associated interstitial pneumonia (infectious or idiopathic), septicemia, and other infections (e.g., cytomegalovirus infections [CMV], recurrent bacterial infection)
   b. Either of the following:
      i. IG is requested within the first 100 days post-transplant.
      ii. Member has a pretreatment serum IgG < 400 mg/dL.
2. Re-authorization of 6 months may be granted when a reduction in the frequency of bacterial infections has been demonstrated since initiation of IG therapy.

I. Multifocal Motor Neuropathy (MMN)

1. Initial authorization of 3 months may be granted when the following criteria are met:
   a. Member experienced progressive, multifocal, asymmetrical weakness without objective sensory loss in 2 or more nerves for at least 1 month
   b. The diagnosis was confirmed by electrodiagnostic studies
2. Re-authorization of 6 months may be granted when significant improvement in disability and maintenance of improvement have occurred since initiation of IG therapy

J. Guillain-Barre Syndrome (GBS)

Authorization of 1 month total may be granted for GBS when the following criteria are met:

1. Member has severe disease with significant weakness (e.g., inability to stand or walk without aid, respiratory weakness)
2. Onset of neurologic symptoms occurred less than 4 weeks from the anticipated start of therapy

K. Lambert-Eaton Myasthenic Syndrome (LEMS)

1. Initial authorization of 6 months may be granted for LEMS when the following criteria are met:
   a. Diagnosis has been confirmed by either of the following:
      i. Neurophysiology studies (e.g., electromyography)
      ii. A positive anti- P/Q type voltage-gated calcium channel antibody test
   b. Anticholinesterases (eg pyridostigmine) and amifampridine (e.g., 3,4-diaminopyridine phosphate, Firdapse) have been tried but were unsuccessful or not tolerated
   c. Weakness is severe or there is difficulty with venous access for plasmapheresis
2. Re-authorization of 6 months may be granted when member is responding to therapy (i.e., there is stability or improvement in symptoms relative to the natural course of LEMS).

L. Kawasaki Syndrome

Authorization of 1 month may be granted for pediatric members with Kawasaki syndrome.

M. Fetal/Neonatal Alloimmune Thrombocytopenia (F/NAIT)
Authorization of 6 months may be granted for treatment of F/NAIT.

N. Parvovirus B19-induced Pure Red Cell Aplasia (PRCA)
Authorization of 6 months may be granted for severe, refractory anemia associated with bone marrow suppression, with parvovirus B19 viremia.

O. Stiff-person Syndrome
Authorization of 6 months may be granted for stiff-person syndrome when the following criteria are met:
1. Diagnosis has been confirmed by anti-glutamic acid decarboxylase (GAD) antibody testing
2. Member had an inadequate response to first-line treatment (benzodiazepines and/or baclofen)

P. Management of immune checkpoint inhibitor-related toxicities
Authorization of 1 month may be granted for management of immune checkpoint-inhibitor toxicities when all of the following criteria are met:
1. Member has experienced a moderate or severe adverse event to a PD-1 or PD-L1 inhibitor (eg, pembrolizumab, nivolumab, atezolizumab, avelumab, durvalumab)
2. The offending medication has been held or discontinued
3. Member experienced one or more of the following nervous system adverse events: myocarditis, bullous dermatitis, Stevens-Johnson syndrome, toxic epidermal necrolysis, pneumonitis, myasthenia gravis, peripheral neuropathy, encephalitis, transverse myelitis, severe inflammatory arthritis, Guillain-Barre syndrome, or steroid-refractory myalgias or myositis

Q. Acquired Red Cell Aplasia
Authorization of 6 months may be granted for acquired red cell aplasia.

R. Acute Disseminated Encephalomyelitis
Authorization of 1 month may be granted for acute disseminated encephalomyelitis in members who have had an insufficient response or a contraindication to intravenous corticosteroid treatment.

S. Autoimmune Mucocutaneous Blistering Disease
Authorization of 6 months may be granted for autoimmune mucocutaneous blistering disease (includes pemphigus vulgaris, pemphigus foliaceus, bullous pemphigoid, mucous membrane pemphigoid, and epidermolysis bullosa aquisita) when the following criteria are met:
1. Diagnosis has been proven by biopsy and confirmed by pathology report, and
2. Condition is rapidly progressing, extensive or debilitating, and
3. Member has failed or experienced significant complications (eg diabetes, steroid-induced osteoporosis) from standard treatment (corticosteroids, immunosuppressive agents).

T. Autoimmune Hemolytic Anemia
Authorization of 6 months may be granted for warm-type autoimmune hemolytic anemia in members who do not respond or have a contraindication to corticosteroids or splenectomy.

U. Autoimmune Neutropenia
Authorization of 6 months may be granted for autoimmune neutropenia where treatment with G-CSF (granulocyte colony stimulating factor) is not appropriate.

V. Birdshot Retinochoroidopathy
Authorization of 6 months may be granted for birdshot (vitiliginous) retinochoroidopathy that is not responsive to immunosuppressives (eg corticosteroids, cyclosporine).

W. BK Virus Associated Nephropathy

Authorization of 6 months may be granted for BK virus associated nephropathy.

X. Churg-Strauss Syndrome
Authorization of 6 months may be granted for severe, active Churg-Strauss syndrome as adjunctive therapy for members who have experienced failure, intolerance, or are contraindicated to other interventions.

Y. Enteroviral Meningoencephalitis
Authorization of 6 months may be granted for severe cases of enteroviral meningoencephalitis.

Z. Hematophagocytic Lymphohistiocytosis (HLH) or Macrophage Activation Syndrome (MAS)
Authorization of 6 months may be granted for treatment of hypogammaglobulinemia in HLH or MAS when total IgG is less than 400 mg/dL or two standard deviations below the mean for age.

AA. Hemolytic Disease of Newborn
Authorization of 6 months may be granted for isoimmune hemolytic disease in neonates.

BB. HIV-associated Thrombocytopenia
Authorization of 6 months may be granted for HIV-associated thrombocytopenia when the following criteria are met:
1. Pediatric members with IgG < 400 mg/dL and has one of the following:
   a. 2 or more bacterial infections in a 1-year period despite antibiotic chemoprophylaxis with TMP-SMZ or another active agent, or
   b. Received 2 doses or measles vaccine and lives in a region with a high prevalence or measles, or
   c. HIV-associated thrombocytopenia despite anti-retroviral therapy, or
   d. Chronic bronchiectasis that is suboptimally responsive to antimicrobial and pulmonary therapy, or
   e. T4 cell count ≥ 200/mm^3
2. Adult members with significant bleeding, platelet count < 20,000/mcL, and failure of RhIG in Rh-positive patients

CC. Hyperimmunoglobulinemia E Syndrome
Authorization of 6 months may be granted to treat severe eczema in hyperimmunoglobulinemia E syndrome.

DD. Hypogammaglobulinemia from CAR-T therapy
Authorization of 6 months may be granted for members with IgG < 400 mg/dL receiving treatment with CAR-T therapy (including but not limited to idecabtagene vicleucel [Abecma], tisagenlecleucel [Kymriah], or axicabtagene ciloleucel [Yescarta]).

EE. Multiple Myeloma
Authorization of 6 months may be granted for multiple myeloma in members who have recurrent, serious infections despite the use of prophylactic antibiotics.

FF. Neonatal Hemochromatosis
Authorization of 6 months may be granted for prophylaxis in members who are pregnant with a history of pregnancy ending in documented neonatal hemochromatosis.

GG. Opsoclonus-myoclonus
Authorization of 6 months may be granted for treatment of either of the following:
1. Paraneoplastic opsoclonus-myoclonus-ataxia associated with neuroblastoma
2. Refractory opsoclonus-myoclonus, as last-resort treatment

HH. Post-transfusion Purpura
Authorization of 1 month may be granted for post-transfusion purpura.

II. Rasmussen Encephalitis
Authorization of 6 months may be granted for Rasmussen encephalitis in members whose symptoms do not improve with anti-epileptic drugs and corticosteroids.

JJ. Renal Transplantation
Authorization of 6 months may be granted for a member undergoing renal transplantation from a live donor with ABO incompatibility or positive cross match.

KK. Secondary Immunosuppression Associated with Major Surgery, Hematological Malignancy, Major Burns, and Collagen-Vascular Diseases
Authorization of 6 months may be granted to prevent or modify recurrent bacterial or viral infections in members with secondary immunosuppression (IgG < 400 mg/dL) associated with major surgery, hematological malignancy, extensive burns, or collagen-vascular disease.

LL. Solid Organ Transplantation
Authorization of 6 months may be granted for solid organ transplantation for allosensitized members.

MM. Toxic Epidermal Necrolysis and Stevens-Johnson Syndrome
Authorization of 1 month may be granted for severe cases of toxic epidermal necrolysis or Stevens-Johnson syndrome.

NN. Toxic Shock Syndrome
Authorization of 1 month may be granted for staphylococcal or streptococcal toxic shock syndrome when the infection is refractory to several hours of aggressive therapy, an undrainable focus is present, or the member has persistent oliguria with pulmonary edema.

OO. Systemic Lupus Erythematosus
Authorization of 6 months may be granted for severe, active SLE in members who have experienced inadequate response, intolerance or have a contraindication to first and second line therapies.

PP. Measles (Rubeola) prophylaxis
Authorization of 1 month may be granted for postexposure prophylaxis to prevent or modify symptoms of measles (rubeola) in susceptible members exposed to the disease less than 6 days previously.

QQ. Tetanus treatment and prophylaxis
Authorization of 1 month may be granted for treatment or postexposure prophylaxis of tetanus as an alternative when tetanus immune globulin (TIG) is unavailable.

RR. Varicella prophylaxis
Authorization of 1 month may be granted for postexposure prophylaxis of varicella in susceptible individuals when varicella-zoster immune globulin (VZIG) is unavailable.

SS. Toxic Necrotizing Fasciitis Due To Group A Streptococcus
Authorization of 1 month may be granted for members with fasciitis due to invasive streptococcal infection.

VI. CONTINUATION OF THERAPY

Authorization may be granted for continuation of therapy when either the following criteria is met:

a. For conditions with reauthorization criteria listed under section III: Members who are currently receiving IG therapy must meet the applicable reauthorization criteria for the member's condition.
b. For all other conditions, all members (including new members) must meet initial authorization criteria.

VII. APPENDICES

Appendix A: Impaired Antibody Response to Pneumococcal Polysaccharide Vaccine

- Age 2 years and older: impaired antibody response demonstrated to vaccination with a pneumococcal polysaccharide vaccine
- Not established for children less than 2 years of age
- Excludes the therapy initiated in the hospital setting

Appendix B: Examples of Risk Factors for Bleeding (not all inclusive)

- Undergoing a medical or dental procedure where blood loss is anticipated
- Comorbidity (eg, peptic ulcer disease, hypertension)
- Mandated anticoagulation therapy
- Profession or lifestyle predisposes patient to trauma (eg, construction worker, fireman, professional athlete)

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SECTION 2

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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

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Reference number(s)
1651-A

SPECIALTY GUIDELINE MANAGEMENT

Revatio (sildenafil)
sildenafil (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
Sildenafil/Revatio is indicated for the treatment of pulmonary arterial hypertension (World Health Organization [WHO] Group 1) in adults to improve exercise ability and delay clinical worsening. Studies establishing effectiveness were short-term (12 to 16 weeks), and included predominantly patients with New York Heart Association (NYHA) Functional Class II-III symptoms. Etiologies were idiopathic or associated with connective tissue disease.

Limitation of use: Adding sildenafil to bosentan therapy does not result in any beneficial effect on exercise capacity.

B. Compendial Use
Secondary Raynaud's phenomenon *(Tablets only)*

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). PAH was confirmed by either criterion (i) or criterion (ii) below:
    i. Pretreatment right heart catheterization with all of the following results:
        a. mPAP > 20 mmHg
        b. PCWP ≤ 15 mmHg
        c. PVR ≥ 3 Wood units
    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

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

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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)

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POLICY Document for SIMPONI ARIA
(golimumab injection for intravenous use)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, lower cost site of care and overall, clinically appropriate use. This document provides specific information to each of the three sections of the overall policy.

Section 1: Site of Care
- Policy information specific to site of care (outpatient, hospital outpatient, home infusion)

Section 2: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 1: Site of Care

CareFirst Site of Care Criteria
Administration of Simponi Aria

POLICY

I. CRITERIA FOR APPROVAL FOR ADMINISTRATION IN OUTPATIENT HOSPITAL SETTING

This policy provides coverage for administration of Simponi Aria in an outpatient hospital setting for 3 months when a member is new to therapy or is reinitiating therapy after not being on therapy for at least 6 months.

This policy provides coverage for administration of Simponi Aria in an outpatient hospital setting for a longer course of treatment when ANY of the following criteria are met:

A. The member has experienced an adverse reaction that did not respond to conventional interventions (eg, acetaminophen, steroids, diphenhydramine, fluids or other pre-medications) or a severe adverse event (anaphylaxis, anaphylactoid reactions, myocardial infarction, thromboembolism, or seizures) during or immediately after an infusion.
B. The member is medically unstable (eg respiratory, cardiovascular, or renal conditions).
C. The member has severe venous access issues that require the use of a special interventions only available in the outpatient hospital setting.
D. The member has significant behavioral issues and/or physical or cognitive impairment that would impact the safety of the infusion therapy AND the patient does not have access to a caregiver.
E. The member is less than 14 years of age.

For situations where administration of Simponi Aria does not meet the criteria for outpatient hospital infusion, coverage for Simponi Aria is provided when administered in alternative sites such as; physician office, home infusion or ambulatory care.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the site of care prior authorization review (where applicable):

A. Medical records supporting the member has experienced an adverse reaction that did not respond to conventional interventions or a severe adverse event during or immediately after an infusion
B. Medical records supporting the member is medically unstable

C. Medical records supporting the member has severe venous access issues that require specialized interventions only available in the outpatient hospital setting
D. Medical records supporting the member has behavioral issues and/or physical or cognitive impairment and no access to a caregiver

Section 2: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

SIMPONI ARIA (golimumab injection for intravenous use)

POLICY

III. INDICATIONS

The indications below including FDA-approved indications and compendial 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) in combination with methotrexate
   2. Active psoriatic arthritis (PsA) in patients 2 years of age and older
   3. Adult patients with active ankylosing spondylitis (AS)
   4. Active polyarticular juvenile idiopathic arthritis (pJIA) in patients 2 years of age and older

B. Compendial Uses
   1. Non-radiographic axial spondyloarthritis
   2. Oligoarticular juvenile idiopathic arthritis

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

IV. 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. Psoriatic arthritis (PsA), ankylosing spondylitis (AS), non-radiographic axial spondyloarthritis (nr-axSpA), and 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. 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.

V. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with one of the following:
A. Rheumatoid arthritis, ankylosing spondylitis, non-radiographic axial spondyloarthritis, and articular juvenile idiopathic arthritis: rheumatologist
B. Psoriatic arthritis: rheumatologist or dermatologist

VI. 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 A).

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 A).
    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 A).

B. Psoriatic arthritis (PsA)

1. Authorization of 12 months may be granted for members 2 years of age and 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 and 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 A), 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 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.

D. Articular juvenile idiopathic arthritis (JIA)

1. Authorization of 12 months may be granted for members 2 years of age and 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 and 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 drug (NSAID) 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.

VII. 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 members 2 years of age and 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 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)

D. Articular juvenile idiopathic arthritis (JIA)
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 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

VIII. 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.

IX. DOSAGE AND ADMINISTRATION

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

X. APPENDICES

Appendix A: Examples of Contraindications to Methotrexate or Leflunomide
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

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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 in adults who are candidates for systemic therapy or phototherapy
B. Active psoriatic arthritis in adults
C. Moderately to severely active Crohn's disease 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
   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. Crohn's disease
   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 or remission.

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 A).

B. Active psoriatic arthritis
Authorization of 12 months may be granted for treatment of active psoriatic arthritis.

C. Moderately to severely active Crohn's disease (CD)
1. Authorization of 12 months may be granted for members who have previously received a biologic indicated for the treatment of Crohn's disease.

2. Authorization of 12 months may be granted for members for the treatment of moderately to severely active CD when the member has had an inadequate response, intolerance, or contraindication to at least one conventional therapy option (see Appendix B).

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. Moderately to severely active 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 Crohn's disease 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 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. Endoscopic appearance of the mucosa
   vii. Improvement on a disease activity scoring tool (e.g., Crohn's Disease Activity Index [CDAI] score)

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 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.

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 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 B: Examples of Conventional Therapy Options for CD

1. Mild to moderate disease – induction of remission:
   a. Oral budesonide
   b. Alternatives: metronidazole, ciprofloxacin, rifaximin
2. Mild to moderate disease – maintenance of remission:

a. Azathioprine, mercaptopurine
b. Alternatives: oral budesonide, methotrexate intramuscular (IM) or subcutaneous (SC), sulfasalazine

3. Moderate to severe disease – induction of remission:
   a. Prednisone, methylprednisolone intravenous (IV)
   b. Alternatives: methotrexate IM or SC
4. Moderate to severe disease – maintenance of remission:
   a. Azathioprine, mercaptopurine
   b. Alternative: methotrexate IM or SC
5. Perianal and fistulizing disease – induction of remission:
   a. Metronidazole ± ciprofloxacin, tacrolimus
6. Perianal and fistulizing disease – maintenance of remission:
   a. Azathioprine, mercaptopurine
   b. Alternative: methotrexate IM or SC

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POLICY Document for SOLIRIS (eculizumab)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, lower cost site of care and overall, clinically appropriate use. This document provides specific information to each of the three sections of the overall policy.

Section 1: Site of Care

- Policy information specific to site of care (outpatient, hospital outpatient, home infusion)

Section 2: Clinical Criteria

- Policy information specific to the clinical appropriateness for the medication

Section 1: Site of Care

CareFirst Site of Care Criteria
Administration of Intravenous Soliris

POLICY

I. CRITERIA FOR APPROVAL FOR ADMINISTRATION IN OUTPATIENT HOSPITAL SETTING

This policy provides coverage for administration of Soliris in an outpatient hospital setting for 12 days (2 doses) when a member is new to therapy or is reinitiating therapy after not being on therapy for at least 6 months.

This policy provides coverage for administration of Soliris in an outpatient hospital setting for a longer course of treatment when ANY of the following criteria are met:

A. The member has experienced an adverse reaction to the medication that did not respond to conventional interventions (eg, acetaminophen, steroids, diphenhydramine, fluids, other pre-medications or slowing of the infusion rate) or a severe adverse event (anaphylaxis, anaphylactoid reactions, myocardial infarction, thromboembolism, or seizures) during or immediately after an infusion.
B. The member is medically unstable (eg respiratory, cardiovascular, or renal conditions).
C. The member has severe venous access issues that require the use of special interventions only available in the outpatient hospital setting.
D. The member has significant behavioral issues and/or physical or cognitive impairment that would impact the safety of the infusion therapy AND the patient does not have access to a caregiver.
E. The member is less than 14 years of age.

For situations where administration of Soliris does not meet the criteria for outpatient hospital infusion, coverage for Soliris is provided when administered in alternative sites such as; physician office, home infusion or ambulatory care.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the site of care prior authorization review (where applicable):

A. Medical records supporting the member has experienced an adverse reaction that did not respond to conventional interventions or a severe adverse event during or immediately after an infusion

B. Medical records supporting the member is medically unstable
C. Medical records supporting the member has severe venous access issues that require specialized interventions only available in the outpatient hospital setting
D. Medical records supporting the member has behavioral issues and/or physical or cognitive impairment and no access to a caregiver

Section 2: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

SOLIRIS (eculizumab) SGM

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.

FDA-Approved Indications
A. Paroxysmal nocturnal hemoglobinuria (PNH) to reduce hemolysis
B. Atypical hemolytic uremic syndrome (aHUS) to inhibit complement-mediated thrombotic microangiopathy
C. Generalized myasthenia gravis (gMG) in adult patients who are anti-acetylcholine receptor (AchR) antibody positive
D. Neuromyelitis optica spectrum disorder (NMOSD) in adult patients who are anti-aquaporin-4 (AQP4) antibody positive

Limitations of Use: Soliris is not indicated for the treatment of patients with Shiga toxin E. coli related hemolytic uremic syndrome (STEC-HUS).

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 new requests for treatment of:
A. For initial requests:
    1. Atypical hemolytic uremic syndrome: ADAMTS 13 level
    2. Paroxysmal nocturnal hemoglobinuria: flow cytometry used to show results of glycosylphosphatidylinositol-anchored proteins (GPI-APs) deficiency
    3. Generalized myasthenia gravis: anti-acetylcholine receptor (AchR) antibody positive, clinical classification of myasthenia gravis score, MG activities of daily living score, use of IVIG, use of two immunosuppressive therapies
    4. Neuromyelitis optica spectrum disorder: 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

A. Atypical hemolytic uremic syndrome
Authorization of 6 months may be granted for treatment of atypical hemolytic uremic syndrome not caused by Shiga toxin when all of the following criteria are met:
1. ADAMTS 13 activity level above 5%
2. Absence of Shiga toxin

B. Paroxysmal nocturnal hemoglobinuria
Authorization of 6 months may be granted for treatment of paroxysmal nocturnal hemoglobinuria (PNH) when all of the following criteria are met:
1. The diagnosis of PNH was confirmed by detecting a deficiency of glycosylphosphatidylinositol-anchored proteins (GPI-APs) as demonstrated by either of the following:
   a. At least 5% PNH cells
   b. At least 51% of GPI-AP deficient poly-morphonuclear cells
2. Flow cytometry is used to demonstrate GPI-APs deficiency

C. Generalized myasthenia gravis (gMG)
Authorization of 6 months may be granted for treatment of generalized myasthenia gravis (gMG) when all of the following criteria are met:
1. Anti-acetylcholine receptor (AchR) antibody positive
2. Myasthenia Gravis Foundation of America (MGFA) clinical classification II to IV
3. MG activities of daily living (MG-ADL) total score ≥6
4. Meets both of the following:
   a. Member has had an inadequate response to at least two immunosuppressive therapies listed below:
      i. azathioprine
      ii. cyclosporine
      iii. mycophenolate mofetil
      iv. tacrolimus
      v. methotrexate
      vi. cyclophosphamide
      vii. rituximab
   b. Member has inadequate response to chronic IVIG

D. Neuromyelitis Optica Spectrum Disorder (NMOSD)
Authorization of 6 months may be granted for treatment of neuromyelitis optica spectrum disorder (NMOSD) when all of the following criteria are met:
1. Anti-aquaporin-4 (AQP4) antibody positive
2. Member exhibits one of the following core clinical characteristics of NMOSD:
   a. Optic neuritis
   b. Acute myelitis
   c. Area postrema syndrome (episode of otherwise unexplained hiccups or nausea and vomiting)
   d. Acute brainstem syndrome
   e. Symptomatic narcolepsy or acute diencephalic clinical syndrome with NMOSD-typical diencephalic MRI lesions
   f. Symptomatic cerebral syndrome with NMOSD-typical brain lesions
3. The member will not receive the requested drug concomitantly with other biologics for the treatment of NMOSD.

IV. CONTINUATION OF THERAPY

A. Atypical hemolytic uremic syndrome
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 and demonstrate a positive response to therapy (e.g., normalization of lactate dehydrogenase (LDH) levels, platelet counts).

B. Paroxysmal nocturnal hemoglobinuria
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 and demonstrate a positive response to therapy (e.g., improvement in hemoglobin levels, normalization of lactate dehydrogenase [LDH] levels).

C. Generalized myasthenia gravis (gMG)
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 and demonstrate a positive response to therapy (e.g., improvement in MG-ADL score, changes compared to baseline in Quantitative Myasthenia Gravis (QMG) total score).

D. Neuromyelitis optica spectrum disorder (NMOSD)
Authorization of 12 months may be granted for continued treatment in members requesting reauthorization when all of the following criteria are met:
1. There is no evidence of unacceptable toxicity or disease progression while on the current regimen.
2. The member demonstrates a positive response to therapy (e.g., reduction in number of relapses).
3. The member will not receive the requested drug concomitantly with other biologics for the treatment of NMOSD.

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.

REFERENCES

SECTION 1
1. Soliris [package insert]. New Haven, CT: Alexion Pharmaceuticals Inc; November 2020.
2. Brodsky RA, Young NS, Antonioli E, et al. Multicenter phase 3 study of the complement inhibitor eculizumab for the treatment of patients with paroxysmal nocturnal hemoglobinuria. *Blood.* 2008;111(4):1840-1847.
3. Hillmen P, Young NS, Schubert J, et al. The complement inhibitor eculizumab in paroxysmal nocturnal hemoglobinuria. *N Engl J Med.* 2006;355(12):1233-1243.

SECTION 2
1. Soliris [package insert]. New Haven, CT: Alexion Pharmaceuticals, Inc.; November 2020.
2. Loirat C, Fakhouri F, Ariceta G, et al. An international consensus approach to the management of atypical hemolytic uremic syndrome in children. *Pediatr Nephrol*. Published online: April 11, 2015.
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5. Jaretzki A, Barohn RJ, Ernstoff RM et al. Myasthenia Gravis: Recommendations for Clinical Research Standards. *Ann Thorac Surg*. 2000;70: 327-34.

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10. Preis M, Lowrey CH. Laboratory tests for paroxysmal nocturnal hemoglobinuria (PNH). Am J Hematol. 2014;89(3):339-341.
11. Lee JW, Sicre de Fontbrune F, Wong LL, et al. Ravulizumab (ALXN1210) vs eculizumab in adult patients with PNH naive to complement inhibitors: The 301 study. Blood. 2018 Dec 3; pii: blood-2018-09-876136.
12. Pittock SJ, Berthele A, Kim HJ, et al. Eculizumab in Aquaporin-4-Positive Neuromyelitis Optica Spectrum Disorder. *N Engl J Med*. 2019 May 3. doi: 10.1056/NEJMoA1900866.
13. Wingerchuk DM, Banwell B, Bennett JL, et al. International consensus diagnostic criteria for neuromyelitis optica spectrum disorders. *Neurology.* 2015; 85:177-189.
14. Parker CJ. Update on the diagnosis and management of paroxysmal nocturnal hemoglobinuria. Hematology Am Soc Hematol Educ Program. 2016;2016(1):208-216.

POLICY Document for SOMAVERT (pegvisomant)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, and overall, clinically appropriate use. This document provides specific information to both sections of the overall policy.

Section 1: Preferred Product
- Policy information specific to preferred medications

Section 2: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 1: Preferred Product

EXCEPTIONS CRITERIA
ACROMEGALY PRODUCTS

PREFERRED PRODUCTS: SANDOSTATIN LAR, SOMATULINE DEPOT

POLICY
This policy informs prescribers of preferred products and provides an exception process for targeted products through prior authorization.

I. PLAN DESIGN SUMMARY

This program applies to the acromegaly products specified in this policy. Coverage for a targeted product is provided based on clinical circumstances that would exclude the use of the preferred products and may be based on previous use of a product. The coverage review process will ascertain situations where a clinical exception can be made. This program applies to all members requesting treatment with a targeted product.

Each referral is reviewed based on all utilization management (UM) programs implemented for the client.

Table. Acromegaly Products

	Product(s)
Preferred*	• **Sandostatin LAR** (octreotide acetate for injectable suspension) • **Somatuline Depot** (lanreotide)
Targeted	• **lanreotide injection** • **Signifor LAR** (pasireotide injectable suspension) • **Somavert** (pegvisomant)

*: Medications considered formulary or preferred on your plan may still require a clinical prior authorization review.

II. EXCEPTION CRITERIA

This program applies to members requesting treatment for an indication that is FDA-approved for both of the preferred products.

A. lanreotide injection

Coverage for the targeted product is provided when all of the following criteria are met:

1. The member has had a documented intolerable adverse event to Somatuline Depot, and the adverse event was not an unexpected adverse event attributed to the active ingredient as described in the prescribing information.
2. The member has a documented inadequate response or intolerable adverse event to Sandostatin LAR.

B. Signifor LAR, Somavert

Coverage for a targeted product is provided when the member has had a documented inadequate response or intolerable adverse event to any of the preferred products.

Section 2: Clinical Criteria

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.

REFERENCES:

SECTION 1

1. Somatuline Depot [package insert]. Basking Ridge, NJ: Ipsen Biopharmaceuticals, Inc.; February 2023.
2. Sandostatin LAR Depot [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; March 2021.
3. Signifor LAR [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Company; June 2020.
4. Somavert [package insert]. New York, NY: Pharmacia & Upjohn Co; August 2021.
5. Lanreotide injection [package insert]. Warren, NJ: Cipla USA, Inc.; December 2021.

SECTION 2

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)
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

1. Sovaldi [package insert]. Foster City, CA: Gilead Sciences, Inc.; 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)
5580-A

SPECIALTY GUIDELINE MANAGEMENT

SPEVIGO (spesolimab-sbzo)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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
For the treatment of generalized pustular psoriasis (GPP) flares 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. Chart notes or medical record documentation of history of GPP.
B. Chart notes or medical record documentation of clinical presentation of pustules and affected area(s).
C. Genetic test results, laboratory results, biopsy results, GPP severity assessment (e.g., Generalized Pustular Psoriasis Physician Global Assessment (GPPPGA) score), if applicable.

III. PRESCRIBER SPECIALTIES

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

IV. CRITERIA FOR INITIAL APPROVAL

Generalized pustular psoriasis (GPP) flare
Authorization of 1 month may be granted for treatment of generalized pustular psoriasis flares in adult members when all of the following criteria are met:
A. Member has a known documented history of GPP (either relapsing [greater than 1 episode] or persistent [greater than 3 months]).
B. Member is presenting with primary, sterile, macroscopically visible pustules on non-acral skin (excluding cases where pustulation is restricted to psoriatic plaques).
C. Member has at least one of the following documented:
    1. IL36RN, CARD14, or AP1S3 gene mutation.
    2. Skin biopsy confirming presence of Kogoj's spongiform pustules.
    3. Systemic symptoms or laboratory abnormalities commonly associated with GPP flare (e.g., fever, asthenia, myalgia, elevated C-reactive protein [CRP], leukocytosis, neutrophilia [above ULN]).
    4. GPP flare of moderate-to-severe intensity (e.g., at least 5% body surface area is covered with erythema and the presence of pustules; Generalized Pustular Psoriasis Physician Global Assessment [GPPPGA] total score of greater or equal to 3).

V. CONTINUATION OF THERAPY

All adult 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.

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

VII. REFERENCES

1. Spevigo [package insert]. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc.; September 2022.
2. Bachelez H, Choon SE, Marrakchi S, et al. Trial of Spesolimab for Generalized Pustular Psoriasis. *N Engl J Med*. 2021;385(26):2431-2440.
3. Ly K, Beck KM, Smith MP, Thibodeaux Q, Bhutani T. Diagnosis and screening of patients with generalized pustular psoriasis. *Psoriasis (Auckl)*. 2019;9:37-42.
4. Fujita H, Gooderham M, Romiti R. Diagnosis of Generalized Pustular Psoriasis. *Am J Clin Dermatol*. 2022;23(Suppl 1):31-38.
5. Choon SE, Navarini AA, Pinter A. Clinical Course and Characteristics of Generalized Pustular Psoriasis. Am J Clin Dermatol. 2022 Jan;23(Suppl 1):21-29.
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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

1. Spravato [package insert]. Titusville, NJ: Janssen Pharmaceuticals, Inc.; July 2020.
2. American Psychological Association. *Depression Assessment Instruments.* Available at: https://www.apa.org/depression-guideline/assessment. Accessed October 5, 2022.
3. Micromedex Solutions [database online]. Ann Arbor, MI: Truven Health Analytics Inc. Available at: www.micromedexsolutions.com [available with subscription]. Accessed October 5, 2022.
4. Thase, M and Connolly, R (2021) Unipolar depression in adults: Choosing treatment for resistant depression, *UpToDate*, Available at www.uptodate.com [available with subscription]. Accessed October 5, 2022.

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.

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© 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

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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.

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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

1. Strensiq [package insert]. Cheshire, CT: Alexion Pharmaceuticals, Inc.; June 2020.
2. Bianchi ML. Hypophosphatasia: an overview of the disease and its treatment. *Osteoporos Int.* 2015; 26(12):2743-57.
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Reference number(s)
1973-A

SPECIALTY GUIDELINE MANAGEMENT

Supprelin LA (histrelin 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
Supprelin LA is indicated for the treatment of children with central precocious puberty (CPP).

B. Compendial Uses
1. Gender dysphoria (also known as gender non-conforming or transgender persons)
2. Preservation of ovarian function
3. Prevention of recurrent menstrual related attacks in acute porphyria

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. PRESCRIBER SPECIALTIES

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 patients less than 18 years of age.

IV. 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. Gender dysphoria

1. Authorization of 12 months may be granted for pubertal hormonal suppression in an adolescent member when all of the following criteria are met:
   i. The member has a diagnosis of gender dysphoria.
   ii. The member has reached Tanner stage 2 of puberty or greater.
   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 transition when all of the following criteria are met:
   i. The member has a diagnosis of gender dysphoria.
   ii. The member will receive Supprelin LA concomitantly with gender-affirming hormones.
   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.

C. Preservation of ovarian function

Authorization of 3 months may be granted for preservation of ovarian function when the member is premenopausal and undergoing chemotherapy.

D. Prevention of recurrent menstrual related attacks in acute porphyria

Authorization of 12 months may be granted for prevention of recurrent menstrual related attacks in members with acute porphyria when the requested medication is prescribed by or in consultation with a physician experienced in the management of porphyrias.

V. CONTINUATION OF THERAPY

A. Central precocious puberty (CPP)

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. Gender dysphoria

1. Authorization of 12 months may be granted for continued treatment for pubertal hormonal suppression 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 has previously reached Tanner stage 2 of puberty or greater.
   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 transition in members requesting reauthorization when all of the following criteria are met:
   i. The member has a diagnosis of gender dysphoria.
   ii. The member will receive Supprelin LA concomitantly with gender-affirming hormones.
   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.

C. All other indications

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

VI. REFERENCES

1. Supprelin LA [package insert]. Malvern, PA: Endo Pharmaceuticals Inc.; April 2022.
2. Kletter GB, Klein KO, Wong YY. A pediatrician's guide to central precocious puberty. *Clin Pediatr.* 2015;54:414-424.
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16. 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
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

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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.
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Reference number
1988-A

SPECIALTY GUIDELINE MANAGEMENT

SYNAGIS (palivizumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Synagis is indicated for the prevention of serious lower respiratory tract disease caused by respiratory syncytial virus (RSV) in pediatric patients:
- with a history of premature birth (less than or equal to 35 weeks gestational age) and who are 6 months of age or younger at the beginning of RSV season,
- with bronchopulmonary dysplasia (BPD) that required medical treatment within the previous 6 months and who are 24 months of age or younger at the beginning of RSV season,
- with hemodynamically significant congenital heart disease (CHD) and who are 24 months of age or younger at the beginning of RSV season

Limitations of Use:
The safety and efficacy of Synagis have not been established for treatment of RSV disease.

B. Compendial Uses
1. RSV prophylaxis in infants with congenital abnormalities of the airway or neuromuscular disease that compromise handling of respiratory secretions
2. RSV prophylaxis in immunocompromised pediatric patients
3. RSV prophylaxis in pediatric patients with cystic fibrosis who have evidence of chronic lung disease or nutritional compromise in the first year of life

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

II. CRITERIA FOR INITIAL APPROVAL

Authorization of up to 5 doses per RSV season may be granted for the prevention of serious lower respiratory tract disease caused by RSV when a member has any of the following diagnoses and meets the criteria pertaining to the diagnosis:
1. Prematurity
2. Chronic lung disease (CLD) of prematurity
3. Congenital heart disease (CHD) (See Appendix B)
4. Congenital airway abnormality
5. Neuromuscular condition
6. Immunocompromised children
7. Cystic fibrosis

A. Prematurity

All of the following criteria are met:
1. Member's gestational age is < 29 weeks, 0 days.
2. Member's chronological age at the start of RSV season is < 12 months.

B. CLD of prematurity

ALL of the following criteria must be met:
1. Member's gestational age is < 32 weeks, 0 days.
2. Requirement for > 21% oxygen for at least the first 28 days after birth.
3. Member meets either of the following criteria:
   i. Member's chronological age at the start of their first RSV season is < 12 months.
   ii. Member's chronological age at the start of the subsequent RSV season is < 24 months and the member continues to require medical support (e.g., chronic corticosteroids, diuretic therapy, supplemental oxygen) during the 6-month period prior to the start of the RSV season.

C. CHD

All of the following criteria are met:
1. CHD is hemodynamically significant.
2. Member meets either of the following criteria:
   i. Member's chronological age at the start of RSV season is < 12 months.
   ii. Member's chronological age at the start of RSV season is between 12 to 24 months and the member will be undergoing cardiac transplantation during the RSV season.

D. Congenital airway abnormality

All of the following criteria must be met:
1. The condition compromises handling of respiratory secretions.
2. Member's chronological age at the start of RSV season is < 12 months.

E. Neuromuscular condition

All of the following criteria must be met:
1. The condition compromises handling of respiratory secretions.
2. Member's chronological age at the start of RSV season is < 12 months.

F. Immunocompromised children

All of the following criteria must be met:
1. Member is profoundly immunocompromised during the RSV season (e.g., SCID, stem cell transplant, bone marrow transplant)
2. Member's chronological age at the start of the RSV season is <24 months

G. Cystic Fibrosis

Either of the following criteria must be met:
1. Member's chronological age at the start of the RSV season is < 12 months and the member has evidence of CLD or nutritional compromise
2. Member's chronological age at the start of RSV season is between 12 to 24 months and the member has manifestations of lung disease (e.g., hospitalizations for pulmonary exacerbations) or weight for length less than the 10th percentile

III. OTHER

For all off-season Synagis requests, authorization of 1 dose per request, up to a maximum of 5 doses per RSV season, may be granted if the RSV activity for the requested region is ≥ 10% (with rapid antigen testing) or ≥

3% (with real-time polymerase chain reaction (PCR) test) within 2 weeks of the intended dose according to the CDC National Respiratory and Enteric Virus Surveillance System (NREVSS).[3] The local health department or the CDC NREVSS will be consulted to assess the RSV activity for that region or state (http://www.cdc.gov/surveillance/nrevss/rsv/index.html). Other Specialty Guideline Management criteria apply.

CVS Caremark PBM Synagis Season will be from November 1st to March 31st. Other health plans may differ.

IV. EXCLUSIONS

Coverage will not be provided for members who have received Beyfortus (nirsevimab-alip) in the same RSV season.

V. APPENDIX

Appendix A: Recommended Use of Synagis for Prevention of RSV Infection

Recommendations from the American Academy of Pediatrics for the prevention of RSV infection with Synagis are summarized in Table below.[2] Synagis should be administered intramuscularly at a dose of 15 mg/kg once per month beginning prior to the onset of the RSV season,[1,2] which typically occurs in November.[2] Because 5 monthly doses of Synagis will provide more than 6 months of serum Synagis concentrations above the desired serum concentration for most infants, administration of more than 5 monthly doses is not recommended within the continental United States.[2]

Table. Recommended Use of Synagis for Prevention of RSV Infection

Prematurity	• Preterm infants born < 29 weeks, 0 days of gestation who are younger than 12 months at the start of the RSV season

Congenital Heart Disease	• Infants and children < 12 months of age with hemodynamically significant CHD
	• Those most likely to benefit from prophylaxis include:
	  ○ Infants with acyanotic heart disease who are receiving medication to control congestive heart failure and will require cardiac surgical procedures
	  ○ Infants with moderate to severe pulmonary hypertension
	• Infants and children < 24 months of age who undergo cardiac transplantation during the RSV season

Chronic Lung Disease of Prematurity	• For the first RSV season during the first year of life:
	Preterm infants who develop CLD of prematurity defined as:
	  ○ Gestational age < 32 weeks, 0 days AND
	  ○ Requirement for > 21% oxygen for at least the first 28 days after birth
	• For the second RSV season during the second year of life:
	Preterm infants who:
	  ○ Satisfy the above definition of CLD of prematurity AND
	  ○ Continue to require medical support* for CLD during the 6-month period prior to the start of the second RSV season

Congenital Abnormality of the Airway/ Neuromuscular Condition	• Infants who have either a significant congenital abnormality of the airway or a neuromuscular condition that compromises handling of respiratory secretions for the first year of life
Immunocompromised children	• Children younger than 24 months of age who are profoundly immunocompromised during the RSV season
Cystic Fibrosis	• For the first year of life, children with clinical evidence of CLD and/or nutritional compromise • For the second year of life, children with manifestations of severe lung disease (previous hospitalization for pulmonary exacerbation in the first year of life or abnormalities on chest radiography or chest computed tomography that persist when stable) OR weight for length less than the 10th percentile.

Abbreviations: CHD = congenital heart disease; CLD = chronic lung disease (formerly bronchopulmonary dysplasia); RSV = respiratory syncytial virus.
* Medical support includes supplemental oxygen, diuretic therapy, or chronic corticosteroid therapy.

Appendix B: Examples of Congenital Heart Anomalies*

- Atrial or ventricular septal defect
- Patent ductus arteriosus
- Coarctation of aorta
- Tetralogy of Fallot
- Pulmonary or aortic valve stenosis
- D-Transposition of great arteries
- Hypoplastic left/right ventricle
- Truncus arteriosus
- Total anomalous pulmonary venous return
- Tricuspid atresia
- Ebstein's anomaly
- Pulmonary atresia
- Single ventricle
- Double-outlet right ventricle

*Must be hemodynamically significant. See Table above for examples of infants and children who are most likely to benefit from Synagis.

VI. REFERENCES

1. Synagis [package insert]. Waltham, MA: Sobi Inc; November 2021.
2. American Academy of Pediatrics. Updated guidance for palivizumab prophylaxis among infants and young children at increased risk of hospitalization for respiratory syncytial virus infection. *Pediatrics.* 2014;134(2):415-20.
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6. American Academy of Pediatrics. Updated Guidance: Use of Palivizumab Prophylaxis to Prevent Hospitalization From Severe Respiratory Syncytial Virus Infection During the 2022-2023 RSV Season. https://www.aap.org/en/pages/2019-novel-coronavirus-covid-19-infections/clinical-guidance/interim-guidance-for-use-of-palivizumab-prophylaxis-to-prevent-hospitalization/. Updated November 17, 2022. Accessed April 28, 2023.

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)
1640-A

SPECIALTY GUIDELINE MANAGEMENT

Adcirca (tadalafil tablet)
Alyq (tadalafil tablet)
tadalafil tablets (generic)
Tadliq (tadalafil 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.

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 NYHA Functional Class II – III symptoms and etiologies of idiopathic or heritable PAH (61%) or PAH associated with connective tissue diseases (23%).

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.

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. mPAP > 20 mmHg
        b. PCWP ≤ 15 mmHg
        c. PVR ≥ 3 Wood units
    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

III. 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.
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16. 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)
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 treatment of patients with metastatic non-small cell lung cancer (NSCLC) with BRAF V600E mutation as detected by an FDA-approved test.
4. 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.
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. Papillary carcinoma
   b. Follicular carcinoma
   c. 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

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. 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 stage III cutaneous melanoma in combination with trametinib (Mekinist) following complete resection or no evidence of disease.

B. Non-Small Cell Lung Cancer (NSCLC)
Authorization of 12 months may be granted for treatment of BRAF V600E mutation-positive recurrent, 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 carcinoma
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 or metastatic anaplastic thyroid carcinoma and 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).

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 2021 National Comprehensive Cancer Network, Inc. Available at: https://www.nccn.org. Accessed November 5, 2021.
3. Micromedex Solutions [database online]. Ann Arbor, MI: Truven Health Analytics Inc. Updated periodically. www.micromedexsolutions.com [available with subscription]. Accessed November 9, 2021.
4. 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.
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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.

POLICY Document for TAFINLAR (dabrafenib)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, and overall, clinically appropriate use. This document provides specific information to both sections of the overall policy.

Section 1: Clinical Criteria

- Policy information specific to the clinical appropriateness for the medication

Section 2: Oncology Clinical Policy

- Policy information specific to regimen review per NCCN Guidelines.

Section 1: Clinical Criteria

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
   i. Anaplastic carcinoma
   ii. Papillary carcinoma
   iii. Follicular carcinoma
   iv. Hűrthle cell carcinoma
8. Hepatobiliary Cancers
   i. Gallbladder Cancer
   ii. Extrahepatic Cholangiocarcinoma
   iii. Intrahepatic Cholangiocarcinoma
9. Histiocytic Neoplasms
   i. Erdheim-Chester Disease
   ii. 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.

Section 2: Oncology Clinical Policy

Oncology Clinical Policy

Program Description

The National Comprehensive Care Network® (NCCN®) is an alliance of leading cancer centers devoted to patient care, research and education dedicated to improving the quality, effectiveness and efficiency of cancer care so patients can live better lives.[1] It is comprised of oncology experts who convene regularly to establish the best treatments for patients. NCCN develops various resources for use by stakeholders in the health care delivery system. These resources include, but are not limited to, the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®), the NCCN Drugs & Biologics Compendium (NCCN Compendium®) and the NCCN Chemotherapy Order Templates (NCCN Templates®).

NCCN templates are based on NCCN Clinical Practice Guidelines and NCCN Compendium. The NCCN Compendium lists the appropriate drugs and biologics for specific cancers using U.S. Food and Drug Administration (FDA)-approved disease indications and specific NCCN panel recommendations. Each recommendation is supported by a level of evidence category.

NCCN Categories of Evidence and Consensus
Category 1: Based on high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2A: Based on lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2B: Based on lower-level evidence, there is NCCN consensus that the intervention is appropriate.
Category 3: Based any level of evidence, there is major NCCN disagreement that the intervention is

appropriate.

Policy for Regimen Prior Authorization

A regimen prior authorization allows submission of a single prior authorization request for all oncology drugs or biologics within an NCCN template that require prior authorization.

This policy provides coverage of a regimen review when *all* of the following criteria are met:

a. Regimen prior authorization reviews, based on NCCN templates, are initiated through the provider portal: https://provider.carefirst.com/providers/home.page
b. If the prior authorization request is submitted via phone or fax, each drug or biologic will need to be submitted and reviewed as a separate prior authorization request for review with drug-specific criteria.
c. 2. The prior authorization review is requested for an oncology drug or biologic that requires prior authorization on the medical benefit.
d. The indication is for a cancer that is eligible for regimen review. Currently, the cancer types in scope for regimen review include breast, lung, colon and rectal cancer.
e. The member is eligible for regimen review.

In addition, the following criteria must be met for approval:

a. The requested regimen for the drug(s) or biologic(s) and indication is consistent with an NCCN recommendation with a level of evidence category of 1 or 2A.
b. The NCCN template must be accepted by the provider without modification.

Authorizations may be granted for 12 months.
Further review may be indicated where the above criteria are not met.

Continuation of Therapy

To submit a request for continuation of therapy, a new regimen prior authorization review must be requested. Upon template selection, the template must be modified to include the appropriate therapies being used for maintenance treatment. The regimen request will be submitted for further review.

Dosage and Administration

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

REFERENCES:

SECTION 1

1. Tafinlar [package insert]. East Hanover, NJ: Novartis Pharmaceutical Corporation; June 2022.
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SECTION 2

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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

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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

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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 Indication
Talzenna is indicated 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.

B. Compendial Uses
1. Recurrent or metastatic human epidermal growth factor receptor 2 (HER2)-negative, BRCA 1/2-germline mutated breast cancer that is hormone receptor-negative, or hormone receptor-positive disease with visceral crisis or endocrine therapy refractory.
2. Recurrent or metastatic HER2-positive BRCA1/2-germline mutated breast cancer that is hormone receptor negative, or hormone receptor positive with or without endocrine 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: BRCA mutation testing results.

III. CRITERIA FOR INITIAL APPROVAL

Breast cancer
Authorization of 12 months may be granted for treatment of locally advanced, recurrent, or metastatic breast cancer as a single agent in members with deleterious or suspected deleterious germline BRCA mutations.

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.; September 2021.

2. The NCCN Drugs & Biologics Compendium 2021 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed December 6, 2021.

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

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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

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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.

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.

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 the treatment of follicular lymphoma, documentation of an EZH2 mutation (where applicable).

III. 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. Tumor is positive for an EZH2 mutation and the member has received at least 2 prior therapies
2. The member does not have any satisfactory alternative treatment options

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.

Reference number(s)
4042-A

SPECIALTY GUIDELINE MANAGEMENT

TECARTUS (brexucabtagene autoleucel)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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. Adult patients with relapsed or refractory mantle cell lymphoma (MCL)
2. Adult patients with relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL)

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 all indications: Chart notes, medical record documentation or claims history supporting previous lines of therapy.
B. For Acute Lymphoblastic Leukemia: Testing or analysis confirming morphological disease in the bone marrow (≥ 5% blasts).

III. EXCLUSIONS

Coverage will not be provided for members with any of the following exclusions:
A. ECOG performance status greater than or equal to 3 (member is not ambulatory and not capable of all self-care, confined to bed or chair more than 50% of waking hours)
B. Inadequate and unstable kidney, liver, pulmonary or cardiac function
C. Active hepatitis B, active hepatitis C or any active uncontrolled infection
D. Active inflammatory disorder

IV. CRITERIA FOR INITIAL APPROVAL

A. Mantle Cell Lymphoma

Authorization of 3 months may be granted for treatment of mantle cell lymphoma in members 18 years of age or older when all of the following criteria are met:
1. The disease is relapsed or refractory.
2. The member has had previous treatment with both chemoimmunotherapy and a bruton tyrosine kinase inhibitor (e.g., ibrutinib).
3. The member has not received a previous treatment course of brexucabtagene autoleucel or another CD19-directed chimeric antigen receptor (CAR) T-cell therapy.

B. Adult Relapsed or Refractory B-cell precursor Acute Lymphoblastic Leukemia (ALL)

Authorization of 3 months may be granted for the treatment of B-cell precursor acute lymphoblastic leukemia (ALL) in members 18 years of age or older when all of the following criteria are met:

1. The member has not received a previous treatment course of the requested medication or another CD19-directed chimeric antigen receptor (CAR-T) therapy, or any prior CD19 directed therapy other than blinatumomab.
2. The member meets either of the following criteria:
    i. Member has Philadelphia chromosome-negative disease that is relapsed or refractory as defined as one of the following:
        a. Primary refractory disease
        b. First relapse with remission of 12 months or less
        c. Relapsed or refractory disease after at least 2 previous lines of systemic therapy
        d. Relapsed or refractory disease after allogeneic stem cell transplant (allo-SCT)
    ii. Member has Philadelphia chromosome-positive disease and meets any of the following:
        a. The member has relapsed or refractory disease despite treatment with at least 2 different tyrosine kinase inhibitors (TKIs) (e.g., bosutinib, dasatinib, imatinib, nilotinib, ponatinib)
        b. The member is intolerant to TKI therapy
3. The member has morphological disease in the bone marrow (≥5% blasts)
4. The member does not have active graft versus host disease.

V. REFERENCES

1. Tecartus [package insert]. Santa Monica, CA: Kite Pharma, Inc.; October 2021.
2. The NCCN Drugs & Biologics Compendium® © 2023 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed June 6, 2023.
3. Wang M, Munoz J, Goy A, et al. KTE-X19 CAR T-Cell Therapy in Relapsed or Refractory Mantle-Cell Lymphoma. NEJM 2020; 382:1331-1342.
4. Shah BD, Ghobadi A, Oluwole OO, et al. KTE-X19 for relapsed or refractory adult B-cell acute lymphoblastic leukaemia: phase 2 results of the single-arm, open-label, multicentre ZUMA-3 study. Lancet. 2021;398(10299):491-502.

V. REFERENCES

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2. The NCCN Drugs & Biologics Compendium® © 2022 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed January 12, 2022.

POLICY Document for TECENTRIQ (atezolizumab)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, and overall, clinically appropriate use. This document provides specific information to both sections of the overall policy.

Section 1: Site of Care
- Policy information specific to site of care (outpatient, hospital outpatient, home infusion)

Section 2: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 3: Oncology Clinical Policy
- Policy information specific to regimen review per NCCN Guidelines.

Section 1: Site of Care

CareFirst Site of Care Criteria
Administration of Intravenous Checkpoint Inhibitors
Bavencio, Imfinzi, Jemperli, Keytruda, Libtayo, Opdivo, Opdualag, Tecentriq, Yervoy and Zynyz

POLICY

I. CRITERIA FOR APPROVAL FOR ADMINISTRATION IN OUTPATIENT HOSPITAL SETTING

This policy provides coverage for administration of a checkpoint inhibitor in an outpatient hospital setting for the initial 6 months approval and up to 45 days for renewal of therapy.

This policy provides coverage for administration of a checkpoint inhibitor in an outpatient hospital setting for a longer course of treatment when ANY of the following criteria are met:

A. The member has experienced an adverse reaction that did not respond to conventional interventions (eg, acetaminophen, steroids, diphenhydramine, fluids, other pre-medications or slowing of infusion rate) or a severe adverse event (anaphylaxis, anaphylactoid reactions, myocardial infarction, thromboembolism, or seizures) during or immediately after an infusion or has experienced severe toxicity requiring continuous monitoring (e.g. Grade 2-4 bullous dermatitis, transaminitis, pneumonitis, Stevens-Johnson syndrome, acute pancreatitis, primary adrenal insufficiency aseptic meningitis, encephalitis, transverse myelitis, myocarditis, pericarditis, arrhythmias, impaired ventricular function, conduction abnormalities).
B. The member is medically unstable (eg respiratory, cardiovascular, or renal conditions).
C. The member has severe venous access issues that require the use of a special interventions only available in the outpatient hospital setting.
D. The member has significant behavioral issues and/or physical or cognitive impairment that would impact the safety of the infusion therapy AND the patient does not have access to a caregiver.
E. The member is receiving provider administered combination chemotherapy.
F. The member is less than 14 years of age.

For situations where administration of a checkpoint inhibitor does not meet the criteria for outpatient hospital infusion, coverage for a checkpoint inhibitor is provided when administered in alternative sites such as physician office, home infusion or ambulatory care.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the site of care prior authorization review (where applicable):

A. Medical records supporting the member has experienced an adverse reaction that did not respond to conventional interventions or a severe adverse event during or immediately after an infusion or a severe toxicity requiring continuous monitoring
B. Medical records supporting the member is medically unstable
C. Medical records supporting the member has severe venous access issues that require specialized interventions only available in the outpatient hospital setting
D. Medical records supporting the member has behavioral issues and/or physical or cognitive impairment and no access to a caregiver
E. Medical records supporting the member is receiving provider administered combination therapy.

Section 2: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

TECENTRIQ (atezolizumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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)
   a. Tecentriq, as a single-agent, is indicated as adjuvant treatment following resection and platinum-based chemotherapy for adult patients with stage II to IIIA non-small cell lung cancer (NSCLC) whose tumors have PD-L1 expression on ≥ 1% of tumor cells, as determined by an FDA-approved test.
   b. Tecentriq, as a single-agent, is indicated for the first line treatment of adult patients with metastatic NSCLC whose tumors have high PD-L1 expression (PD-L1 stained ≥ 50% of tumor cells [TC ≥ 50%] or PD-L1 stained tumor-infiltrating immune cells [IC] covering ≥ 10% of the tumor area [IC ≥ 10%]), as determined by an FDA-approved test, with no EGFR or ALK genomic tumor aberrations.
   c. Tecentriq, in combination with bevacizumab, paclitaxel, and carboplatin, is indicated for the first-line treatment, of adult patients with metastatic non-squamous NSCLC with no EGFR or ALK genomic tumor aberrations.
   d. Tecentriq, in combination with paclitaxel protein-bound and carboplatin, is indicated for the first-line treatment of adult patients with metastatic non-squamous NSCLC with no EGFR or ALK genomic tumor aberrations.
   e. Tecentriq as a single agent is indicated for the treatment of adult patients with metastatic NSCLC who have disease progression during or following platinum-containing chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for NSCLC harboring these aberrations prior to receiving Tecentriq.

2. Small cell lung cancer (SCLC)
   Tecentriq, in combination with carboplatin and etoposide, is indicated for the first-line treatment of adult patients with extensive-stage small cell lung cancer (ES-SCLC).

3. Hepatocellular Carcinoma (HCC)

Tecentriq, in combination with bevacizumab, is indicated for the treatment of patients with unresectable or metastatic HCC who have not received prior systemic therapy.

4. Melanoma
   Tecentriq, in combination with cobimetinib and vemurafenib, is indicated for the treatment of patients with BRAF V600 mutation-positive unresectable or metastatic melanoma.

5. Alveolar Soft Part Sarcoma (ASPS)
   Tecentriq, as a single agent, is indicated for the treatment of adult and pediatric patients age 2 years and older with unresectable or metastatic ASPS.

B. Compendial Uses
   1. Urothelial carcinoma
      a. Bladder cancer
      b. Primary carcinoma of the urethra
      c. Upper genitourinary tract tumors
      d. Urothelial carcinoma of the prostate
   2. Non-small cell lung cancer (NSCLC)
   3. Malignant Peritoneal Mesothelioma, Pericardial Mesothelioma, Tunica Vaginalis Testis Mesothelioma
   4. Cervical Cancer

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. Test results confirming PD-L1 tumor expression (where applicable)
B. Test results confirming tumor is positive for BRAF V600 mutation (where applicable)
C. Test results confirming the presence of EGFR exon 19 deletions or L858R mutations or ALK rearrangements (where applicable)

III. EXCLUSIONS

Coverage will not be provided for members who have experienced disease progression while on PD-1 or PD-L1 inhibitor therapy

IV. CRITERIA FOR INITIAL APPROVAL

A. Urothelial Carcinoma - Bladder Cancer
Authorization of 6 months may be granted for treatment as a single agent for bladder cancer when the requested medication is used as first line therapy in cisplatin ineligible members whose tumors express PD-L1 (defined as PD-L1 stained tumor-infiltrating immune cells [IC] covering greater than or equal to 5% of the tumor area) or in members who are not eligible for any platinum containing chemotherapy regardless of PD-L1 expression for any of the following:
1. Stage II or Stage IIIa disease if tumor is present following reassessment of tumor status 2-3 months after primary treatment with either concurrent chemoradiotherapy, radiotherapy alone, or TURBT
2. Stage IIIb disease as downstaging systemic therapy or following partial response or progression after primary treatment with concurrent chemoradiotherapy
3. Locally advanced or metastatic disease
4. Metastatic or local recurrence post-cystectomy

5. Muscle invasive local recurrence or persistent disease in a preserved bladder

B. Urothelial Carcinoma - Primary Carcinoma of the Urethra
Authorization of 6 months may be granted for treatment as a single agent for primary carcinoma of the urethra when the requested medication is used as first line therapy for recurrent, locally advanced or metastatic disease in cisplatin ineligible members whose tumors express PD-L1 (defined as PD-L1 stained tumor-infiltrating immune cells [IC] covering greater than or equal to 5% of the tumor area) or in members who are not eligible for any platinum containing chemotherapy regardless of PD-L1 expression.

C. Urothelial Carcinoma - Upper Genitourinary Tract Tumors or Urothelial Carcinoma of the Prostate
Authorization of 6 months may be granted for treatment as a single agent for upper genitourinary tract tumors or urothelial carcinoma of the prostate when the requested medication is used as first line therapy for locally advanced or metastatic disease in cisplatin ineligible members whose tumors express PD-L1 (defined as PD-L1 stained tumor-infiltrating immune cells [IC] covering greater than or equal to 5% of the tumor area) or in members who are not eligible for any platinum containing chemotherapy regardless of PD-L1 expression.

D. Non-Small Cell Lung Cancer (NSCLC)
1. Authorization of 6 months may be granted for treatment of recurrent, advanced or metastatic non-small cell lung cancer when there are no EGFR exon 19 deletions or L858R mutations or ALK rearrangements (unless testing is not feasible due to insufficient tissue) and any of the following criteria are met:
   a. The requested medication will be used as continued maintenance therapy as a single agent or in combination with bevacizumab.
   b. The requested medication will be used as first line or subsequent therapy in combination with chemotherapy.
   c. The requested medication will be used as first line therapy for PD-L1 expression positive (≥50%) tumors as a single agent.
2. Authorization of 6 months may be granted for treatment of recurrent, advanced or metastatic non-small cell lung cancer as single agent subsequent therapy.
3. Authorization of 6 months may be granted for treatment of stage II to IIIB non-small cell lung cancer that is PD-L1 positive as single agent adjuvant therapy.

E. Small Cell Lung Cancer (SCLC)
Authorization of 6 months may be granted for treatment of small cell lung cancer when the requested medication will be used as initial treatment in combination with etoposide and carboplatin (followed by single agent maintenance) for extensive-stage disease.

F. Hepatocellular Carcinoma (HCC)
Authorization of 6 months may be granted for treatment of unresectable or metastatic HCC when the requested medication will be used as initial treatment in combination with bevacizumab.

G. Melanoma
Authorization of 6 months may be granted for the treatment of BRAF V600 mutation-positive unresectable or metastatic melanoma when the requested medication will be used in combination with cobimetinib (Cotellic) and vemurafenib (Zelboraf).

H. Malignant Peritoneal Mesothelioma, Pericardial Mesothelioma, Tunica Vaginalis Testis Mesothelioma
Authorization of 6 months may be granted for the subsequent treatment of malignant peritoneal mesothelioma, pericardial mesothelioma, or tunica vaginalis testis mesothelioma when used in combination with bevacizumab.

I. Alveolar Soft Part Sarcoma (ASPS)
Authorization of 6 months may be granted for the treatment of unresectable or metastatic alveolar soft part

sarcoma when used as a single agent.

J. Cervical Cancer
Authorization of 6 months may be granted for the treatment of persistent, recurrent or metastatic small cell neuroendocrine carcinoma of the cervix (NECC) when used in combination with etoposide and either cisplatin or carboplatin.

V. **CONTINUATION OF THERAPY**

A. Adjuvant treatment of Non-Small Cell Lung Cancer (NSCLC)
Authorization of 6 months may be granted (up to 12 months total) for continued treatment in members requesting reauthorization of adjuvant therapy of non-small cell lung cancer who have not experienced disease recurrence or an unacceptable toxicity.

B. All other indications
Authorization of 6 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.

Section 3: Oncology Clinical Policy

Oncology Clinical Policy

Program Description

The National Comprehensive Care Network® (NCCN®) is an alliance of leading cancer centers devoted to patient care, research and education dedicated to improving the quality, effectiveness and efficiency of cancer care so patients can live better lives.[1] It is comprised of oncology experts who convene regularly to establish the best treatments for patients. NCCN develops various resources for use by stakeholders in the health care delivery system. These resources include, but are not limited to, the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®), the NCCN Drugs & Biologics Compendium (NCCN Compendium®) and the NCCN Chemotherapy Order Templates (NCCN Templates®).

NCCN templates are based on NCCN Clinical Practice Guidelines and NCCN Compendium. The NCCN Compendium lists the appropriate drugs and biologics for specific cancers using U.S. Food and Drug Administration (FDA)-approved disease indications and specific NCCN panel recommendations. Each recommendation is supported by a level of evidence category.

NCCN Categories of Evidence and Consensus[2]

a. Category 1: Based on high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
b. Category 2A: Based on lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
c. Category 2B: Based on lower-level evidence, there is NCCN consensus that the intervention is appropriate.
d. Category 3: Based any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

Policy for Regimen Prior Authorization

A regimen prior authorization allows submission of a single prior authorization request for all oncology drugs or biologics within an NCCN template that require prior authorization.

This policy provides coverage of a regimen review when *all* of the following criteria are met:

a. Regimen prior authorization reviews, based on NCCN templates, are initiated through the provider portal: https://provider.carefirst.com/providers/home.page
b. If the prior authorization request is submitted via phone or fax, each drug or biologic will need to be submitted and reviewed as a separate prior authorization request for review with drug-specific criteria.
c. The prior authorization review is requested for an oncology drug or biologic that requires prior authorization on the medical benefit.
d. The indication is for a cancer that is eligible for regimen review. Currently, the cancer types in scope for regimen review include breast, lung, colon and rectal cancer.
e. The member is eligible for regimen review.

In addition, the following criteria must be met for approval:

a. The requested regimen for the drug(s) or biologic(s) and indication is consistent with an NCCN recommendation with a level of evidence category of 1 or 2A.
b. The NCCN template must be accepted by the provider without modification.

Authorizations may be granted for 12 months.
Further review may be indicated where the above criteria are not met.

Continuation of Therapy

To submit a request for continuation of therapy, a new regimen prior authorization review must be requested. Upon template selection, the template must be modified to include the appropriate therapies being used for maintenance treatment. The regimen request will be submitted for further review.

Dosage and Administration

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

REFERENCES:

SECTION 1

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2. Bavencio [package insert]. Rockland, MA: EMD Serono, Inc; July 2020.
3. Imfinzi [prescribing information]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; November 2022.
4. Jemperli [prescribing information]. Philadelphia, PA: GlaxoSmithKline LLC; February 2023.
5. Keytruda [prescribing information]. Rahway, NJ: Merck Sharp & Dome LLC.; April 2023.
6. Libtayo [prescribing information]. Tarrytown, NY: Regeneron Pharmaceuticals, Inc.; April 2023.
7. Tecentriq [package insert]. South San Francisco, CA: Genentech, Inc.; December 2022.
8. Yervoy [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; February 2023.
9. Opdualag [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; March 2022.
10. Zynyz [package insert]. Wilmington, DE: Incyte Corporation; March 2023.

SECTION 2

1. Tecentriq [package insert]. South San Francisco, CA: Genentech, Inc.; December 2022.
2. The NCCN Drugs & Biologics Compendium® © 2023 National Comprehensive Cancer Network, Inc. Available at: https://www.nccn.org. Accessed January 25, 2023.

SECTION 3

1. National Comprehensive Cancer Network. About NCCN website. https://www.nccn.org/about/default.aspx, accessed September 16, 2019.
2. National Comprehensive Cancer Network. NCCN Categories of Evidence and Consensus website. https://www.nccn.org/professionals/physician_gls/categories_of_consensus.aspx, accessed September 16, 2019.
3. National Comprehensive Cancer Network. NCCN Guidelines website. http://www.nccn.org/professionals/physician_gls/f_guidelines.asp, accessed September 16, 2019. *(Note: An account may be required.)*
4. National Comprehensive Cancer Network. NCCN Drugs and Biologics Compendium® website. http://www.nccn.org/professionals/drug_compendium/content/contents.asp, accessed September 16, 2019. *(Note: A subscription may be required.)*
5. National Comprehensive Cancer Network. NCCN Chemotherapy Order Templates (NCCN Templates) website. https://www.nccn.org/professionals/OrderTemplates/Default.aspx, accessed September 16, 2019. *(Note: A subscription may be required.)*

POLICY Document for TEGSEDI (inotersen)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, and overall, clinically appropriate use. This document provides specific information to both sections of the overall policy.

Section 1: Preferred Product
- Policy information specific to preferred medications

Section 2: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 1: Preferred Product

EXCEPTIONS CRITERIA

hATTR DISORDERS

PREFERRED PRODUCT: ONPATTRO

POLICY
This policy informs prescribers of preferred products and provides an exception process for targeted products through prior authorization.

I. PLAN DESIGN SUMMARY

This program applies to the products for the treatment of polyneuropathy of hereditary transthyretin-mediated amyloidosis specified in this policy. Coverage for the targeted product is provided based on clinical circumstances that would exclude the use of the preferred product and may be based on previous use of a product. The coverage review process will ascertain situations where a clinical exception can be made. This program applies to members who are new to treatment with a targeted product for the first time.

Each referral is reviewed based on all utilization management (UM) programs implemented for the client.

Table. Polyneuropathy of hereditary transthyretin-mediated (hATTR) amyloidosis Products

	Product(s)
Preferred*	• **Onpattro** (patisiran) injection
Targeted	• **Amvuttra** (vutrisiran) injection • **Tegsedi** (inotersen) injection

*: Medications considered formulary or preferred on your plan may still require a clinical prior authorization review.

II. EXCEPTION CRITERIA

This program applies to members requesting treatment for an indication that is FDA-approved for the preferred product.

Coverage for the targeted product is provided when either of the following criteria is met:

A. Member is currently receiving treatment with the targeted product, excluding when the requested targeted product is obtained as samples or via manufacturer's patient assistance programs.
B. Member has a documented inadequate response or intolerable adverse event with the preferred product.

CVS/caremark

Section 2: Clinical Criteria

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.

CVS/caremark

REFERENCES:

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1. Onpattro [package insert]. Cambridge, MA: Alnylam Pharmaceuticals, Inc.; January 2023.
2. Tegsedi [package insert]. Waltham, MA: Sobi Inc; June 2022.
3. Amvuttra [package insert]. Cambridge, MA: Alnylam Pharmaceuticals, Inc.; June 2022.

SECTION 2

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.
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POLICY Document for TECENTRIQ (atezolizumab)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, and overall, clinically appropriate use. This document provides specific information to both sections of the overall policy.

Section 1: Site of Care
- Policy information specific to site of care (outpatient, hospital outpatient, home infusion)

Section 2: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 3: Oncology Clinical Policy
- Policy information specific to regimen review per NCCN Guidelines.

Section 1: Site of Care

CareFirst Site of Care Criteria
Administration of Intravenous Checkpoint Inhibitors

Bavencio, Imfinzi, Jemperli, Keytruda, Libtayo, Opdivo, Opdualag, Tecentriq, and Yervoy

POLICY

I. CRITERIA FOR APPROVAL FOR ADMINISTRATION IN OUTPATIENT HOSPITAL SETTING

This policy provides coverage for administration of a checkpoint inhibitor in an outpatient hospital setting for the initial 6 months approval and up to 45 days for renewal of therapy.

This policy provides coverage for administration of a checkpoint inhibitor in an outpatient hospital setting for a longer course of treatment when ANY of the following criteria are met:

A. The member has experienced an adverse reaction that did not respond to conventional interventions (eg, acetaminophen, steroids, diphenhydramine, fluids, other pre-medications or slowing of infusion rate) or a severe adverse event (anaphylaxis, anaphylactoid reactions, myocardial infarction, thromboembolism, or seizures) during or immediately after an infusion or has experienced severe toxicity requiring continuous monitoring (e.g. Grade 2-4 bullous dermatitis, transaminitis, pneumonitis, Stevens-Johnson syndrome, acute pancreatitis, primary adrenal insufficiency aseptic meningitis, encephalitis, transverse myelitis, myocarditis, pericarditis, arrhythmias, impaired ventricular function, conduction abnormalities).
B. The member is medically unstable (eg respiratory, cardiovascular, or renal conditions).
C. The member has severe venous access issues that require the use of a special interventions only available in the outpatient hospital setting.
D. The member has significant behavioral issues and/or physical or cognitive impairment that would impact the safety of the infusion therapy AND the patient does not have access to a caregiver.
E. The member is receiving provider administered combination chemotherapy.
F. The member is less than 14 years of age.

For situations where administration of a checkpoint inhibitor does not meet the criteria for outpatient hospital infusion, coverage for a checkpoint inhibitor is provided when administered in alternative sites such as physician office, home infusion or ambulatory care.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the site of care prior authorization review (where applicable):

A. Medical records supporting the member has experienced an adverse reaction that did not respond to conventional interventions or a severe adverse event during or immediately after an infusion or a severe toxicity requiring continuous monitoring
B. Medical records supporting the member is medically unstable
C. Medical records supporting the member has severe venous access issues that require specialized interventions only available in the outpatient hospital setting
D. Medical records supporting the member has behavioral issues and/or physical or cognitive impairment and no access to a caregiver
E. Medical records supporting the member is receiving provider administered combination therapy.

Section 2: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

TECENTRIQ (atezolizumab)

POLICY

III. INDICATIONS

The indications below including FDA-approved indications and compendial 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)
   a. Tecentriq, as a single-agent, is indicated as adjuvant treatment following resection and platinum-based chemotherapy for adult patients with stage II to IIIA non-small cell lung cancer (NSCLC) whose tumors have PD-L1 expression on ≥ 1% of tumor cells, as determined by an FDA-approved test.
   b. Tecentriq, as a single-agent, is indicated for the first line treatment of adult patients with metastatic NSCLC whose tumors have high PD-L1 expression (PD-L1 stained ≥ 50% of tumor cells [TC ≥ 50%] or PD-L1 stained tumor-infiltrating immune cells [IC] covering ≥ 10% of the tumor area [IC ≥ 10%]), as determined by an FDA-approved test, with no EGFR or ALK genomic tumor aberrations.
   c. Tecentriq, in combination with bevacizumab, paclitaxel, and carboplatin, is indicated for the first-line treatment, of adult patients with metastatic non-squamous NSCLC with no EGFR or ALK genomic tumor aberrations.
   d. Tecentriq, in combination with paclitaxel protein-bound and carboplatin, is indicated for the first-line treatment of adult patients with metastatic non-squamous NSCLC with no EGFR or ALK genomic tumor aberrations.
   e. Tecentriq as a single agent is indicated for the treatment of adult patients with metastatic NSCLC who have disease progression during or following platinum-containing chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for NSCLC harboring these aberrations prior to receiving Tecentriq.

2. Small cell lung cancer (SCLC)
   Tecentriq, in combination with carboplatin and etoposide, is indicated for the first-line treatment of adult patients with extensive-stage small cell lung cancer (ES-SCLC).

3. Hepatocellular Carcinoma (HCC)
   Tecentriq, in combination with bevacizumab, is indicated for the treatment of patients with unresectable or metastatic HCC who have not received prior systemic therapy.

4. Melanoma
   Tecentriq, in combination with cobimetinib and vemurafenib, is indicated for the treatment of patients with BRAF V600 mutation-positive unresectable or metastatic melanoma.

5. Alveolar Soft Part Sarcoma (ASPS)
   Tecentriq, as a single agent, is indicated for the treatment of adult and pediatric patients age 2 years and older with unresectable or metastatic ASPS.

B. Compendial Uses
   1. Urothelial carcinoma
      a. Bladder cancer
      b. Primary carcinoma of the urethra
      c. Upper genitourinary tract tumors
      d. Urothelial carcinoma of the prostate
   2. Non-small cell lung cancer (NSCLC)
   3. Malignant Peritoneal Mesothelioma, Pericardial Mesothelioma, Tunica Vaginalis Testis Mesothelioma
   4. Cervical Cancer

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

IV. REQUIRED DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
A. Test results confirming PD-L1 tumor expression (where applicable)
B. Test results confirming tumor is positive for BRAF V600 mutation (where applicable)
C. Test results confirming the presence of EGFR exon 19 deletions or L858R mutations or ALK rearrangements (where applicable)

V. EXCLUSIONS

Coverage will not be provided for members who have experienced disease progression while on PD-1 or PD-L1 inhibitor therapy

VI. CRITERIA FOR INITIAL APPROVAL

A. Urothelial Carcinoma - Bladder Cancer
Authorization of 6 months may be granted for treatment as a single agent for bladder cancer when the requested medication is used as first line therapy in cisplatin ineligible members whose tumors express PD-L1 (defined as PD-L1 stained tumor-infiltrating immune cells [IC] covering greater than or equal to 5% of the tumor area) or in members who are not eligible for any platinum containing chemotherapy regardless of PD-L1 expression for any of the following:
1. Stage II or Stage IIIa disease if tumor is present following reassessment of tumor status 2-3 months after primary treatment with either concurrent chemoradiotherapy, radiotherapy alone, or TURBT
2. Stage IIIb disease as downstaging systemic therapy or following partial response or progression after primary treatment with concurrent chemoradiotherapy

3. Locally advanced or metastatic disease
4. Metastatic or local recurrence post-cystectomy
5. Muscle invasive local recurrence or persistent disease in a preserved bladder

B. Urothelial Carcinoma - Primary Carcinoma of the Urethra
Authorization of 6 months may be granted for treatment as a single agent for primary carcinoma of the urethra when the requested medication is used as first line therapy for recurrent, locally advanced or metastatic disease in cisplatin ineligible members whose tumors express PD-L1 (defined as PD-L1 stained tumor-infiltrating immune cells [IC] covering greater than or equal to 5% of the tumor area) or in members who are not eligible for any platinum containing chemotherapy regardless of PD-L1 expression.

C. Urothelial Carcinoma - Upper Genitourinary Tract Tumors or Urothelial Carcinoma of the Prostate
Authorization of 6 months may be granted for treatment as a single agent for upper genitourinary tract tumors or urothelial carcinoma of the prostate when the requested medication is used as first line therapy for locally advanced or metastatic disease in cisplatin ineligible members whose tumors express PD-L1 (defined as PD-L1 stained tumor-infiltrating immune cells [IC] covering greater than or equal to 5% of the tumor area) or in members who are not eligible for any platinum containing chemotherapy regardless of PD-L1 expression.

D. Non-Small Cell Lung Cancer (NSCLC)
1. Authorization of 6 months may be granted for treatment of recurrent, advanced or metastatic non-small cell lung cancer when there are no EGFR exon 19 deletions or L858R mutations or ALK rearrangements (unless testing is not feasible due to insufficient tissue) and any of the following criteria are met:
   a. The requested medication will be used as continued maintenance therapy as a single agent or in combination with bevacizumab.
   b. The requested medication will be used as first line or subsequent therapy in combination with chemotherapy.
   c. The requested medication will be used as first line therapy for PD-L1 expression positive (≥50%) tumors as a single agent.
2. Authorization of 6 months may be granted for treatment of recurrent, advanced or metastatic non-small cell lung cancer as single agent subsequent therapy.
3. Authorization of 6 months may be granted for treatment of stage II to IIIB non-small cell lung cancer that is PD-L1 positive as single agent adjuvant therapy.

E. Small Cell Lung Cancer (SCLC)
Authorization of 6 months may be granted for treatment of small cell lung cancer when the requested medication will be used as initial treatment in combination with etoposide and carboplatin (followed by single agent maintenance) for extensive-stage disease.

F. Hepatocellular Carcinoma (HCC)
Authorization of 6 months may be granted for treatment of unresectable or metastatic HCC when the requested medication will be used as initial treatment in combination with bevacizumab.

G. Melanoma
Authorization of 6 months may be granted for the treatment of BRAF V600 mutation-positive unresectable or metastatic melanoma when the requested medication will be used in combination with cobimetinib (Cotellic) and vemurafenib (Zelboraf).

H. Malignant Peritoneal Mesothelioma, Pericardial Mesothelioma, Tunica Vaginalis Testis Mesothelioma
Authorization of 6 months may be granted for the subsequent treatment of malignant peritoneal mesothelioma, pericardial mesothelioma, or tunica vaginalis testis mesothelioma when used in combination with bevacizumab.

I. Alveolar Soft Part Sarcoma (ASPS)
Authorization of 6 months may be granted for the treatment of unresectable or metastatic alveolar soft part sarcoma when used as a single agent.

J. Cervical Cancer
Authorization of 6 months may be granted for the treatment of persistent, recurrent or metastatic small cell neuroendocrine carcinoma of the cervix (NECC) when used in combination with etoposide and either cisplatin or carboplatin.

VII. **CONTINUATION OF THERAPY**

A. Adjuvant treatment of Non-Small Cell Lung Cancer (NSCLC)
Authorization of 6 months may be granted (up to 12 months total) for continued treatment in members requesting reauthorization of adjuvant therapy of non-small cell lung cancer who have not experienced disease recurrence or an unacceptable toxicity.

B. All other indications
Authorization of 6 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.

Section 3: Oncology Clinical Policy

Oncology Clinical Policy

Program Description

The National Comprehensive Care Network® (NCCN®) is an alliance of leading cancer centers devoted to patient care, research and education dedicated to improving the quality, effectiveness and efficiency of cancer care so patients can live better lives.[1] It is comprised of oncology experts who convene regularly to establish the best treatments for patients. NCCN develops various resources for use by stakeholders in the health care delivery system. These resources include, but are not limited to, the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®), the NCCN Drugs & Biologics Compendium (NCCN Compendium®) and the NCCN Chemotherapy Order Templates (NCCN Templates®).

NCCN templates are based on NCCN Clinical Practice Guidelines and NCCN Compendium. The NCCN Compendium lists the appropriate drugs and biologics for specific cancers using U.S. Food and Drug Administration (FDA)-approved disease indications and specific NCCN panel recommendations. Each recommendation is supported by a level of evidence category.

NCCN Categories of Evidence and Consensus[2]

a. Category 1: Based on high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
b. Category 2A: Based on lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
c. Category 2B: Based on lower-level evidence, there is NCCN consensus that the intervention is appropriate.
d. Category 3: Based any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

Policy for Regimen Prior Authorization

A regimen prior authorization allows submission of a single prior authorization request for all oncology drugs or

biologics within an NCCN template that require prior authorization.

This policy provides coverage of a regimen review when *all* of the following criteria are met:

a. Regimen prior authorization reviews, based on NCCN templates, are initiated through the provider portal: https://provider.carefirst.com/providers/home.page
b. If the prior authorization request is submitted via phone or fax, each drug or biologic will need to be submitted and reviewed as a separate prior authorization request for review with drug-specific criteria.
c. The prior authorization review is requested for an oncology drug or biologic that requires prior authorization on the medical benefit.
d. The indication is for a cancer that is eligible for regimen review. Currently, the cancer types in scope for regimen review include breast, lung, colon and rectal cancer.
e. The member is eligible for regimen review.

In addition, the following criteria must be met for approval:

a. The requested regimen for the drug(s) or biologic(s) and indication is consistent with an NCCN recommendation with a level of evidence category of 1 or 2A.
b. The NCCN template must be accepted by the provider without modification.

Authorizations may be granted for 12 months.
Further review may be indicated where the above criteria are not met.

Continuation of Therapy

To submit a request for continuation of therapy, a new regimen prior authorization review must be requested. Upon template selection, the template must be modified to include the appropriate therapies being used for maintenance treatment. The regimen request will be submitted for further review.

Dosage and Administration

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

REFERENCES:

SECTION 1

1. Opdivo [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; July 2022.
2. Bavencio [package insert]. Rockland, MA: EMD Serono, Inc; July 2020.
3. Imfinzi [prescribing information]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; October 2022.
4. Jemperli [prescribing information]. Philadelphia, PA: GlaxoSmithKline LLC; April 2022.
5. Keytruda [prescribing information]. Whitehouse Station, NJ: Merck & Co., Inc.; August 2022.
6. Libtayo [prescribing information]. Tarrytown, NY: Regeneron Pharmaceuticals, Inc.; November 2022.
7. Tecentriq [package insert]. South San Francisco, CA: Genentech, Inc.; January 2022.
8. Yervoy [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; May 2022.
9. Opdualag [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; March 2022

SECTION 2

1. Tecentriq [package insert]. South San Francisco, CA: Genentech, Inc.; December 2022.
2. The NCCN Drugs & Biologics Compendium® © 2023 National Comprehensive Cancer Network, Inc. Available at: https://www.nccn.org. Accessed January 25, 2023.

SECTION 3

1. National Comprehensive Cancer Network. About NCCN website. https://www.nccn.org/about/default.aspx, accessed September 16, 2019.
2. National Comprehensive Cancer Network. NCCN Categories of Evidence and Consensus website. https://www.nccn.org/professionals/physician_gls/categories_of_consensus.aspx, accessed September 16, 2019.
3. National Comprehensive Cancer Network. NCCN Guidelines website. http://www.nccn.org/professionals/physician_gls/f_guidelines.asp, accessed September 16, 2019. *(Note: An account may be required.)*
4. National Comprehensive Cancer Network. NCCN Drugs and Biologics Compendium® website. http://www.nccn.org/professionals/drug_compendium/content/contents.asp, accessed September 16, 2019. *(Note: A subscription may be required.)*
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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.

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: Documentation of score of items 1 to 7 of the Abnormal Involuntary Movement Scale (AIMS) for tardive dyskinesia

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 3, 2022.
3. AHFS Drug Information. http://online.lexi.com/lco. Accessed March 3, 2022.
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]. Westin, FL: Apotex Corp.; September 2018.
8. 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)
2368-A

SPECIALTY GUIDELINE MANAGEMENT

THALOMID (thalidomide)

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. Thalomid in combination with dexamethasone is indicated for the treatment of patients with newly diagnosed multiple myeloma.
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: not indicated as monotherapy for ENL treatment in the presence of moderate to severe neuritis

B. Compendial Uses
1. Myelofibrosis-related anemia
2. Multicentric Castleman's disease
3. AIDS-related aphthous stomatitis
4. Kaposi's sarcoma
5. Chronic graft-versus-host disease
6. Crohn's disease
7. 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-related Anemia
Authorization of 12 months may be granted for treatment of myelofibrosis-related 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 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 erythropoietic stimulating agents

C. Erythema Nodosum Leprosum
Authorization of 12 months may be granted for treatment of erythema nodosum leprosum.

D. Crohn's Disease
Authorization of 12 months may be granted for treatment of Crohn's disease.

E. Kaposi's Sarcoma
Authorization of 12 months may be granted for treatment of Kaposi's 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's Disease
Authorization of 12 months may be granted for treatment of multicentric Castleman's disease.

H. AIDS-related Aphthous Stomatitis
Authorization of 12 months may be granted for treatment of AIDS-related aphthous stomatitis.

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's Disease, Histiocytic Neoplasms, and Kaposi's sarcoma
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.

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's disease, histiocytic neoplasms, or Kaposi's sarcoma, who have improvement in symptoms and no unacceptable toxicity.

IV. REFERENCES

1. Thalomid [package insert]. Summit, NJ: Celgene Corporation; February 2021.
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3. The NCCN Drugs & Biologics Compendium® © 2021 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed October 5, 2021.
4. DRUGDEX® System (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. Available at: http://www.micromedexsolutions.com. Accessed October 5, 2021.

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.
2. The NCCN Drugs & Biologics Compendium® © 2022 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed May 26, 2022.

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

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3. TOBI Podhaler [package insert]. Morgantown, WV: Mylan Specialty L.P.; October 2020.

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POLICY Document for TORISEL (temsirolimus)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, and overall, clinically appropriate use. This document provides specific information to both sections of the overall policy.

Section 1: Clinical Criteria

- Policy information specific to the clinical appropriateness for the medication

Section 2: Oncology Clinical Policy

- Policy information specific to regimen review per NCCN Guidelines.

Section 1: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

TORISEL (temsirolimus)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Advanced renal cell carcinoma (RCC)

B. Compendial Uses
1. Relapsed or stage IV renal cell carcinoma
2. Endometrial carcinoma
3. Soft tissue sarcoma subtypes:
   a. Perivascular epithelioid cell tumors (PEComa)
   b. Rhabdomyosarcoma
   c. Angiomyolipoma
   d. Lymphangioleiomyomatosis
5. Mantle cell lymphoma (MCL)
6. Uterine Sarcoma

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 as a single agent for treatment of advanced, relapsed, or stage IV renal cell carcinoma.

B. Endometrial Carcinoma

Authorization of 12 months may be granted as a single agent for subsequent treatment of recurrent endometrial carcinoma.

C. Soft Tissue Sarcoma

1. Authorization of 12 months may be granted for treatment of any of the following subtypes of soft tissue sarcoma as single agent therapy: locally advanced unresectable or metastatic perivascular epithelioid cell tumor (PEComa), recurrent angiomyolipoma, or recurrent lymphangioleiomyomatosis.
2. Authorization of 12 months may be granted for treatment of rhabdomyosarcoma in combination with cyclophosphamide and vinorelbine.

D. Mantle Cell Lymphoma

Authorization of 12 months may be granted for treatment of relapsed or refractory mantle cell lymphoma.

E. Uterine Sarcoma

Authorization of 12 months may be granted as a single agent for subsequent treatment of advanced, recurrent/metastatic or inoperable PEComa.

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.

Section 2: Oncology Clinical Policy

PROGRAM DESCRIPTION

The National Comprehensive Care Network® (NCCN®) is an alliance of leading cancer centers devoted to patient care, research and education dedicated to improving the quality, effectiveness, and efficiency of cancer care so patients can live better lives.[1] It is comprised of oncology experts who convene regularly to establish the best treatments for patients. NCCN develops various resources for use by stakeholders in the health care delivery system. These resources include, but are not limited to, the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®), the NCCN Drugs & Biologics Compendium (NCCN Compendium®) and the NCCN Chemotherapy Order Templates (NCCN Templates®).

NCCN Templates® are based on NCCN Guidelines® and NCCN Compendium®. The NCCN Compendium lists the appropriate drugs and biologics as treatment options for specific cancers using U.S. Food and Drug Administration (FDA)-approved disease indications and specific NCCN panel recommendations. Each recommendation is supported by a level of evidence category.

NCCN Categories of Evidence and Consensus[2]

- Category 1: Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
- Category 2A: Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
- Category 2B: Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.
- Category 3: Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

POLICY

Policy for Regimen Prior Authorization
A regimen prior authorization allows submission of a single prior authorization request for all oncology drugs or biologics within an NCCN template that require prior authorization.

PROCEDURE

This policy provides coverage of a regimen review when all of the following criteria are met:
1. Regimen prior authorization reviews, based on NCCN templates, are initiated through the provider portal.
    - If the prior authorization request is submitted via phone or fax, each drug or biologic will need to be submitted and reviewed as a separate prior authorization request for review with drug-specific criteria.
2. The prior authorization review is requested for an oncology drug or biologic.
3. The member is eligible for regimen review.
4. The indication is for a cancer that is eligible for regimen review. Currently, the cancer types in scope for regimen review include the following:
    - Ampullary Adenocarcinoma
    - Anal Carcinoma
    - B-Cell Lymphomas
    - Basal Cell Skin Cancer
    - Biliary Tract Cancers
    - Bone Cancer
    - Breast Cancer
    - Bladder Cancer
    - Central Nervous System Cancers
    - Cervical Cancer
    - Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma
    - Chronic Myeloid leukemia
    - Colon Cancer
    - Dermatofibrosarcoma Protuberans
    - Esophageal Cancer
    - Gastric Cancer
    - Gastrointestinal Stromal Tumors
    - Gestational Trophoblastic Neoplasms
    - Hairy Cell Leukemia
    - Head and Neck Cancers
    - Hodgkin Lymphoma
    - Hepatocellular Carcinoma
    - Kaposi Sarcoma
    - Kidney Cancer
    - Melanoma: Cutaneous
    - Melanoma: Uveal
    - Merkel Cell Carcinoma
    - Mesothelioma: Peritoneal
    - Mesothelioma: Pleural
    - Myelodysplastic Syndromes
    - Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Gene Fusions
    - Myeloproliferative Neoplasms
    - Neuroendocrine and Adrenal Tumors
    - Non-Small Cell Lung Cancer
    - Occult Primary
    - Ovarian Cancer
    - Pancreatic Cancer
    - Penile Cancer
    - Prostate Cancer
    - Rectal Cancer

- Small Bowl Adenocarcinoma
- Small Cell Lung Cancer
- Soft Tissue Sarcoma
- Squamous Cell Skin Cancer
- Systemic Mastocytosis
- Systemic Light Chain Amyloidosis
- Testicular Cancer
- Thymomas and Thymic Carcinomas
- Thyroid Carcinoma
- Uterine Neoplasms
- Vulvar Cancer
- Waldenström Macroglobulinemia / Lymphoplasmacytic Lymphoma

In addition, the following criteria must be met for approval:

1. The requested regimen for the drug(s) or biologic(s) and indication is consistent with an NCCN recommendation with a level of evidence category of 1 or 2A.
2. The NCCN template must be accepted by the provider without modification.

Further review may be indicated when the above criteria are not met.

Authorizations may be granted for 12 months or as medically required, based on the member's condition and provider's assessment.

Supportive Care: Myeloid Growth Factor Therapy
Granulocyte colony stimulating factors are recommended for primary prophylaxis based on the febrile neutropenia risk of the chemotherapy regimen. Febrile neutropenia risk levels vary by NCCN Chemotherapy Order template and are listed at the top of the template. Regimens associated with a high or intermediate risk of febrile neutropenia may include a granulocyte colony stimulating factor as part of the prior authorization.

Continuation of Therapy
To submit a request for continuation of therapy, a new regimen prior authorization review must be requested. Upon template selection, the template must be modified to include the appropriate therapies being used for maintenance treatment. The regimen request will be submitted for further review.

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

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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.

POLICY Document for TRELSTAR (triptorelin pamoate)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, and overall, clinically appropriate use. This document provides specific information to both sections of the overall policy.

Section 1: Preferred Product
- Policy information specific to preferred medications

Section 2: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 3: Oncology Clinical Policy
- Policy information specific to regimen review per NCCN Guidelines.

Section 1: Preferred Product

EXCEPTIONS CRITERIA
GONADOTROPIN RELEASING HORMONE AGONISTS

PREFERRED PRODUCT: ELIGARD

POLICY
This policy informs prescribers of preferred products and provides an exception process for targeted products through prior authorization.

I. PLAN DESIGN SUMMARY

This program applies to the gonadotropin releasing hormone agonist products specified in this policy. Coverage for targeted products is provided based on clinical circumstances that would exclude the use of the preferred product and may be based on previous use of a product. The coverage review process will ascertain situations where a clinical exception can be made. This program applies to all members requesting treatment with Camcevi and Lupron Depot. This program also applies to members who are new to treatment with Firmagon, Trelstar, or Zoladex for the first time.

Each referral is reviewed based on all utilization management (UM) programs implemented for the client.

Table. Gonadotropin releasing hormone agonists

	Product(s)
Preferred*	• **Eligard** (leuprolide acetate)
Targeted	• **Camcevi** (leuprolide mesylate) • **Firmagon** (degarelix) • **Lupron Depot** (leuprolide acetate for depot suspension) • **Trelstar** (triptorelin) • **Zoladex** (goserelin acetate)

*: Medications considered formulary or preferred on your plan may still require a clinical prior authorization review.

II. EXCEPTION CRITERIA

This program applies to members requesting treatment for prostate cancer.

A. Firmagon, Trelstar, and Zoladex

Coverage for the Firmagon, Trelstar, and Zoladex is provided when any of the following criteria is met:

1. Member is currently receiving treatment with the requested targeted product, excluding when the requested targeted product is obtained as samples or via manufacturer's patient assistance programs.
2. Member has a documented hypersensitivity to the preferred product.

B. Camcevi and Lupron Depot

Coverage for Camcevi and Lupron Depot is provided when the member has a documented hypersensitivity to the preferred product.

Section 2: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

TRELSTAR (triptorelin pamoate)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Trelstar is indicated for the palliative treatment of advanced prostate cancer

B. Compendial Uses
1. Prostate cancer
2. Preservation of ovarian function
3. Breast cancer – ovarian suppression
4. Gender dysphoria (also known as gender non-conforming or transgender persons)

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 testing results (where applicable).

III. PRESCRIBER SPECIALTIES

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 patients less than 18 years of age.

IV. CRITERIA FOR INITIAL APPROVAL

A. Prostate cancer
Authorization of 12 months may be granted for treatment of prostate cancer.

B. Preservation of ovarian function
Authorization of 3 months may be granted for preservation of ovarian function when the member is premenopausal and undergoing chemotherapy.

C. Breast cancer – ovarian suppression
Authorization of 12 months may be granted for ovarian suppression in premenopausal members with hormone-receptor positive breast cancer at higher risk for recurrence (e.g., young age, high-grade tumor, lymph-node involvement) when used in combination with endocrine therapy.

D. Gender dysphoria
1. Authorization of 12 months may be granted for pubertal hormonal suppression in an adolescent member when all of the following criteria are met:
   i. The member has a diagnosis of gender dysphoria.
   ii. The member has reached Tanner stage 2 of puberty or greater.
   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 transition when all of the following criteria are met:
   i. The member has a diagnosis of gender dysphoria.
   ii. The member will receive Trelstar concomitantly with gender-affirming hormones.
   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.

V. CONTINUATION OF THERAPY

A. Prostate cancer
Authorization of 12 months may be granted for continued treatment in members requesting reauthorization who are experiencing clinical benefit to therapy (e.g., serum testosterone less than 50 ng/dL) and who have not experienced an unacceptable toxicity.

B. Breast cancer – ovarian suppression
Authorization of 12 months may be granted (up to 5 years total) for continued treatment in members requesting reauthorization who were premenopausal at diagnosis and are still undergoing treatment with endocrine therapy.

C. Gender dysphoria
1. Authorization of 12 months may be granted for continued treatment for pubertal hormonal suppression 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 has previously reached Tanner stage 2 of puberty or greater.
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 transition in members requesting reauthorization when all of the following criteria are met:
   i. The member has a diagnosis of gender dysphoria.
   ii. The member will receive Trelstar concomitantly with gender-affirming hormones.
   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.

D. Preservation of ovarian function

All members (including new members) requesting authorization for continuation of therapy for preservation of ovarian function must meet all initial authorization criteria.

Section 3: Oncology Clinical Policy

Oncology Clinical Policy

Program Description

The National Comprehensive Care Network® (NCCN®) is an alliance of leading cancer centers devoted to patient care, research and education dedicated to improving the quality, effectiveness and efficiency of cancer care so patients can live better lives.[1] It is comprised of oncology experts who convene regularly to establish the best treatments for patients. NCCN develops various resources for use by stakeholders in the health care delivery system. These resources include, but are not limited to, the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®), the NCCN Drugs & Biologics Compendium (NCCN Compendium®) and the NCCN Chemotherapy Order Templates (NCCN Templates®).

NCCN templates are based on NCCN Clinical Practice Guidelines and NCCN Compendium. The NCCN Compendium lists the appropriate drugs and biologics for specific cancers using U.S. Food and Drug Administration (FDA)-approved disease indications and specific NCCN panel recommendations. Each recommendation is supported by a level of evidence category.

NCCN Categories of Evidence and Consensus[2]

Category 1: Based on high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2A: Based on lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2B: Based on lower-level evidence, there is NCCN consensus that the intervention is appropriate.
Category 3: Based any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

Policy for Regimen Prior Authorization

A regimen prior authorization allows submission of a single prior authorization request for all oncology drugs or biologics within an NCCN template that require prior authorization.

This policy provides coverage of a regimen review when *all* the following criteria are met:

a. Regimen prior authorization reviews, based on NCCN templates, are initiated through the provider portal: https://provider.carefirst.com/providers/home.page
b. If the prior authorization request is submitted via phone or fax, each drug or biologic will need to be submitted and reviewed as a separate prior authorization request for review with drug-specific criteria.

c. The prior authorization review is requested for an oncology drug or biologic that requires prior authorization on the medical benefit.
d. The indication is for a cancer that is eligible for regimen review. Currently, the cancer types in scope for regimen review include breast, lung, colon and rectal cancer.
e. The member is eligible for regimen review.

In addition, the following criteria must be met for approval:

a. The requested regimen for the drug(s) or biologic(s) and indication is consistent with an NCCN recommendation with a level of evidence category of 1 or 2A.
b. The NCCN template must be accepted by the provider without modification.

Authorizations may be granted for 12 months.
Further review may be indicated where the above criteria are not met.

Continuation of Therapy

To submit a request for continuation of therapy, a new regimen prior authorization review must be requested. Upon template selection, the template must be modified to include the appropriate therapies being used for maintenance treatment. The regimen request will be submitted for further review.

Dosage and Administration

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

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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.
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7. Tuberculosis (TB). TB risk factors. Centers for Disease Control and Prevention. Retrieved on 15 November 2021 from: https://www.cdc.gov/tb/topic/basics/risk.htm.
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.

Reference number(s)
2985-A

SPECIALTY GUIDELINE MANAGEMENT

TRETTEN (coagulation Factor XIII A-Subunit [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
Tretten is indicated for routine prophylaxis of bleeding in patients with congenital factor XIII A-subunit deficiency.

Tretten is not for use in patients with congenital factor XIII B-subunit deficiency.

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

II. CRITERIA FOR INITIAL APPROVAL

Congenital Factor XIII A-Subunit Deficiency
Authorization of 12 months may be granted for prophylaxis of bleeding in members with congenital factor XIII A-subunit deficiency.

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. REFERENCES

1. Tretten [package insert]. Plainsboro, NJ: Novo Nordisk Inc.; June 2020.
2. 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 October 4, 2022.

Reference number(s)
1644-A

SPECIALTY GUIDELINE MANAGEMENT

Remodulin (treprostinil injection)
treprostinil 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. Treatment of pulmonary arterial hypertension (PAH; World Health Organization [WHO] Group 1) to diminish symptoms associated with exercise. Studies establishing effectiveness included patients with New York Heart Association (NYHA) Functional Class II-IV symptoms and etiologies of idiopathic or heritable PAH, PAH associated with congenital systemic-to-pulmonary shunts, or PAH associated with connective tissue diseases.
B. In patients with PAH requiring transition from epoprostenol, to diminish the rate of clinical deterioration. The risks and benefits of each drug should be carefully considered prior to transition.

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)
Indefinite authorization 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

Indefinite authorization 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. Treprostinil [package insert]. Princeton, NJ: Sandoz, Inc.; April 2019.
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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)
2504-A

SPECIALTY GUIDELINE MANAGEMENT

TRIPTODUR (triptorelin)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Triptodur is indicated for the treatment of pediatric patients 2 years of age and older with central precocious puberty (CPP).

B. Compendial Uses
1. Gender dysphoria (also known as gender non-conforming or transgender persons)
2. Preservation of ovarian function
3. Prevention of recurrent menstrual related attacks in acute porphyria

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. PRESCRIBER SPECIALTIES

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 patients less than 18 years of age.

IV. 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. Gender dysphoria

1. Authorization of 12 months may be granted for pubertal hormonal suppression in an adolescent member when all of the following criteria are met:
   i. The member has a diagnosis of gender dysphoria.
   ii. The member has reached Tanner stage 2 of puberty or greater.
   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 transition when all of the following criteria are met:
   i. The member has a diagnosis of gender dysphoria.
   ii. The member will receive Triptodur concomitantly with gender-affirming hormones.
   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.

C. Preservation of ovarian function

Authorization of 3 months may be granted for preservation of ovarian function when the member is premenopausal and undergoing chemotherapy.

D. Prevention of recurrent menstrual related attacks in acute porphyria

Authorization of 12 months may be granted for prevention of recurrent menstrual related attacks in members with acute porphyria when the requested medication is prescribed by or in consultation with a physician experienced in the management of porphyrias.

V. CONTINUATION OF THERAPY

A. Central precocious puberty (CPP)

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. Gender dysphoria

1. Authorization of 12 months may be granted for continued treatment for pubertal hormonal suppression 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 has previously reached Tanner stage 2 of puberty or greater.
   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 transition in members requesting reauthorization when all of the following criteria are met:
   i. The member has a diagnosis of gender dysphoria.
   ii. The member will receive Triptodur concomitantly with gender-affirming hormones.
   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.

C. All other indications

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

VI. REFERENCES

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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.
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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
Tymlos is indicated for the treatment of postmenopausal women with osteoporosis at high risk for fracture defined as history of osteoporotic fracture, 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

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:

A. Member has a history of fragility fractures
B. 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:
    1. 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)
    2. Member has failed prior treatment with or is intolerant to previous injectable osteoporosis therapy (e.g., zoledronic acid [Reclast], denosumab [Prolia])
    3. 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)

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 experienced clinical benefit as evidenced by a bone mass measurement showing an improvement or stabilization in T-score compared with the previous bone mass measurement and member has not experienced any adverse effects.
B. Member has experienced clinical benefit (e.g. no new fracture seen on radiography) and has 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. 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 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. September 2021.
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POLICY Document for TYSABRI (natalizumab)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, lower cost site of care and overall, clinically appropriate use. This document provides specific information to each of the three sections of the overall policy.

Section 1: Site of Care

- Policy information specific to site of care (outpatient, hospital outpatient, home infusion)

Section 2: Clinical Criteria

- Policy information specific to the clinical appropriateness for the medication

Section 1: Site of Care

CareFirst Site of Care Criteria
Administration of Intravenous Natalizumab
Tyruko, Tysabri

POLICY

I. CRITERIA FOR APPROVAL FOR ADMINISTRATION IN OUTPATIENT HOSPITAL SETTING

This policy provides coverage for administration of natalizumab in an outpatient hospital setting for up to 45 days when ANY of the following criteria are met:

A. The member is new to therapy or reinitiating therapy after not being on therapy for at least 6 months
B. The member has experienced a gap in therapy of greater than 2 infusions.

This policy provides coverage for administration of natalizumab in an outpatient hospital setting for a longer course of treatment when ANY of the following criteria are met:

A. The member has experienced an adverse reaction to the medication that did not respond to conventional interventions (eg, acetaminophen, steroids, diphenhydramine, fluids or other pre-medications) or a severe adverse event (anaphylaxis, anaphylactoid reactions, myocardial infarction, thromboembolism, or seizures) during or immediately after an infusion.
B. The member has developed antibodies to natalizumab which increases the risk for infusion related reactions.
C. The member is medically unstable (eg respiratory, cardiovascular, or renal conditions).
D. The member has severe venous access issues that require the use of special interventions only available in the outpatient hospital setting.
E. The member has significant behavioral issues and/or physical or cognitive impairment that would impact the safety of the infusion therapy AND the patient does not have access to a caregiver.
F. The member is less than 14 years of age.

For situations where administration of natalizumab does not meet the criteria for outpatient hospital infusion, coverage for natalizumab is provided when administered in alternative specially certified sites such as; physician office or ambulatory care. Natalizumab is not indicated for home infusion.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the site of care prior authorization review (where applicable):

A. Medical records supporting the member has experienced an adverse reaction that did not respond to conventional interventions or a severe adverse event during or immediately after an infusion
B. Medical records supporting the member has developed antibodies to natalizumab
C. Medical records supporting the member is medically unstable
D. Medical records supporting the member has severe venous access issues that require specialized interventions only available in the outpatient hospital setting
E. Medical records supporting the member has behavioral issues and/or physical or cognitive impairment and no access to a caregiver

Section 2: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

TYSABRI (natalizumab)

POLICY

III. INDICATIONS

The indications below including FDA-approved indications and compendial 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. Tysabri is indicated for inducing and maintaining clinical response and remission in adult patients with moderately to severely active Crohn's disease (CD) with evidence of inflammation who have had an inadequate response to, or are unable to tolerate, conventional CD therapies and inhibitors of tumor necrosis factor alpha (TNF-α). Tysabri should not be used in combination with immunosuppressants (e.g., 6-mercaptopurine, azathioprine, cyclosporine, or methotrexate) or inhibitors of TNF-α.
B. Tysabri is indicated as monotherapy for the treatment of relapsing forms of multiple sclerosis, to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults. Tysabri increases the risk of progressive multifocal leukoencephalopathy (PML). When initiating and continuing treatment with Tysabri, physicians should consider whether the expected benefit of Tysabri is sufficient to offset this risk.

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

IV. DOCUMENTATION

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

Crohn's disease (CD):

A. 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.
B. Continuation requests: Chart notes or medical record documentation supporting positive clinical response to therapy or remission.

V. PRESCRIBER SPECIALTIES

The medication must be prescribed by or in consultation with one of the following:

A. Crohn's disease: gastroenterologist
B. Multiple sclerosis: neurologist

VI. CRITERIA FOR INITIAL APPROVAL

A. Crohn's disease (CD)
Authorization of 12 months may be granted to adult members who have received any other biologic indicated for the treatment of moderately to severely active Crohn's disease and who have been tested for anti-JCV antibodies.

B. 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) and those who have been tested for anti-JCV antibodies.

C. Clinically isolated syndrome (CIS)
Authorization of 12 months may be granted to members for the treatment of clinically isolated syndrome of multiple sclerosis and those who have been tested for anti-JCV antibodies.

VII. CONTINUATION OF THERAPY

A. 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. Endoscopic appearance of the mucosa
   vii. Improvement on a disease activity scoring tool (e.g., Crohn's Disease Activity Index [CDAI] score)

B. Relapsing forms of multiple sclerosis (MS) or clinically isolated syndrome (CIS)
Authorization of 12 months may be granted for all members (including new members) who achieve or maintain a positive clinical response with the requested drug as evidenced by experiencing disease stability or improvement.

VIII. OTHER

For all indications: Members cannot use the requested drug concomitantly with any other disease modifying multiple sclerosis agents (Note: Ampyra and Nuedexta are not disease modifying), immunosuppressants, or TNF inhibitors (e.g., adalimumab, infliximab).

IX. DOSAGE AND ADMINISTRATION

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

REFERENCES

SECTION 1

1. Tysabri [package insert]. Cambridge, MA: Biogen Inc.; April 2023.
2. Tyruko [package insert]. Princeton, NJ: Sandoz Inc.; August 2023.
3. O'Connor P, Goodman A, Kappos L, et al. Long-term safety and effectiveness of natalizumab redosing and treatment in the STRATA MS Study. *Neurology.* 2014;83(1):78-86.
4. Polman CH, O'Connor PW, Havrdova E, et al. A randomized, placebo-controlled trial of natalizumab for relapsing multiple sclerosis. *N Engl J Med*. 2006;354(9):899-910.

SECTION 2

1. Tysabri [package insert]. Cambridge, MA: Biogen Inc; June 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.
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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

1. Tyvaso [package insert]. Research Triangle Park, NC: United Therapeutics Corp.; May 2022.
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.
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Reference number
5678-A

SPECIALTY GUIDELINE MANAGEMENT

TZIELD (teplizumab-mzwv)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Tzield is indicated to delay the onset of Stage 3 type 1 diabetes in adults and pediatric patients 8 years of age and older with Stage 2 type 1 diabetes.

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. Presence of two or more pancreatic islet cell autoantibodies within the past 6 months
B. Abnormal oral glucose tolerance test (OGTT) results within the past 2 months

III. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with an endocrinologist.

IV. CRITERIA FOR INITIAL APPROVAL

Delay of Stage 3 Type 1 Diabetes
Authorization of 1 month may be granted for members with Stage 2 type 1 diabetes to delay the onset of Stage 3 type 1 diabetes when all of the following criteria are met:
A. Member is 8 years of age and older
B. Member has two or more of the following pancreatic islet cell autoantibodies detected in two samples obtained within the past 6 months:
    1. Glutamic acid decarboxylase 65 (GAD) autoantibodies
    2. Insulin autoantibody (IAA)
    3. Insulinoma-associated antigen 2 autoantibody (IA-2A)
    4. Zinc transporter 8 autoantibody (ZnT8A)
    5. Islet cell autoantibody (ICA)
C. Member has an abnormal oral glucose tolerance test (OGTT) confirming dysglycemia within the past 2 months when any of the following are met:
    1. Fasting blood glucose level of 110 to 125 mg/dL (6.1 to 6.9 mmol/L)
    2. 2-hour postprandial plasma glucose level of at least 140 mg/dL (7.8 mmol/L) and less than 200 mg/dL (11.1 mmol/L)

3. Intervening postprandial glucose level at 30, 60, or 90 minutes of greater than 200 mg per deciliter (11.1 mmol/L) on two occasions

D. Member does not have symptoms associated with type 1 diabetes (e.g., increased urination, excessive thirst, weight loss)

E. Member will not exceed a one-time 14-day treatment course consisting of the following dosing schedule:
   1. Day 1: 65 mcg/m^2
   2. Day 2: 125 mcg/m^2
   3. Day 3: 250 mcg/m^2
   4. Day 4: 500 mcg/m^2
   5. Days 5 through 14: 1,030 mcg/m^2

V. REFERENCES

1. Tzield [package insert]. Red Bank, NJ: Provention Bio, Inc.; November 2022.
2. Herold KC, Bundy BN, Long SA, et al. An Anti-CD3 Antibody, Teplizumab, in Relatives at Risk for Type 1 Diabetes. N Engl J Med 2019; 381:603-613. https://www.nejm.org/doi/full/10.1056/nejmoa1902226.

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.

POLICY Document for UPLIZNA (inebilizumab-cdon)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, lower cost site of care and overall, clinically appropriate use. This document provides specific information to each of the three sections of the overall policy.

Section 1: Site of Care

- Policy information specific to site of care (outpatient, hospital outpatient, home infusion)

Section 2: Clinical Criteria

- Policy information specific to the clinical appropriateness for the medication

Section 1: Site of Care

CareFirst Site of Care Criteria
Administration of Intravenous Uplizna

POLICY

I. CRITERIA FOR APPROVAL FOR ADMINISTRATION IN OUTPATIENT HOSPITAL SETTING

This policy provides coverage for administration of Uplizna in an outpatient hospital setting for up to 45 days when a member is new to therapy or is reinitiating therapy after not being on therapy for at least 6 months.

This policy provides coverage for administration of Uplizna in an outpatient hospital setting for a longer course of treatment when ANY of the following criteria are met:

A. The member has experienced an adverse reaction to Uplizna that did not respond to conventional interventions (eg, acetaminophen, steroids, diphenhydramine, fluids, other pre-medications or slowing of infusion rate) or a severe adverse event (anaphylaxis, anaphylactoid reactions, myocardial infarction, thromboembolism, or seizures) during or immediately after an infusion.
B. The member is medically unstable (eg respiratory, cardiovascular, or renal conditions).
C. The member has severe venous access issues that require the use of special interventions only available in the outpatient hospital setting.
D. The member has significant behavioral issues and/or physical or cognitive impairment that would impact the safety of the infusion therapy AND the patient does not have access to a caregiver.
E. The member is less than 14 years of age.

For situations where administration of Uplizna does not meet the criteria for outpatient hospital infusion, coverage for Uplizna is provided when administered in alternative sites such as physician office, home infusion or ambulatory care.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the site of care prior authorization review (where applicable):

A. Medical records supporting the member has experienced an adverse reaction that did not respond to conventional interventions or a severe adverse event during or immediately after an infusion

B. Medical records supporting the member is medically unstable
C. Medical records supporting the member has severe venous access issues that requires specialized interventions only available in the outpatient hospital setting
D. Medical records supporting the member has behavioral issues and/or physical or cognitive impairment and no access to a caregiver

Section 2: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

UPLIZNA (inebilizumab-cdon)

POLICY

III. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Uplizna is 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.

IV. 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.

V. CRITERIA FOR INITIAL APPROVAL

Neuromyelitis optica spectrum disorder (NMOSD)
A. Authorization of 12 months may be granted for treatment of neuromyelitis optica spectrum disorder (NMOSD) when all of the following criteria are met:
   1. Anti-aquaporin-4 (AQPR) antibody positive
   2. Member exhibits one of the following core clinical characteristics of NMOSD:
      i. Optic neuritis
      ii. Acute myelitis
      iii. Area postrema syndrome (episode of otherwise unexplained hiccups or nausea and vomiting)
      iv. Acute brainstem syndrome
      v. Symptomatic narcolepsy or acute diencephalic clinical syndrome with NMOSD-typical diencephalic magnetic resonance imaging (MRI) lesions
      vi. Symptomatic cerebral syndrome with NMOSD-typical brain lesions
   3. The member will not receive the requested drug concomitantly with other biologics for the treatment of NMOSD.

VI. 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.

REFERENCES

SECTION 1

1. Uplizna [package insert]. Gaithersburg, MD: Viela Bio, Inc.; July 2021.

SECTION 2

1. Uplizna [package insert]. Baithersburg, MD: Viela Bio, Inc.; December 2020.
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POLICY Document for ULTOMIRIS (ravulizumab)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, lower cost site of care and overall, clinically appropriate use. This document provides specific information to each of the three sections of the overall policy.

Section 1: Site of Care

- Policy information specific to site of care (outpatient, hospital outpatient, home infusion)

Section 2: Clinical Criteria

- Policy information specific to the clinical appropriateness for the medication

Section 1: Site of Care

CareFirst Site of Care Criteria
Administration of Intravenous Ultomiris

POLICY

I. CRITERIA FOR APPROVAL FOR ADMINISTRATION IN OUTPATIENT HOSPITAL SETTING

This policy provides coverage for administration of Ultomiris in an outpatient hospital setting for up to 45 days when a member is new to therapy or is reinitiating therapy after not being on therapy for at least 6 months.

This policy provides coverage for administration of Ultomiris in an outpatient hospital setting for a longer course of treatment when ANY of the following criteria are met:

A. The member has experienced an adverse reaction to the drug that did not respond to conventional interventions (eg, acetaminophen, steroids, diphenhydramine, fluids, other pre-medications or slowing of infusion rate) or a severe adverse event (anaphylaxis, anaphylactoid reactions, myocardial infarction, thromboembolism, or seizures) during or immediately after an infusion.
B. The member is medically unstable (eg respiratory, cardiovascular, or renal conditions).
C. The member has severe venous access issues that require the use of special interventions only available in the outpatient hospital setting.
D. The member has significant behavioral issues and/or physical or cognitive impairment that would impact the safety of the infusion therapy AND the patient does not have access to a caregiver.
E. The member is less than 14 years of age.

For situations where administration of Ultomiris does not meet the criteria for outpatient hospital infusion, coverage for Ultomiris is provided when administered in alternative sites such as; physician office, home infusion or ambulatory care.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the site of care prior authorization review (where applicable):

A. Medical records supporting the member has experienced an adverse reaction that did not respond to conventional interventions or a severe adverse event during or immediately after an infusion

B. Medical records supporting the member is medically unstable
C. Medical records supporting the member has severe venous access issues that requires specialized interventions only available in the outpatient hospital setting
D. Medical records supporting the member has behavioral issues and/or physical or cognitive impairment and no access to a caregiver

Section 2: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

ULTOMIRIS (ravulizumab)

POLICY

III. INDICATIONS

The indications below including FDA-approved indications and compendial 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. Ultomiris is indicated for the treatment of adult and pediatric patients one month of age and older with paroxysmal nocturnal hemoglobinuria (PNH).
2. Ultomiris is indicated for the treatment of adults and pediatric patients one month of age and older with atypical hemolytic uremic syndrome (aHUS) to inhibit complement-mediated thrombotic microangiopathy (TMA).
3. Ultomiris is indicated for the treatment of adult patients with generalized myasthenia gravis (gMG) who are anti-acetylcholine receptor (AChR) antibody-positive.

Limitations of Use: Ultomiris is not indicated for the treatment of patients with Shiga toxin E. coli related hemolytic uremic syndrome (STEC-HUS).

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

IV. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review for new requests for treatment of:

A. For initial requests:
   1. Paroxysmal nocturnal hemoglobinuria: flow cytometry used to show results of glycosylphosphatidylinositol-anchored proteins (GPI-APs) deficiency
   2. Atypical hemolytic uremic syndrome: ADAMTS 13 level
   3. Generalized myasthenia gravis: anti-acetylcholine receptor (AchR) antibody positive, clinical classification of myasthenia gravis score, MG activities of daily living score, use of IVIG, use of two immunosuppressive therapies
B. For continuation requests: Chart notes or medical record documentation supporting positive clinical response.

V. CRITERIA FOR INITIAL APPROVAL

A. Paroxysmal nocturnal hemoglobinuria
Authorization of 6 months may be granted for treatment of paroxysmal nocturnal hemoglobinuria (PNH) when all of the following criteria are met:
A. The diagnosis of PNH was confirmed by detecting a deficiency of glycosylphosphatidylinositol-anchored proteins (GPI-APs) as demonstrated by either of the following:
   1. At least 5% PNH cells
   2. At least 51% of GPI-AP deficient poly-morphonuclear cells
B. Flow cytometry is used to demonstrate GPI-APs deficiency

B. Atypical hemolytic uremic syndrome (aHUS)
Authorization of 6 months may be granted for treatment of atypical hemolytic uremic syndrome (aHUS) not caused by Shiga toxin when all of the following criteria are met:
1. Absence of Shiga toxin
2. ADAMTS 13 activity level above 5%

C. Generalized myasthenia gravis (gMG)
Authorization of 6 months may be granted for treatment of generalized myasthenia gravis (gMG) when all of the following criteria are met:
1. Anti-acetylcholine receptor (AchR) antibody positive
2. Myasthenia Gravis Foundation of America (MGFA) clinical classification II to IV
3. MG activities of daily living (MG-ADL) total score ≥6
4. Meets both of the following:
   a. Member has had an inadequate response to at least two immunosuppressive therapies listed below:
      i. azathioprine
      ii. cyclosporine
      iii. mycophenolate mofetil
      iv. tacrolimus
      v. methotrexate
      vi. cyclophosphamide
      vii. rituximab
   b. Member has inadequate response to chronic IVIG

VI. CONTINUATION OF THERAPY

A. Paroxysmal nocturnal hemoglobinuria
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 and demonstrate a positive response to therapy (e.g., improvement in hemoglobin levels, normalization of lactate dehydrogenase [LDH] levels).

B. Atypical hemolytic uremic syndrome (aHUS)
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 and demonstrate a positive response to therapy (e.g., normalization of lactate dehydrogenase (LDH) levels, platelet counts).

C. Generalized myasthenia gravis (gMG)
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 and member demonstrates a positive response to therapy (e.g., improvement in MG-ADL score, changes compared to baseline in Quantitative Myasthenia Gravis (QMG) total score).

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.

REFERENCES

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SECTION 2

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2. The NCCN Drugs & Biologics Compendium® © 2022 National Comprehensive Cancer Network, Inc. Available at: https://www.nccn.org. Accessed March 8, 2022.

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, 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. 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

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Reference number(s)
5156-A

SPECIALTY GUIDELINE MANAGEMENT

VABYSMO (faricimab-svoa)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Vabysmo is indicated for the treatment of:
A. Diabetic macular edema
B. Neovascular (wet) age-related macular degeneration
C. Macular edema following retinal vein occlusion

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

II. CRITERIA FOR INITIAL APPROVAL

A. Diabetic Macular Edema
Authorization of 6 months may be granted for treatment of diabetic macular edema.

B. Neovascular (Wet) Age-Related Macular Degeneration
Authorization of 6 months may be granted for treatment of neovascular (wet) age-related macular degeneration.

C. Macular Edema Following Retinal Vein Occlusion
Authorization of 6 months may be granted for treatment of macular edema following retinal vein occlusion.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment of an indication listed in Section II for members who have demonstrated a positive clinical response to therapy (e.g., improvement or maintenance in best corrected visual acuity [BCVA] or visual field, or a reduction in the rate of vision decline or the risk of more severe vision loss).

IV. REFERENCES

1. Vabysmo [package insert]. South San Francisco, CA: Genentech, Inc.; October 2023.
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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.

POLICY Document for VECTIBIX (panitumumab)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, and overall, clinically appropriate use. This document provides specific information to both sections of the overall policy.

Section 1: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 2: Oncology Clinical Policy
- Policy information specific to regimen review per NCCN Guidelines.

Section 1: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

VECTIBIX (panitumumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Vectibix is indicated for the treatment of patients with wild-type *RAS* (defined as wild-type in both *KRAS* and *NRAS* as determined by an FDA-approved test for this use) metastatic colorectal cancer (mCRC):
   a. As first-line therapy in combination with FOLFOX (fluorouracil, leucovorin, and oxaliplatin).
   b. As monotherapy following disease progression after prior treatment with fluoropyrimidine-, oxaliplatin-, and irinotecan-containing chemotherapy.

Limitation of Use: Vectibix is not indicated for the treatment of patients with *RAS*-mutant mCRC or for whom *RAS* mutation status is unknown.

B. Compendial Use
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:
A. Documentation of *RAS* wild-type status, where applicable.
B. Documentation of *BRAF* mutation status, where applicable.

III. CRITERIA FOR INITIAL APPROVAL

Colorectal Cancer (CRC)
Authorization of 6 months may be granted for the treatment of colorectal cancer, including appendiceal adenocarcinoma and anal adenocarcinoma, for unresectable/inoperable, advanced, or metastatic disease and the member has not previously experienced clinical failure on cetuximab when all of the following criteria are met:

1. The *RAS (KRAS* and *NRAS)* mutation status is negative (wild-type)
2. If the tumor is positive for BRAF V600E mutation, the requested medication will be used in combination with encorafenib (Braftovi)
3. For colon cancer, the tumor is left-sided only

IV. CONTINUATION OF THERAPY

Authorization of 6 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.

Section 2: Oncology Clinical Policy

PROGRAM DESCRIPTION

The National Comprehensive Care Network® (NCCN®) is an alliance of leading cancer centers devoted to patient care, research and education dedicated to improving the quality, effectiveness, and efficiency of cancer care so patients can live better lives.[1] It is comprised of oncology experts who convene regularly to establish the best treatments for patients. NCCN develops various resources for use by stakeholders in the health care delivery system. These resources include, but are not limited to, the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®), the NCCN Drugs & Biologics Compendium (NCCN Compendium®) and the NCCN Chemotherapy Order Templates (NCCN Templates®).

NCCN Templates® are based on NCCN Guidelines® and NCCN Compendium®. The NCCN Compendium lists the appropriate drugs and biologics as treatment options for specific cancers using U.S. Food and Drug Administration (FDA)-approved disease indications and specific NCCN panel recommendations. Each recommendation is supported by a level of evidence category.

NCCN Categories of Evidence and Consensus[2]

- Category 1: Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
- Category 2A: Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
- Category 2B: Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.
- Category 3: Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

POLICY

Policy for Regimen Prior Authorization
A regimen prior authorization allows submission of a single prior authorization request for all oncology drugs or biologics within an NCCN template that require prior authorization.

PROCEDURE

This policy provides coverage of a regimen review when all of the following criteria are met:
1. Regimen prior authorization reviews, based on NCCN templates, are initiated through the provider portal.
    - If the prior authorization request is submitted via phone or fax, each drug or biologic will need to be submitted and reviewed as a separate prior authorization request for review with drug-specific criteria.
2. The prior authorization review is requested for an oncology drug or biologic.
3. The member is eligible for regimen review.
4. The indication is for a cancer that is eligible for regimen review. Currently, the cancer types in scope for regimen review include the following:
    - Ampullary Adenocarcinoma
    - Anal Carcinoma
    - B-Cell Lymphomas
    - Basal Cell Skin Cancer
    - Biliary Tract Cancers
    - Bone Cancer
    - Breast Cancer
    - Bladder Cancer
    - Central Nervous System Cancers
    - Cervical Cancer
    - Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma
    - Chronic Myeloid leukemia
    - Colon Cancer
    - Dermatofibrosarcoma Protuberans
    - Esophageal Cancer
    - Gastric Cancer
    - Gastrointestinal Stromal Tumors
    - Gestational Trophoblastic Neoplasms
    - Hairy Cell Leukemia
    - Head and Neck Cancers
    - Hodgkin Lymphoma
    - Hepatocellular Carcinoma
    - Kaposi Sarcoma
    - Kidney Cancer
    - Melanoma: Cutaneous
    - Melanoma: Uveal
    - Merkel Cell Carcinoma
    - Mesothelioma: Peritoneal
    - Mesothelioma: Pleural
    - Myelodysplastic Syndromes
    - Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Gene Fusions
    - Myeloproliferative Neoplasms
    - Neuroendocrine and Adrenal Tumors
    - Non-Small Cell Lung Cancer
    - Occult Primary
    - Ovarian Cancer
    - Pancreatic Cancer
    - Penile Cancer
    - Prostate Cancer
    - Rectal Cancer
    - Small Bowl Adenocarcinoma
    - Small Cell Lung Cancer
    - Soft Tissue Sarcoma
    - Squamous Cell Skin Cancer
    - Systemic Mastocytosis
    - Systemic Light Chain Amyloidosis

- Testicular Cancer
- Thymomas and Thymic Carcinomas
- Thyroid Carcinoma
- Uterine Neoplasms
- Vulvar Cancer
- Waldenström Macroglobulinemia / Lymphoplasmacytic Lymphoma

In addition, the following criteria must be met for approval:

1. The requested regimen for the drug(s) or biologic(s) and indication is consistent with an NCCN recommendation with a level of evidence category of 1 or 2A.
2. The NCCN template must be accepted by the provider without modification.

Further review may be indicated when the above criteria are not met.

Authorizations may be granted for 12 months or as medically required, based on the member's condition and provider's assessment.

Supportive Care: Myeloid Growth Factor Therapy
Granulocyte colony stimulating factors are recommended for primary prophylaxis based on the febrile neutropenia risk of the chemotherapy regimen. Febrile neutropenia risk levels vary by NCCN Chemotherapy Order template and are listed at the top of the template. Regimens associated with a high or intermediate risk of febrile neutropenia may include a granulocyte colony stimulating factor as part of the prior authorization.

Continuation of Therapy
To submit a request for continuation of therapy, a new regimen prior authorization review must be requested. Upon template selection, the template must be modified to include the appropriate therapies being used for maintenance treatment. The regimen request will be submitted for further review.

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

REFERENCES:

SECTION 1

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2. The NCCN Drugs & Biologics Compendium® © 2022 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed July 11, 2022.
3. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines): Colon Cancer. Version 1.2022. Accessed July 14, 2022 https://www.nccn.org/professionals/physician_gls/pdf/colon.pdf
4. 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

SECTION 2

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2. National Comprehensive Cancer Network. NCCN Categories of Evidence and Consensus website, https://www.nccn.org/guidelines/guidelines-process/development-and-update-of-guidelines, accessed June 6, 2023.
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4. National Comprehensive Cancer Network. NCCN Drugs and Biologics Compendium website https://www.nccn.org/compendia-templates/compendia/drugs-and-biologics-compendia, accessed June 6, 2023. (Note: A subscription may be required.)
5. National Comprehensive Cancer Network. NCCN Chemotherapy Order Templates (NCCN Templates) website. https://www.nccn.org/compendia-templates/nccn-templates-main/browse-by-cancer-type, accessed June 6, 2023. (Note: A subscription may be required.)

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.
2. The NCCN Drugs & Biologics Compendium® © 2022 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed March 8, 2022.

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) (WHO Group 1) to improve a composite endpoint consisting of exercise tolerance, symptoms (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. 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

1. Ventavis [package insert]. South San Francisco, CA: Actelion Pharmaceuticals US, Inc.; March 2022.
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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5. Simonneau G, Robbins IM, Beghetti M, et al. Updated clinical classification of pulmonary hypertension. *J Am Coll Cardiol.* 2013;62:D34-S41.
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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)
2342-A

SPECIALTY GUIDELINE MANAGEMENT

VERZENIO (abemaciclib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Verzenio is indicated:
1. Early Breast Cancer
    a. In combination with endocrine therapy (tamoxifen or an aromatase inhibitor) for the adjuvant treatment of adult patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, node-positive, early breast cancer at high risk of recurrence and a Ki-67 score ≥20% as determined by an FDA approved test.
2. Advanced or Metastatic Breast Cancer
    a. In combination with an aromatase inhibitor as initial endocrine-based therapy for the treatment of postmenopausal women, and men, with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer.
    b. In combination with fulvestrant for the treatment of adult patients with HR-positive, HER2-negative advanced or metastatic breast cancer with disease progression following endocrine therapy.
    c. As monotherapy for the treatment of adult patients with HR-positive, HER2-negative advanced or metastatic breast cancer with disease progression following endocrine therapy and prior chemotherapy in the metastatic setting.

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 the following information is necessary to initiate the prior authorization review:
A. Documentation of laboratory results confirming hormone receptor (HR) status
B. Documentation of laboratory results confirming HER2 status
C. Documentation of test results confirming Ki-67 score, where applicable

III. CRITERIA FOR INITIAL APPROVAL

Breast Cancer
1. Authorization of 12 months may be granted for the treatment of HR-positive, HER2-negative, early breast cancer when all of the following criteria are met:
    a. The requested medication is used as adjuvant treatment, in combination with endocrine therapy (tamoxifen or an aromatase inhibitor)

b. The member has either:
   i. Four or more positive lymph nodes; or
   ii. One to three positive lymph nodes and at least one of the following: grade 3 disease, tumor size of 5 cm or greater, or a Ki-67 score of 20% or greater

2. Authorization of 12 months may be granted for the treatment of HR-positive, HER2-negative, recurrent, advanced, or metastatic breast cancer and the requested medication is used in any of the following regimens:
   a. As monotherapy for a member who has experienced disease progression following endocrine therapy and prior chemotherapy in the metastatic setting; or
   b. In combination with fulvestrant; or
   c. In combination with an aromatase inhibitor (e.g., letrozole, anastrazole, exemestane).

IV. CONTINUATION OF THERAPY

A. Early Breast Cancer

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for early breast cancer until completion of 2 years of treatment or until disease recurrence or unacceptable toxicity while on the current regimen.

B. Recurrent, Advanced, or Metastatic Breast Cancer

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for recurrent, advanced, or metastatic breast cancer when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

V. REFERENCES

1. Verzenio [package insert]. Indianapolis, IN: Eli Lilly and Company; October 2021.
2. The NCCN Drugs & Biologics Compendium © 2021 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed November 30, 2021.
3. Dickler MN, Tolaney SM, Rugo HS, et al. MONARCH 1, a phase II study of abemaciclib, a CDK4 and CDK6 inhibitor, as a single agent, in patients with refractory HR+/HER2- metastatic breast cancer. *Clin Cancer Res.* 2017;23(17):5218-5224.
4. Sledge, GW Jr, Toi M, Neven P, et al. MONARCH 2: abemaciclib in combination with fulvestrant in women with HR+/HER2- advanced breast cancer who had progressed while receiving endocrine therapy. *J Clin Oncol*. 2017;35(25):2875-2884.

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 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[1-3]

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[1-3,6-11]
Authorization of 4 weeks may be granted for treatment of infantile spasms in members less than 2 years of age.

B. Complex Partial Seizures[1-6,12,13]
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; March 2020.

3. Vigadrone [package insert]. Maple grove, MN: Upsher-Smith Laboratories, LLC; February 2020.
4. CVS Caremark Clinical Program Review. Focus on Seizure Disorders Programs; October 1, 2013.
5. Livingston JH, Beaumont D, Arzimanoglou A, et al: Vigabatrin in the treatment of epilepsy in children. *Br J Clin Pharmacol*. 1989; 27:109S-112S.
6. 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.
7. Pellock JM, Hrachovy R, Shinnar S, et al. Infantile spasms: A U.S. consensus report. *Epilepsia*. 2010:51:2175-2189.
8. 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.
9. Hancock EC, Osborne JP, Edwards SW. Treatment of infantile spasms. *Cochrane Database Syst Rev*. 2013;6:CD001770.
10. Riikonen R. Recent advances in the pharmacotherapy of infantile spasms. *CNS Drugs* 2014; 28:279-290.
11. 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.
12. Willmore LJ, Abelson MB, Ben-Menachem E, Pellock JM, Shields WD. Vigabatrin: 2008 Update. *Epilepsia.* 2009; 50(2):163-173.
13. 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.

POLICY Document for VILTEPSO (viltolarsen)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, lower cost site of care and overall, clinically appropriate use. This document provides specific information to each of the three sections of the overall policy.

Section 1: Site of Care

- Policy information specific to site of care (outpatient, hospital outpatient, home infusion)

Section 2: Clinical Criteria

- Policy information specific to the clinical appropriateness for the medication

Section 1: Site of Care

CareFirst Site of Care Criteria
Administration of Intravenous Viltepso

POLICY

I. CRITERIA FOR APPROVAL FOR ADMINISTRATION IN OUTPATIENT HOSPITAL SETTING

This policy provides coverage for administration of Viltepso in an outpatient hospital setting for up to 45 days when a member is new to therapy or reinitiating therapy after not being on therapy for at least 6 months.

This policy provides coverage for administration of Viltepso in an outpatient hospital setting for a longer course of treatment when ANY of the following criteria are met:

A. The member has experienced an adverse reaction to the drug that did not respond to conventional interventions (eg, acetaminophen, steroids, diphenhydramine, fluids or other pre-medications) or a severe adverse event (anaphylaxis, anaphylactoid reactions, myocardial infarction, thromboembolism, or seizures) during or immediately after an infusion.
B. The member is medically unstable (eg respiratory, cardiovascular, or renal conditions).
C. The member has severe venous access issues that require the use of special interventions only available in the outpatient hospital setting.
D. The member has significant behavioral issues and/or physical or cognitive impairment that would impact the safety of the infusion therapy AND the patient does not have access to a caregiver.
E. The member is less than 14 years of age.

For situations where administration of Viltepso does not meet the criteria for outpatient hospital infusion, coverage for Viltepso is provided when administered in alternative sites such as; physician office, home infusion or ambulatory care.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the site of care prior authorization review (where applicable):

A. Medical records supporting the member has experienced an adverse reaction that did not respond to conventional interventions or a severe adverse event during or immediately after an infusion
B. Medical records supporting the member is medically unstable

C. Medical records supporting the member has severe venous access issues that requires specialized interventions only available in the outpatient hospital setting
D. Medical records supporting the member has behavioral issues and/or physical or cognitive impairment and no access to a caregiver

Section 2: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

VILTEPSO (viltolarsen)

POLICY

III. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Viltepso is indicated for the treatment of Duchenne muscular dystrophy (DMD) in patients who have a confirmed mutation of the DMD gene that is amenable to exon 53 skipping.

This indication is approved under accelerated approval based on an increase in dystrophin production in skeletal muscle observed in patients treated with Viltepso. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.

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

IV. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
A. Initial requests: laboratory confirmation of Duchenne muscular dystrophy (DMD) diagnosis with a *DMD* gene mutation that is amenable to exon 53 skipping (refer to examples in Appendix).
B. Continuation of therapy requests: documentation (e.g., chart notes) of response to therapy.

V. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with a physician who specializes in the treatment of Duchenne muscular dystrophy (DMD).

VI. 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. Genetic testing was conducted to confirm the diagnosis of DMD and to identify the specific type of *DMD* gene mutation.
B. The *DMD* gene mutation is amenable to exon 53 skipping (refer to examples in Appendix).
C. Treatment with Viltepso is initiated before the age of 10.
D. Member is able to walk independently without assistive devices.
E. Member will not exceed a dose of 80 mg/kg once weekly.
F. The requested medication will not be used concomitantly with golodirsen.

VII. 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 has demonstrated a response to therapy as evidenced by remaining ambulatory (e.g., not wheelchair dependent).
B. The member will not exceed a dose of 80 mg/kg once weekly.
C. The requested medication will not be used concomitantly with golodirsen.

VIII. APPENDIX

Examples of DMD gene mutations (exon deletions) amenable to exon 53 skipping (not an all-inclusive list):

1. Deletion of exon 52
2. Deletion of exon 45-52
3. Deletion of exon 47-52
4. Deletion of exon 48-52
5. Deletion of exon 49-52
6. Deletion of exon 50-52

REFERENCES

SECTION 1

1. Viltepso [package insert]. Paramus, NJ: NS Pharma Inc; March 2021.

SECTION 2

2. Viltepso [package insert]. Paramus, NJ: NS Pharma, Inc.; March 2021.
3. Watanabe N, Nagata T, Satou Y, et al. NS-065/NCNP-01: An Antisense Oligonucleotide for Potential Treatment of Exon 53 Skipping in Duchenne Muscular Dystrophy. *Mol Ther Nucleic Acids*. 2018;13:442–449. doi:10.1016/j.omtn.2018.09.017

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.; March 2021.
2. The NCCN Drugs & Biologics Compendium® © 2022 National Comprehensive Cancer Network, Inc. Available at: https://www.nccn.org. Accessed July 20, 2022.

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.

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)
1951-A

SPECIALTY GUIDELINE MANAGEMENT

VONVENDI (von Willebrand factor [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
Vonvendi is indicated for use in adults (age 18 and older) diagnosed with von Willebrand disease (VWD) for:
1. On-demand treatment and control of bleeding episodes
2. Perioperative management of bleeding.
3. Routine Prophylaxis to reduce the frequency of bleeding episodes in patients with severe Type 3 VWD receiving on-demand therapy

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

II. PRESCRIBER SPECIALTIES

Must be prescribed by or in consultation with a hematologist.

III. CRITERIA FOR INITIAL APPROVAL

Von Willebrand Disease
Authorization of 12 months may be granted for VWD when any of the following criteria is met:
A. Member has type 1, 2A, 2M, or 2N VWD and has had an insufficient response to desmopressin or a documented clinical reason for not using desmopressin (see Appendix).
B. Member has type 2B or type 3 VWD.

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 is experiencing benefit from therapy (e.g., reduced frequency or severity of bleeds).

V. APPENDIX

Clinical Reasons for Not Utilizing Desmopressin in Patients with Type 1, 2A, 2M and 2N VWD
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. Severe type 1 von Willebrand disease
J. Stimate Nasal Spray is unavailable due to backorder/shortage issues (where applicable)

VI. REFERENCES

1. Vonvendi [package insert]. Lexington, MA: Baxalta US Inc.; January 2022.
2. 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 October 3, 2022.
3. National Hemophilia Foundation. MASAC recommendations regarding the treatment of von Willebrand disease. Revised February 2021. MASAC Document #266. https://www.hemophilia.org/sites/default/files/document/files/266.pdf. Accessed October 3, 2022.
4. National Institutes of Health. The diagnosis, evaluation, and management of von Willebrand disease. Bethesda, MD: US Dept of Health and Human Services, National Institutes of Health; 2007. NIH publication No. 08-5832.
5. Stimate [package insert]. King of Prussia, PA: CSL Behring LLC; June 2021.
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)
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)
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®

POLICY Document for VYEPTI

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, lower cost site of care and overall, clinically appropriate use. This document provides specific information to each of the three sections of the overall policy.

Section 1: Site of Care

- Policy information specific to site of care (outpatient, hospital outpatient, home infusion)

Section 2: Clinical Criteria

- Policy information specific to the clinical appropriateness for the medication

Section 1: Site of Care

CareFirst Site of Care Criteria
Administration of Intravenous Vyepti

POLICY

I. CRITERIA FOR APPROVAL FOR ADMINISTRATION IN OUTPATIENT HOSPITAL SETTING

This policy provides coverage for administration of Vyepti in an outpatient hospital setting for up to 90 days when a member is new to therapy or is reinitiating therapy after not being on therapy for at least 6 months.

This policy provides coverage for administration of Vyepti in an outpatient hospital setting for a longer course of treatment when ANY of the following criteria are met:

A. The member has experienced an adverse reaction that did not respond to conventional interventions (eg, acetaminophen, steroids, diphenhydramine, fluids or other pre-medications) or a severe adverse event (anaphylaxis, anaphylactoid reactions, myocardial infarction, thromboembolism, or seizures) during or immediately after an infusion.
B. The member is medically unstable (eg respiratory, cardiovascular, or renal conditions).
C. The member has severe venous access issues that require the use of special interventions only available in the outpatient hospital setting.
D. The member has significant behavioral issues and/or physical or cognitive impairment that would impact the safety of the infusion therapy AND the patient does not have access to a caregiver.
E. The member is less than 14 years of age.

For situations where administration of Vyepti does not meet the criteria for outpatient hospital infusion, coverage for Vyepti is provided when administered in alternative sites such as; physician office, home infusion or ambulatory care.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the site of care prior authorization review (where applicable):

A. Medical records supporting the member has experienced an adverse reaction that did not respond to conventional interventions or a severe adverse event during or immediately after an infusion
B. Medical records supporting the member is medically unstable
C. Medical records supporting the member has severe venous access issues that requires specialized interventions only available in the outpatient hospital setting

D. Medical records supporting the member has behavioral issues and/or physical or cognitive impairment and no access to a caregiver

Section 2: Clinical Criteria

PRIOR AUTHORIZATION 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	***Ref # 2581-C***
Type: Initial Prior Authorization	***Ref # REG 3160-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

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.

CVS/caremark™

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 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)
  AND
  - The requested drug will not be used concurrently with another CGRP receptor antagonist
  AND
  - The request is for Aimovig, Ajovy, Emgality 120mg, or Vyepti

OR

- The request is for Emgality 100mg for treatment of episodic cluster headaches in an adult patient
  AND
  - The patient received at least 3 weeks treatment with the requested drug and had a reduction in weekly cluster headache attack frequency from baseline
    OR
  - The patient experienced an inadequate treatment response to any of the following: A) sumatriptan (subcutaneous or nasal), B) zolmitriptan (nasal or oral)
    OR
  - The patient experienced an intolerance or contraindication to any of the following: A) sumatriptan (subcutaneous or nasal), B) zolmitriptan (nasal or oral)
  AND
  - The requested drug will not be used concurrently with another CGRP receptor antagonist

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. Aimovig, Ajovy, Emgality, and Vyepti are indicated for the preventive treatment of migraine in adults.[1-4] Emgality is also indicated for the treatment of episodic cluster headache in adults.[3]

In the Aimovig clinical study, a protocol amendment that was implemented during the enrollment period allowed the enrollment of patients with concomitant use of one migraine-preventive medication taken at a stable dose (i.e., with no changes to the dose within 2 months before the baseline phase or at any time during the trial).[11,,12] In the Ajovy clinical study, a subset of patients was allowed to use one additional concomitant preventive medication.[13,14] In the Emgality clinical study, a subset of patients was allowed to use one concomitant migraine preventive medication[3]. In the Vyepti clinical study 2, patients were allowed to use acute migraine or headache preventive medication.[4]

For prevention of migraine headache, the American Academy of Neurology (AAN) and the American Headache Society (AHS) 2012 guideline update recommendations state that the following medications are established as effective and should be offered for migraine prevention: β-adrenergic blocking agents, metoprolol, propranolol, timolol; and antiepileptic drugs (AEDs), divalproex sodium, topiramate, sodium valproate. Additionally the following medications are probably effective: antidepressants, amitriptyline, venlafaxine; and β-adrenergic blocking agents, atenolol, nadolol and should be considered for migraine prevention.[7,8,9] Although triptans are recommended by the AAN and AHS guideline, (frovatriptan as effective, naratriptan and zolmitriptan as probably effective), triptans were not included as a criteria trial option because recommended use was for short-term prophylaxis of menstruation-associated migraine (MAM).[7,8] Calcium channel blockers (CCBs) are not included as a criteria trial option based on the AAN and AHS guideline which categorizes nicardipine as possibly effective and nifedipine, nimodipine, verapamil as having inadequate or conflicting data to support or refute medication use.[7,8,9] Therefore, the trial drug criteria options will include the drugs in the drug classes the AAN and AHS guideline recommended as effective and should be offered or probably effective and should be considered for migraine prevention.

The American Academy of Neurology and the American Headache Society Position Statement recommends to give oral preventive treatments an adequate trial of at least 8 weeks at a target or usual effective dose to optimize the possibility of a therapeutic response. Before lack of effectiveness can be determined in patients with chronic migraine, prevention plans should be followed for a minimum of 8 weeks at a target therapeutic dose for oral treatments. If there is no response to treatment after 8 weeks at a target or usual effective dose switching preventive treatments is recommended.[10] Therefore, for coverage of the requested drug, patients with migraine headache must have had a trial for eight weeks, or had an intolerance or contraindication that would prohibit eight-week trials.

The recommended dosage of Aimovig is 70mg injected subcutaneously once monthly. Some patients may benefit from a dosage of 140mg injected subcutaneously once monthly. Aimovig is supplied as SureClick Autoinjector or Prefilled Syringe in a pack of one 70mg/mL or one 140mg/mL single-dose prefilled autoinjector or syringe.[1] Therefore, the limit is set at a quantity of one 140mg/mL autoinjector or syringe and two 70mg/mL autoinjectors or syringes per month.

Two subcutaneous dosing options of Ajovy are available to administer the recommended dosage: 225mg monthly, or 675mg every 3 months (quarterly) administered as three consecutive subcutaneous injections of 225mg each. When switching dosage options, administer the first dose of the new regimen on the next scheduled date of administration. Ajovy is supplied as a carton of one 225mg/1.5mL single-dose prefilled syringe or autoinjector. It is also supplied as a pack of three 225mg/1.5mL single-dose prefilled autoinjectors.[2] Therefore, the limit is set at a quantity of 3 prefilled syringes or autoinjectors per a 3 month period.

The recommended dosage of Emgality for migraines is 240mg (two consecutive subcutaneous injections of 120mg each) once as a loading dose, followed by monthly doses of 120mg injected subcutaneously. Emgality is supplied in a carton of one 120mg/mL single-dose prefilled pen or single-dose prefilled syringe and in a carton of two.[3] Therefore, the initial limit is set at a quantity of 2 prefilled pens or prefilled syringes for initiation of therapy. Thereafter, the limit will be 1 prefilled pen or prefilled syringe per month.

The recommended dosage of Vyepti is 100 mg administered by intravenous infusion every 3 months. Some patients may benefit from a dosage of 300 mg administered by intravenous infusion every 3 months. Dilute only in 100 mL 0.9% Sodium Chloride Injection, USP. Vyepti is for intravenous infusion only; infuse over approximately 30 minutes. Vyepti is supplied in a carton containing one 100 mg/mL single-dose vial.[4] Therefore, the limit is set at a quantity of three 100gm/mL single dose vials per a 3 month period.

The efficacy of Aimovig was evaluated as a preventive treatment of episodic or chronic migraine in three randomized, double-blind, placebo-controlled studies: two studies in patients with episodic migraine (4 to 14 migraine days per month) and one study in patients with chronic migraine (≥ 15 headache days per month with ≥ 8 migraine days per month). The primary efficacy endpoint in Study 1 was the change from baseline in mean monthly migraine days over months 4 to 6. In Study 2 and 3, the primary efficacy endpoint was the change from baseline in mean monthly migraine days at month 3 [1,11,12] The efficacy of Ajovy was evaluated as a preventive treatment of episodic or chronic migraine in two multicenter, randomized, 3-month, double-blind, placebo-controlled studies: one study in patients with episodic

migraine (<15 headache days per month) and one study in patients with chronic migraine (≥15 headache days per month).[2, 13,14] The efficacy of Emgality was evaluated as a preventive treatment of episodic or chronic migraine in three multicenter, randomized, double-blind, placebo-controlled studies: two 6-month studies in patients with episodic migraine and one 3-month study in patients with chronic migraine.[3,15] The efficacy of Vyepti was evaluated as a preventive treatment of episodic and chronic migraine in two randomized, multicenter, placebo-controlled studies, both with 6-month double-blind periods: one study in patients with episodic migraine and one study in patients with chronic migraine. Vyepti was administered by intravenous infusion every 3 months in both studies; however, the primary endpoint was measured at 12 weeks. The primary efficacy endpoints were the change from baseline in mean monthly migraine days over months 1-3.[4] Therefore, after 3 months of therapy with these agents the patient should have improvement in the change from baseline in migraine days for approval. The duration of approval for initial starts will be 3 months and for continuation will be 12 months. The duration of approval for initial starts for the REG 3160-C criteria is 12 months to comply with regulatory standards.

Cluster headaches are an extremely debilitating primary headache disorder.[16] Episodic cluster headache is six times more common than the chronic form. Patients with the episodic cluster headaches have at least two cluster periods of at least one week but less than one year, with remission for at least one month.[17] The American Headache Society (AHS) 2016 guideline update for the treatment of cluster headaches and a meta-analysis published in Neurology recommends for the treatment of cluster headache state that the following medications are established as effective for acute treatment of cluster headaches: sumatriptan subcutaneous, zolmitriptan nasal spray, and oxygen. Additionally, the following medications are probably effective: sumatriptan nasal spray and zolmitriptan oral.[16,18] The American Academy of Family Physicians (AAFP) also recommends triptans (subcutaneous or nasal sumatriptan and nasal or oral zolmitriptan) and supplemental oxygen for first line abortive therapies for cluster headaches.[17] Other therapies for acute treatment (e.g. octreotide, dihydroergotamine nasal spray, prednisone) are classified as possibly effective or insufficient evidence to make recommendation by the AHS and in the meta-analysis for acute treatment of cluster headache.[16,,18] The AAFP also states there is weaker supporting evidence for intranasal lidocaine, octreotide, dihydroergotamine, and prednisone for acute treatment of cluster headache.[17] Therefore, the trial drug criteria options will include the drugs in the Neurology meta-analysis and AHS guideline recommended as effective and should be offered or probably effective and should be considered for treatment of episodic cluster headache.

The recommended dosage of Emgality for cluster headaches is 300 mg (three consecutive subcutaneous injections of 100 mg each) at the onset of the cluster period, and then monthly until the end of the cluster period. If a dose of Emgality is missed during a cluster period, administer as soon as possible. Thereafter, Emgality can be scheduled monthly form the date of the last dose until the end of the cluster period. Emgality is supplied in a carton of three 100mg/mL single-dose prefilled syringes.[3]

The efficacy of Emgality was evaluated for the treatment of episodic cluster headache in a randomized, 8-week double-blind, placebo-controlled study. The primary efficacy endpoint was the mean change from baseline in weekly cluster headache attack frequency across Weeks 1 to 3. A secondary endpoint was the percentage of patients who achieved a response (defined as a reduction from baseline of 50% or greater in the weekly cluster headache attack frequency) at Week 3.[3] Therefore, after 3 weeks of therapy the patient should have improvement in the change from baseline in weekly cluster headache attack frequency. Thus, when Emgality is prescribed for the treatment of cluster headache in adults, the duration of approval for initial starts will be 1 month and for continuation will be 12 months.

To avoid potential duplications in therapy, the criteria will screen for concurrent use with other CGRP receptor antagonists.

REFERENCES

SECTION 1

1. Vyepti [package insert]. Bothell, WA: Lundbeck Seattle BioPharmaceuticals, Inc.; October 2022.

SECTION 2

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Reference number(s)
5996-A

SPECIALTY GUIDELINE MANAGEMENT

VYJUVEK (beremagene geperpavec-svdt)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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]
Vyjuvek is indicated for the treatment of wounds in patients 6 months of age and older with dystrophic epidermolysis bullosa with mutation(s) in the collagen type VII alpha 1 chain (COL7A1) gene.

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. Medical records documenting clinical manifestations of disease.
   2. Genetic test results confirming a mutation in the COL7A1 gene.

III. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with a dermatologist or wound care specialist.

IV. CRITERIA FOR INITIAL APPROVAL

Dystrophic Epidermolysis Bullosa (DEB)
Authorization of 12 months may be granted for treatment of wounds in members with dystrophic epidermolysis bullosa (DEB) when all of the following criteria are met:
A. Member is 6 months of age and older.
B. Member has clinical manifestations of disease (e.g., extensive skin blistering, skin erosions, scarring).
C. Member has genetic test results confirming a mutation in the COL7A1 gene.
D. Member does not have a history of squamous cell carcinoma in the affected wound(s) that will receive treatment.
E. Vyjuvek will be administered once weekly to the affected wound(s) by a healthcare professional either at a healthcare professional setting (e.g., clinic) or a home setting.
F. Vyjuvek will not be administered to wound(s) that are currently healed.

V. REFERENCES

1. Vyjuvek [package insert]. Pittsburgh, PA: Krystal Biotech, Inc.; May 2023.
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POLICY Document for VYONDYS 53 (golodirsen)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, lower cost site of care and overall, clinically appropriate use. This document provides specific information to each of the three sections of the overall policy.

Section 1: Site of Care

- Policy information specific to site of care (outpatient, hospital outpatient, home infusion)

Section 2: Clinical Criteria

- Policy information specific to the clinical appropriateness for the medication

Section 1: Site of Care

CareFirst Site of Care Criteria
Administration of Intravenous Vyondys 53

POLICY

I. CRITERIA FOR APPROVAL FOR ADMINISTRATION IN OUTPATIENT HOSPITAL SETTING

This policy provides coverage for administration of Vyondys 53 in an outpatient hospital setting for up to 45 days when a member is new to therapy or reinitiating therapy after not being on therapy for at least 6 months.

This policy provides coverage for administration of Vyondys 53 in an outpatient hospital setting for a longer course of treatment when ANY of the following criteria are met:

A. The member has experienced an adverse reaction to the drug that did not respond to conventional interventions (eg, acetaminophen, steroids, diphenhydramine, fluids, other pre-medications or slowing of infusion rate) or a severe adverse event (anaphylaxis, anaphylactoid reactions, myocardial infarction, thromboembolism, or seizures) during or immediately after an infusion.
B. The member is medically unstable (eg respiratory, cardiovascular, or renal conditions).
C. The member has severe venous access issues that require the use of special interventions only available in the outpatient hospital setting.
D. The member has significant behavioral issues and/or physical or cognitive impairment that would impact the safety of the infusion therapy AND the patient does not have access to a caregiver.
E. The member is less than 14 years of age.

For situations where administration of Vyondys 53 does not meet the criteria for outpatient hospital infusion, coverage for Vyondys 53 is provided when administered in alternative sites such as; physician office, home infusion or ambulatory care.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the site of care prior authorization review (where applicable):

A. Medical records supporting the member has experienced an adverse reaction that did not respond to conventional interventions or a severe adverse event during or immediately after an infusion
B. Medical records supporting the member is medically unstable
C. Medical records supporting the member has severe venous access issues that requires specialized interventions only available in the outpatient hospital setting

D. Medical records supporting the member has behavioral issues and/or physical or cognitive impairment and no access to a caregiver

Section 2: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

VYONDYS 53 (golodirsen)

POLICY

III. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Vyondys 53 is indicated for the treatment of Duchenne muscular dystrophy (DMD) in patients who have a confirmed mutation of the DMD gene that is amenable to exon 53 skipping.

This indication is approved under accelerated approval based on an increase in dystrophin production in skeletal muscle observed in patients treated with Vyondys 53. Continued approval for this indication may be contingent upon verification of a clinical benefit in confirmatory trials.

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

IV. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
A. Initial requests: laboratory confirmation of Duchenne muscular dystrophy (DMD) diagnosis with a *DMD* gene mutation that is amenable to exon 53 skipping (refer to examples in Appendix).
B. Continuation of therapy requests: documentation (e.g., chart notes) of response to therapy.

V. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with a physician who specializes in the treatment of Duchenne muscular dystrophy (DMD).

VI. 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. Genetic testing was conducted to confirm the diagnosis of DMD and to identify the specific type of *DMD* gene mutation.
B. The *DMD* gene mutation is amenable to exon 53 skipping (refer to examples in Appendix).
C. Treatment with Vyondys 53 is initiated before the age of 16.
D. Member is able to achieve an average distance of at least 250 meters while walking independently over 6 minutes.

E. Member will not exceed a dose of 30 mg/kg once weekly.
F. The requested medication will not be used concomitantly with viltolarsen.

VII. 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 has demonstrated a response to therapy as evidenced by remaining ambulatory (e.g., able to walk with or without assistance, not wheelchair dependent).
B. The member will not exceed a dose of 30 mg/kg once weekly.
C. The requested medication will not be used concomitantly with viltolarsen.

VIII. APPENDIX

Examples of DMD gene mutations (exon deletions) amenable to exon 53 skipping (not an all-inclusive list):

1. Deletion of exon 52
2. Deletion of exon 45-52
3. Deletion of exon 47-52
4. Deletion of exon 48-52
5. Deletion of exon 49-52
6. Deletion of exon 50-52

REFERENCES

SECTION 1

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SECTION 2

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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

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Reference number(s)
5102-A

SPECIALTY GUIDELINE MANAGEMENT

VYVGART (efgartigimod alfa-fcab)
VYVGART HYTRULO (efgartigiomod alfa and hyaluronidase-qvfc)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Vyvgart and Vyvgart Hytrulo are indicated for the treatment of generalized myasthenia gravis (gMG) in adult patients who are anti-acetylcholine receptor (AChR) 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 chart notes, medical records, or claims history documenting:
   1. Positive anti-acetylcholine receptor (AChR) antibody test
   2. Clinical classification of myasthenia gravis score
   3. MG activities of daily living score
   4. Use of an acetylcholinesterase (AChE) inhibitor, steroid, or non-steroidal immunosuppressive therapy (NSIST)
B. For continuation requests: Chart notes or medical record documentation supporting positive clinical response.

III. CRITERIA FOR INITIAL APPROVAL

Generalized myasthenia gravis (gMG)
Authorization of 6 months may be granted for treatment of generalized myasthenia gravis (gMG) when all of the following criteria are met:
1. Anti-acetylcholine receptor (AChR) antibody positive
2. Myasthenia Gravis Foundation of America (MGFA) clinical classification II to IV
3. MG activities of daily living (MG-ADL) total score of 5 or more with at least 50% of the score due to non-ocular symptoms
4. On a stable dose of at least one of the following:
   a. Acetylcholinesterase inhibitors (e.g., pyridostigmine)
   b. Steroids (at least 3 months of treatment)
   c. Nonsteroidal immunosuppressive therapy (NSIST) (at least 6 months of treatment) (e.g., azathioprine, mycophenolate mofetil)

IV. CONTINUATION OF THERAPY

Authorization of 6 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 and member demonstrates a positive response to therapy (e.g., improvement in MG-ADL score, changes compared to baseline in Quantitative Myasthenia Gravis (QMG) total score).

V. REFERENCES

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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 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 (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; March 2021.
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Reference number(s)
1952-A

SPECIALTY GUIDELINE MANAGEMENT

WILATE (von Willebrand factor/coagulation factor VIII complex [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
   1. Wilate is indicated in children and adults with von Willebrand Disease (VWD) for:
      a. On-demand treatment and control of bleeding episodes
      b. Perioperative management of bleeding
   2. Wilate is indicated in adolescents and adults with hemophilia A for:
      a. Routine prophylaxis to reduce the frequency of bleeding episodes
      b. On-demand treatment and control of bleeding episodes

B. Compendial Use
   Acquired von Willebrand Syndrome

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

II. PRESCRIBER SPECIALTIES

Must be prescribed by or in consultation with a hematologist.

III. CRITERIA FOR INITIAL APPROVAL

A. Von Willebrand Disease
Authorization of 12 months may be granted for members with VWD when either of the following criteria is met:
1. Member has type 1, 2A, 2M, or 2N VWD and has had an insufficient response to desmopressin or a documented clinical reason for not using desmopressin (see Appendix B).
2. Member has type 2B or type 3 VWD.

B. Acquired von Willebrand Syndrome
Authorization of 12 months may be granted for treatment of acquired von Willebrand syndrome.

C. Hemophilia A
Authorization of 12 months may be granted for hemophilia A when the requested medication will be used for either of the following:

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).

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 is experiencing benefit from therapy (e.g., reduced frequency or severity of bleeds).

V. 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

*Factor assay levels are required to determine the diagnosis and are of value in monitoring treatment response.

Appendix B: Clinical Reasons For Not Utilizing Desmopressin in Patients with Hemophilia A and Type 1, 2A, 2M and 2N VWD

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. Severe type 1 von Willebrand disease
J. Stimate Nasal Spray is unavailable due to backorder/shortage issues (where applicable)

V. REFERENCES

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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. NSCLC, recurrent, advanced or metastatic ALK rearrangement-positive or ROS1 rearrangement-positive tumors
2. NSCLC, recurrent, advanced or metastatic MET exon 14 skipping positive tumors
3. NSCLC with high-level MET amplification
4. Inflammatory myofibroblastic tumor (IMT) with ALK translocation
5. Anaplastic large cell lymphoma, relapsed or refractory ALK-positive
6. 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.

C. Anaplastic Large Cell Lymphoma (ALCL)

Authorization of 12 months may be granted for treatment of relapsed or refractory ALK-positive ALCL as a single agent.

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 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)

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 2022 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed March 4, 2022.

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

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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.
3. 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.
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12. 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.
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.

POLICY Document for XOLAIR (omalizumab)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, lower cost site of care and overall, clinically appropriate use. This document provides specific information to each of the three sections of the overall policy.

Section 1: Site of Care

- Policy information specific to site of care (outpatient, hospital outpatient, home infusion)

Section 2: Clinical Criteria

- Policy information specific to the clinical appropriateness for the medication

Section 1: Site of Care

CareFirst Site of Care Criteria
Administration of Subcutaneous Xolair

POLICY

I. CRITERIA FOR APPROVAL FOR ADMINISTRATION IN OUTPATIENT HOSPITAL SETTING

This policy provides coverage for administration of Xolair* in an outpatient hospital setting for up to 60 days when a member is new to therapy or is reinitiating therapy after not being on therapy for 3 months or more. .

This policy provides coverage for administration of Xolair in an outpatient hospital setting for a longer course of treatment when ANY of the following criteria are met:

A. The member has experienced an adverse reaction to the medication that did not respond to conventional interventions (eg, acetaminophen, steroids, diphenhydramine, fluids or other pre-medications) or a severe adverse event (anaphylaxis, anaphylactoid reactions, myocardial infarction, thromboembolism, or seizures) during or immediately after administration.
B. The member is medically unstable (eg respiratory, cardiovascular, or renal conditions).
C. The member has significant behavioral issues and/or physical or cognitive impairment that would impact the safety of the administration AND the patient does not have access to a caregiver.
D. The member is less than 14 years of age.

For situations where administration of Xolair does not meet the criteria for outpatient hospital administration, coverage for Xolair is provided when administered in alternative specially certified sites such as; physician office or ambulatory care. Xolair reconstituted solution is not indicated for home administration.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the site of care prior authorization review (where applicable):

A. Medical records supporting the member has experienced an adverse reaction that did not respond to conventional interventions or a severe adverse event during or immediately after administration
B. Medical records supporting the member is medically unstable
C. interventions only available in the outpatient hospital setting

D. Medical records supporting the member has behavioral issues and/or physical or cognitive impairment and no access to a caregiver

Section 2: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

XOLAIR (omalizumab)

POLICY

III. INDICATIONS

The indications below including FDA-approved indications and compendial 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. Allergic asthma
      Xolair is indicated for patients 6 years of age and older with moderate to severe persistent asthma who have a positive skin test or in vitro reactivity to a perennial aeroallergen and whose symptoms are inadequately controlled with inhaled corticosteroids.

      Limitations of use: Xolair is not indicated for the relief of acute bronchospasm or status asthmaticus, or for treatment of other allergic conditions.

   2. Chronic spontaneous urticaria (CSU)
      Xolair is indicated for the treatment of adults and adolescents 12 years of age and older with chronic spontaneous urticaria (CSU) who remain symptomatic despite H1 antihistamine treatment.

      Limitations of use: Xolair is not indicated for treatment of other forms of urticaria.

   3. Nasal polyps
      Xolair is indicated for add-on maintenance treatment of nasal polyps in adult patients 18 years of age and older with inadequate response to nasal corticosteroids.

B. Compendial Uses
   1. Immune checkpoint inhibitor-related toxicities
   2. Systemic mastocytosis

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

IV. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
A. Asthma:
   1. Initial Requests:
      i. Member's chart or medical record showing pre-treatment IgE level
      ii. Chart notes, medical record documentation, or claims history supporting previous medications tried

2. Continuation requests: Chart notes or medical record documentation supporting improvement in asthma control.

B. CSU:
   1. Initial Requests: Member's chart or medical record documentation, or claims history supporting previous medications tried showing an inadequate treatment response to a second-generation H1 antihistamine
   2. Continuation Requests: Chart notes or medical record documentation supporting response to therapy

C. Nasal polyps:
   1. 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. Continuation Requests: Chart notes or medical record documentation supporting response to therapy

D. Immune checkpoint inhibitor-related toxicity (initial requests): Member's chart or medical record showing pre-treatment IgE level

E. Systemic mastocytosis (initial requests):
   1. Chart notes or medical record documentation supporting diagnosis of systemic mastocytosis
   2. Chart notes, medical record documentation, or claims history of prerequisite therapies (if applicable)

V. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with one of the following:

A. Asthma: allergist/immunologist or pulmonologist
B. Chronic spontaneous urticaria: allergist/immunologist or dermatologist
C. Nasal polyps: allergist/immunologist or otolaryngologist

VI. CRITERIA FOR INITIAL APPROVAL

A. Asthma

Authorization of 6 months may be granted for treatment of asthma when all of the following criteria are met:

1. Member is 6 years of age or older.
2. Member has a positive skin test or in vitro reactivity to at least one perennial aeroallergen.
3. Member has a pre-treatment IgE level greater than or equal to 30 IU/mL.
4. 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).
5. Member has inadequate asthma control despite current treatment with both of the following medications at optimized doses:
   i. Medium-to-high-dose inhaled corticosteroid
   ii. Additional controller (i.e., long acting beta$_2$-agonist, long acting muscarinic antagonist, leukotriene modifier, or sustained-release theophylline)
6. Member will continue to use maintenance asthma treatments (e.g., inhaled corticosteroid, additional controller) in combination with Xolair.
7. Member will not use Xolair concomitantly with other biologics indicated for asthma (e.g., Cinqair, Dupixent, Fasenra, Nucala, Tezspire).

B. Chronic spontaneous urticaria

Authorization of 6 months may be granted for treatment of chronic spontaneous urticaria when all of the following criteria are met:

1. Member is 12 years of age or older.
2. Member remains symptomatic despite treatment with up-dosing (in accordance with EAACI/GA^{2}LEN/EDF/WAO guidelines) of a second-generation H_1 antihistamine (e.g., cetirizine, fexofenadine, levocetirizine, loratadine) for at least 2 weeks.
3. Member has been evaluated for other causes of urticaria, including bradykinin-related angioedema and interleukin-1-associated urticarial syndromes (auto-inflammatory disorders, urticarial vasculitis).
4. Member has experienced a spontaneous onset of wheals, angioedema, or both, for at least 6 weeks.

C. Nasal polyps

Authorization of 6 months may be granted for treatment of nasal polyps when all of the following criteria are met:

1. Member is 18 years of age or older.
2. Member has bilateral nasal polyps and chronic symptoms of sinusitis despite intranasal corticosteroid treatment for at least 2 months unless contraindicated or not tolerated.
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 Xolair, unless contraindicated or not tolerated.
6. Member will not use Xolair concomitantly with other biologics indicated for nasal polyps (e.g., Dupixent, Nucala).

D. Immune checkpoint inhibitor-related toxicity

Authorization of 1 month may be granted for treatment of immune checkpoint inhibitor-related toxicity when both of the following are met:

1. The member has a refractory case of immune-therapy related severe (G3) pruritus
2. The member has elevated IgE levels

E. Systemic mastocytosis

Authorization of 12 months may be granted for the treatment of systemic mastocytosis when both of the following are met:

1. The major and at least one minor diagnostic criterion for systemic mastocytosis are present or three or more minor diagnostic criteria are present (see Appendix)
2. Xolair will be used in any of the following treatment settings:
   i. Used as stepwise prophylactic treatment for chronic mast cell mediator-related cardiovascular and pulmonary symptoms when the member has tried both of the following:
      a. H1 blockers and H2 blockers
      b. Corticosteroids
   ii. Used for prevention of recurrent unprovoked anaphylaxis
   iii. Used for prevention of hymenoptera or food-induced anaphylaxis, with negative specific IgE or negative skin test
   iv. Used to improve tolerability of venom immunotherapy

VII. CONTINUATION OF THERAPY

A. Asthma

Authorization of 12 months may be granted for continuation of treatment of asthma when all of the following criteria are met:

1. Member is 6 years of age or older.
2. Asthma control has improved on Xolair 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[9]
3. Member will continue to use maintenance asthma treatments (e.g., inhaled corticosteroid, additional controller) in combination with Xolair.
4. Member will not use Xolair concomitantly with other biologics indicated for asthma (e.g., Cinqair, Dupixent, Fasenra, Tezspire, Nucala).

B. Chronic spontaneous urticaria

Authorization of 12 months may be granted for continuation of treatment of chronic spontaneous urticaria when all of the following criteria are met:

1. Member is 12 years of age or older.
2. Member has experienced a response (e.g., improved symptoms, decrease in weekly urticaria activity score [UAS7]) since initiation of therapy.

C. Nasal polyps

Authorization of 12 months may be granted for continuation of treatment of nasal polyps when all of the following criteria are met:

1. Member is 18 years of age or older.
2. Member has experienced a response as evidenced by improvement in signs and symptoms (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).
3. Member will not use Xolair concomitantly with other biologics indicated for nasal polyps (e.g., Dupixent, Nucala).

D. Immune checkpoint inhibitor-related toxicities and systemic mastocytosis

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

VIII. OTHER

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.

IX. APPENDIX

2017 WHO Diagnostic Criteria for Systemic Mastocytosis

A. Major Criteria: multifocal, dense infiltrates of mast cells (at least 15 mast cells in aggregates) detected in sections of bone marrow and/or other extracutaneous organs
B. Minor Criteria
   1. In biopsy sections of bone marrow or other extracutaneous organs, greater than 25% of mast cells in the infiltrate are spindle-shaped or have atypical morphology, or greater than 25% of all mast cells in bone marrow aspirate smears are immature or atypical
   2. Detection of an activating point mutation at codon 816 of *KIT* in the bone marrow, blood, or another extracutaneous organ

3. Mast cells in bone marrow, blood, or other extracutaneous organs express CD25, with or without CD2, in addition to normal mast cell markers
4. Serum total tryptase persistently greater than 20 ng/mL (unless there is an associated myeloid neoplasm, in which case this parameter is not valid)

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10. ClinicalTrials.gov. National Library of Medicine (US). Identifier NCT03280537, A Clinical Trial of Omalizumab in Participants with Chronic Rhinosinusitis with Nasal Polyps (POLYP 2) 2017 Sep 12. Available from: https://clinicaltrials.gov/ct2/show/NCT03280537.
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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.
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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.

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
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 the treatment of multiple myeloma in any of the following settings:
1. The requested medication will be used in combination with dexamethasone 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 in combination with bortezomib and dexamethasone in members who have received at least one prior therapy.
3. The requested medication will be used in combination with daratumumab and dexamethasone in members who have received at least one prior therapy.
4. The requested medication will be used in combination with carfilzomib and dexamethasone when the member has relapsed or progressive disease.

5. The requested medication will be used in combination with pomalidomide and dexamethasone in members who have received at least two prior therapies, including an immunomodulatory agent and a proteasome inhibitor.

B. Diffuse Large B-Cell Lymphoma
Authorization of 12 months may be granted for the treatment of relapsed or refractory diffuse large B-cell lymphoma (DLBCL), not otherwise specified, including DLBCL arising from follicular lymphoma, as a single agent when the member has received at least 2 prior lines of systemic 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. Xpovio [package insert]. Newton, MA: Karyopharm Therapeutics Inc.; April 2021.
2. The NCCN Drugs & Biologics Compendium® 2022 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed January 12, 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.

FDA-Approved Indications
Xtandi is indicated for the treatment of patients with:
A. Castration-resistant prostate cancer (CRPC)
B. Metastatic castration-sensitive prostate cancer (mCSPC)

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 analog.

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 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. Xtandi [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 July 6, 2022.

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.
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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

1. Xywav is indicated for the treatment of cataplexy or excessive daytime sleepiness (EDS) in patients 7 years of age and older with narcolepsy.
2. Xywav is indicated for the treatment of idiopathic hypersomnia 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 RESTRICTION

This medication must be prescribed by or in consultation with a sleep specialist.

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 (amphetamine, dextroamphetamine, methylphenidate) OR
   ii. The member has a contraindication to at least one central nervous system (CNS) stimulant (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.; August 2021.
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 11, 2022.
4. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. http://www.micromedexsolutions.com/. Accessed March 11, 2022.
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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.

DOCUMENT HISTORY

Created:	Specialty Clinical Development (RZ/FS) 07/2020
Revised:	LP 03/2021, 08/2021 (IH), CM 02/2022 (added documentation requirements and updated cataplexy episode requirement), 03/2022 (annual), 07/2022 (CPO recommendation)
Reviewed:	CHART/ 08/06/2020, 03/25/2021, 09/02/2021, 10/07/2021, 02/24/2022, 03/31/2022, 08/03/2022
External Review:	05/2021, 09/2021, 06/2022

POLICY Document for YERVOY (ipilimumab)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, and overall, clinically appropriate use. This document provides specific information to both sections of the overall policy.

Section 1: Site of Care
- Policy information specific to site of care (outpatient, hospital outpatient, home infusion)

Section 2: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 3: Oncology Clinical Policy
- Policy information specific to regimen review per NCCN Guidelines.

Section 1: Site of Care

CareFirst Site of Care Criteria
Administration of Intravenous Checkpoint Inhibitors
Bavencio, Imfinzi, Jemperli, Keytruda, Libtayo, Opdivo, Opdualag, Tecentriq, Yervoy and Zynyz

POLICY

I. CRITERIA FOR APPROVAL FOR ADMINISTRATION IN OUTPATIENT HOSPITAL SETTING

This policy provides coverage for administration of a checkpoint inhibitor in an outpatient hospital setting for the initial 6 months approval and up to 45 days for renewal of therapy.

This policy provides coverage for administration of a checkpoint inhibitor in an outpatient hospital setting for a longer course of treatment when ANY of the following criteria are met:

A. The member has experienced an adverse reaction that did not respond to conventional interventions (eg, acetaminophen, steroids, diphenhydramine, fluids, other pre-medications or slowing of infusion rate) or a severe adverse event (anaphylaxis, anaphylactoid reactions, myocardial infarction, thromboembolism, or seizures) during or immediately after an infusion or has experienced severe toxicity requiring continuous monitoring (e.g. Grade 2-4 bullous dermatitis, transaminitis, pneumonitis, Stevens-Johnson syndrome, acute pancreatitis, primary adrenal insufficiency aseptic meningitis, encephalitis, transverse myelitis, myocarditis, pericarditis, arrhythmias, impaired ventricular function, conduction abnormalities).
B. The member is medically unstable (eg respiratory, cardiovascular, or renal conditions).
C. The member has severe venous access issues that require the use of a special interventions only available in the outpatient hospital setting.
D. The member has significant behavioral issues and/or physical or cognitive impairment that would impact the safety of the infusion therapy AND the patient does not have access to a caregiver.
E. The member is receiving provider administered combination chemotherapy.
F. The member is less than 14 years of age.

For situations where administration of a checkpoint inhibitor does not meet the criteria for outpatient hospital infusion, coverage for a checkpoint inhibitor is provided when administered in alternative sites such as physician office, home infusion or ambulatory care.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the site of care prior authorization review (where applicable):

A. Medical records supporting the member has experienced an adverse reaction that did not respond to conventional interventions or a severe adverse event during or immediately after an infusion or a severe toxicity requiring continuous monitoring
B. Medical records supporting the member is medically unstable
C. Medical records supporting the member has severe venous access issues that require specialized interventions only available in the outpatient hospital setting
D. Medical records supporting the member has behavioral issues and/or physical or cognitive impairment and no access to a caregiver
E. Medical records supporting the member is receiving provider administered combination therapy.

Section 2: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

YERVOY (ipilimumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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. Unresectable or Metastatic Melanoma
   Yervoy is indicated as a single agent or in combination with nivolumab for the treatment of unresectable or metastatic melanoma in adult and pediatric patients 12 years and older.

2. Adjuvant Treatment of Melanoma
   Yervoy is indicated for the adjuvant treatment of adult patients with cutaneous melanoma with pathologic involvement of regional lymph nodes of more than 1 mm who have undergone complete resection, including total lymphadenectomy.

3. Advanced Renal Cell Carcinoma
   Yervoy, in combination with nivolumab, is indicated for the first-line treatment of adult patients with intermediate or poor risk advanced renal cell carcinoma (RCC).

4. Microsatellite Instability-High (MSI-H) or Mismatch Repair Deficient (dMMR) Metastatic Colorectal Cancer
   Yervoy, in combination with nivolumab, is indicated for the treatment of adult and pediatric patients 12 years of age and older with microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) metastatic colorectal cancer (CRC) that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan.

5. Hepatocellular Carcinoma
   Yervoy, in combination with nivolumab, is indicated for the treatment of adult patients with hepatocellular carcinoma who have been previously treated with sorafenib.

6. Metastatic Non-small Cell Lung Cancer
   a. Yervoy, in combination with nivolumab, is indicated for the first-line treatment of adult patients with metastatic non-small cell lung cancer (NSCLC) whose tumors express PD-L1 (≥1%) as determined by an FDA-approved test, with no EGFR or ALK genomic tumor aberrations.

b. Yervoy, in combination with nivolumab and 2 cycles of platinum-doublet chemotherapy, is indicated for the first-line treatment of adult patients with metastatic or recurrent non-small cell lung cancer with no EGFR or ALK genomic tumor aberrations.

7. Malignant Pleural Mesothelioma
   Yervoy, in combination with nivolumab, is indicated for the first-line treatment of adult patients with unresectable malignant pleural mesothelioma.

8. Esophageal Cancer
   Yervoy, in combination with nivolumab, is indicated for the first-line treatment of adult patients with unresectable advanced or metastatic esophageal squamous cell carcinoma (ESCC).

B. Compendial Uses
1. Cutaneous melanoma
2. Uveal melanoma
3. Central nervous system (CNS) brain metastases
4. Non-small cell lung cancer
5. Renal cell carcinoma
6. Colorectal cancer, including appendiceal adenocarcinoma and anal adenocarcinoma
7. Malignant pleural mesothelioma
8. Malignant peritoneal mesothelioma
9. Hepatocellular carcinoma
10. Small bowel adenocarcinoma
11. Ampullary adenocarcinoma
12. Esophageal/Esophagogastric Junction Cancers
13. Kaposi Sarcoma
14. Bone Cancer
15. Biliary Tract Cancers
    a. Cholangiocarcinoma
    b. Gallbladder Cancer
16. Soft Tissue Sarcoma
    a. Extremity/body wall sarcoma
    b. Head/neck sarcoma
    c. Retroperitoneal/intra-abdominal sarcoma
    d. Rhabdomyosarcoma
    e. Angiosarcoma
17. Merkel Cell Carcinoma

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 MSI-H or mismatch repair deficient (dMMR) tumor status, where applicable.
B. Documentation of molecular testing for EGFR exon 19 deletions or exon 21 L858R mutations and ALK rearrangements, where applicable

III. CRITERIA FOR INITIAL APPROVAL

A. Cutaneous Melanoma

Authorization of 6 months may be granted for treatment of cutaneous melanoma in any of the following settings:
1. The requested medication will be used as a single agent or in combination with nivolumab (for 4 doses followed by nivolumab as a single agent) for progressive, metastatic or unresectable disease.

2. The requested medication will be used as a single agent or in combination with nivolumab as adjuvant treatment of stage III or IV disease if no evidence of disease following metastasis-directed therapy (i.e., complete resection).
3. The requested medication will be used as subsequent therapy at a low dose in combination with pembrolizumab, or nivolumab for metastatic or unresectable disease in members who progressed on single-agent anti-programmed death 1 (PD-1) immunotherapy or BRAF-targeted therapy.
4. The requested medication will be used as a single agent for limited resectable local recurrence after prior anti-PD-1 therapy.

B. Uveal Melanoma
Authorization of 6 months may be granted as a single agent or in combination with nivolumab for treatment of uveal melanoma for distant metastatic disease.

C. CNS Brain Metastases
Authorization of 6 months may be granted as a single agent or in combination with nivolumab for treatment of CNS brain metastases in members with melanoma.

D. Non-Small Cell Lung Cancer (NSCLC)
Authorization of 6 months may be granted for treatment of recurrent, advanced or metastatic non-small cell lung cancer if there are no EGFR exon 19 deletions or exon 21 L858R mutations or ALK rearrangements (unless testing is not feasible due to insufficient tissue) and the requested medication will be used in a regimen containing nivolumab.

E. Renal Cell Carcinoma
Authorization of 6 months may be granted for treatment of renal cell carcinoma in combination with nivolumab (for 4doses, followed by single agent nivolumab) for relapsed, advanced, or stage IV disease with clear cell histology as:
1. First-line therapy for poor or intermediate risk.
2. First-line therapy for favorable risk.
3. Subsequent therapy.

F. Colorectal Cancer
Authorization of 6 months may be granted for treatment of colorectal cancer, including appendiceal adenocarcinoma and anal adenocarcinoma, for microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) tumors when used in combination with nivolumab (for 4 doses followed by nivolumab as a single agent) for advanced, metastatic, unresectable, or inoperable disease.

G. Malignant Pleural or Peritoneal Mesothelioma
Authorization of 6 months may be granted in combination with nivolumab for treatment of malignant pleural or peritoneal mesothelioma, including pericardial mesothelioma and tunica vaginalis testis mesothelioma.

H. Hepatocellular Carcinoma
Authorization of 6 months may be granted as a single agent or in combination with nivolumab (for 4 doses followed by nivolumab as a single agent) for treatment of hepatocellular carcinoma.

I. Small Bowel Adenocarcinoma
Authorization of 6 months may be granted in combination with nivolumab for treatment of advanced or metastatic small bowel adenocarcinoma for microsatellite-instability high (MSI-H) or mismatch repair deficient (dMMR) tumors.

J. Ampullary Adenocarcinoma
Authorization of 6 months may be granted in combination with nivolumab for treatment of progressive, unresectable, or metastatic microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) ampullary adenocarcinoma.

K. Esophageal and Esophagogastric Junction Cancers
Authorization of 6 months may be granted in combination with nivolumab for the first-line treatment of unresectable locally advanced, recurrent or metastatic esophageal squamous cell carcinoma (ESCC).

L. Kaposi Sarcoma
Authorization of 6 months may be granted in combination with nivolumab for subsequent treatment of relapsed/refractory classic Kaposi Sarcoma.

M. Bone Cancer
Authorization of 6 months may be granted in combination with nivolumab for unresectable or metastatic disease when all of the following are met:
1. Disease has tumor mutation burden-high (TMB-H) [≥10 mutations/megabase (mut/Mb)] tumors
2. Disease has progressed following prior treatment and has no satisfactory alternative treatment options

N. Biliary Tract Cancer (Cholangiocarcinoma and Gallbladder Cancer)
Authorization of 6 months may be granted as subsequent treatment in combination with nivolumab for unresectable or resected gross residual (R2) disease, progressive or metastatic disease that is tumor mutation burden-high (TMB-H).

O. Soft Tissue Sarcoma
Authorization of 6 months may be granted in combination with nivolumab for treatment of extremity/body wall sarcomas, head/neck sarcomas and retroperitoneal/intra-abdominal sarcomas, rhabdomyosarcoma and angiosarcoma.

P. Merkel Cell Carcinoma
Authorization of 6 months may be granted in combination with nivolumab for treatment of progressive, unresectable, recurrent, or stage IV Merkel cell carcinoma.

IV. CONTINUATION OF THERAPY

A. Adjuvant Treatment of Melanoma
Authorization of 6 months may be granted (up to 3 years) for continued treatment in members requesting reauthorization for adjuvant melanoma when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

B. Cutaneous Melanoma, Renal Cell Carcinoma, Colorectal Cancer, Hepatocellular Cancer
Authorization of 6 months may be granted (up to 4 doses maximum, if member has not already received 4 doses) for continued treatment in members requesting reauthorization for cutaneous melanoma, renal cell carcinoma, colorectal cancer, and hepatocellular cancer when treatment guidelines do not specify a limited number of total doses (see above) and there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

C. Non-Small Cell Lung Cancer, Esophageal/Esophagogastric Junction Cancers, or Malignant Pleural Mesothelioma
Authorization of 6 months may be granted (up to 24 months total) for continued treatment in members requesting reauthorization for non-small cell lung cancer, esophageal cancer, or malignant pleural mesothelioma, including pericardial mesothelioma and tunica vaginalis testis mesothelioma subtypes, when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

D. All Other Indications
Authorization of 6 months may be granted for continued treatment in members requesting reauthorization for all other indications listed in Section III when treatment guidelines do not specify a limited number of total

doses (see above) and there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

Section 3: Oncology Clinical Policy

PROGRAM DESCRIPTION

The National Comprehensive Care Network® (NCCN®) is an alliance of leading cancer centers devoted to patient care, research and education dedicated to improving the quality, effectiveness, and efficiency of cancer care so patients can live better lives.[1] It is comprised of oncology experts who convene regularly to establish the best treatments for patients. NCCN develops various resources for use by stakeholders in the health care delivery system. These resources include, but are not limited to, the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®), the NCCN Drugs & Biologics Compendium (NCCN Compendium®) and the NCCN Chemotherapy Order Templates (NCCN Templates®).

NCCN Templates® are based on NCCN Guidelines® and NCCN Compendium®. The NCCN Compendium lists the appropriate drugs and biologics as treatment options for specific cancers using U.S. Food and Drug Administration (FDA)-approved disease indications and specific NCCN panel recommendations. Each recommendation is supported by a level of evidence category.

NCCN Categories of Evidence and Consensus[2]

- Category 1: Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
- Category 2A: Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
- Category 2B: Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.
- Category 3: Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

POLICY

Policy for Regimen Prior Authorization
A regimen prior authorization allows submission of a single prior authorization request for all oncology drugs or biologics within an NCCN template that require prior authorization.

PROCEDURE

This policy provides coverage of a regimen review when all of the following criteria are met:
1. Regimen prior authorization reviews, based on NCCN templates, are initiated through the provider portal.
   - If the prior authorization request is submitted via phone or fax, each drug or biologic will need to be submitted and reviewed as a separate prior authorization request for review with drug-specific criteria.
2. The prior authorization review is requested for an oncology drug or biologic.
3. The member is eligible for regimen review.
4. The indication is for a cancer that is eligible for regimen review. Currently, the cancer types in scope for regimen review include the following:
   - Ampullary Adenocarcinoma
   - Anal Carcinoma
   - B-Cell Lymphomas
   - Basal Cell Skin Cancer
   - Biliary Tract Cancers
   - Bone Cancer
   - Breast Cancer
   - Bladder Cancer
   - Central Nervous System Cancers

- Cervical Cancer
- Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma
- Chronic Myeloid leukemia
- Colon Cancer
- Dermatofibrosarcoma Protuberans
- Esophageal Cancer
- Gastric Cancer
- Gastrointestinal Stromal Tumors
- Gestational Trophoblastic Neoplasms
- Hairy Cell Leukemia
- Head and Neck Cancers
- Hodgkin Lymphoma
- Hepatocellular Carcinoma
- Kaposi Sarcoma
- Kidney Cancer
- Melanoma: Cutaneous
- Melanoma: Uveal
- Merkel Cell Carcinoma
- Mesothelioma: Peritoneal
- Mesothelioma: Pleural
- Myelodysplastic Syndromes
- Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Gene Fusions
- Myeloproliferative Neoplasms
- Neuroendocrine and Adrenal Tumors
- Non-Small Cell Lung Cancer
- Occult Primary
- Ovarian Cancer
- Pancreatic Cancer
- Penile Cancer
- Prostate Cancer
- Rectal Cancer
- Small Bowl Adenocarcinoma
- Small Cell Lung Cancer
- Soft Tissue Sarcoma
- Squamous Cell Skin Cancer
- Systemic Mastocytosis
- Systemic Light Chain Amyloidosis
- Testicular Cancer
- Thymomas and Thymic Carcinomas
- Thyroid Carcinoma
- Uterine Neoplasms
- Vulvar Cancer
- Waldenström Macroglobulinemia / Lymphoplasmacytic Lymphoma

In addition, the following criteria must be met for approval:

1. The requested regimen for the drug(s) or biologic(s) and indication is consistent with an NCCN recommendation with a level of evidence category of 1 or 2A.
2. The NCCN template must be accepted by the provider without modification.

Further review may be indicated when the above criteria are not met.

Authorizations may be granted for 12 months or as medically required, based on the member's condition and provider's assessment.

Supportive Care: Myeloid Growth Factor Therapy

Granulocyte colony stimulating factors are recommended for primary prophylaxis based on the febrile neutropenia risk of

the chemotherapy regimen. Febrile neutropenia risk levels vary by NCCN Chemotherapy Order template and are listed at the top of the template. Regimens associated with a high or intermediate risk of febrile neutropenia may include a granulocyte colony stimulating factor as part of the prior authorization.

Continuation of Therapy
To submit a request for continuation of therapy, a new regimen prior authorization review must be requested. Upon template selection, the template must be modified to include the appropriate therapies being used for maintenance treatment. The regimen request will be submitted for further review.

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

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5. National Comprehensive Cancer Network. NCCN Chemotherapy Order Templates (NCCN Templates) website. https://www.nccn.org/compendia-templates/nccn-templates-main/browse-by-cancer-type, accessed June 6, 2023. (Note: A subscription may be required.)

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.

FDA-Approved Indication
Yonsa is indicated in combination with methylprednisolone for the treatment of patients with metastatic castration-resistant prostate cancer (CRPC).

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 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. Yonsa [package insert]. Cranbury, NJ: Sun Pharmaceutical Industries, Inc.; March 2021.
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POLICY Document for ZALTRAP (ziv-aflibercept)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, and overall, clinically appropriate use. This document provides specific information to both sections of the overall policy.

Section 1: Clinical Criteria

- Policy information specific to the clinical appropriateness for the medication

Section 2: Oncology Clinical Policy

- Policy information specific to regimen review per NCCN Guidelines.

Section 1: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

ZALTRAP (ziv-aflibercept)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Zaltrap is indicated for use in combination with 5-fluorouracil, leucovorin, and irinotecan (FOLFIRI) in patients with metastatic colorectal cancer (mCRC) that is resistant to or has progressed following an oxaliplatin-containing regimen.

B. Compendial Uses
1. Colorectal cancer with unresectable metachronous metastases and previous adjuvant FOLFOX (fluorouracil, leucovorin, and oxaliplatin) or CapeOX (capecitabine and oxaliplatin) within the past 12 months, as initial treatment in combination with irinotecan or FOLFIRI (fluorouracil, leucovorin, and irinotecan)
2. Colorectal cancer (including anal adenocarcinoma and appendiceal adenocarcinoma), advanced or metastatic disease in combination with irinotecan or with FOLFIRI regimen not previously treated with irinotecan-based therapy, as subsequent therapy for disease progression

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

II. CRITERIA FOR INITIAL APPROVAL

Colorectal cancer (CRC)
Authorization of 12 months may be granted for treatment of advanced or metastatic CRC, including anal adenocarcinoma and appendiceal adenocarcinoma, in combination with 5-fluorouracil, leucovorin, and irinotecan (FOLFIRI) or in combination with irinotecan.

III. CONTINUATION OF THERAPY

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

Section 2: Oncology Clinical Policy

PROGRAM DESCRIPTION

The National Comprehensive Care Network® (NCCN®) is an alliance of leading cancer centers devoted to patient care, research and education dedicated to improving the quality, effectiveness, and efficiency of cancer care so patients can live better lives.[1] It is comprised of oncology experts who convene regularly to establish the best treatments for patients. NCCN develops various resources for use by stakeholders in the health care delivery system. These resources include, but are not limited to, the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®), the NCCN Drugs & Biologics Compendium (NCCN Compendium®) and the NCCN Chemotherapy Order Templates (NCCN Templates®).

NCCN Templates® are based on NCCN Guidelines® and NCCN Compendium®. The NCCN Compendium lists the appropriate drugs and biologics as treatment options for specific cancers using U.S. Food and Drug Administration (FDA)-approved disease indications and specific NCCN panel recommendations. Each recommendation is supported by a level of evidence category.

NCCN Categories of Evidence and Consensus[2]

• Category 1: Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
• Category 2A: Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
• Category 2B: Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.
• Category 3: Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

POLICY

Policy for Regimen Prior Authorization
A regimen prior authorization allows submission of a single prior authorization request for all oncology drugs or biologics within an NCCN template that require prior authorization.

PROCEDURE

This policy provides coverage of a regimen review when all of the following criteria are met:
1. Regimen prior authorization reviews, based on NCCN templates, are initiated through the provider portal.
   - If the prior authorization request is submitted via phone or fax, each drug or biologic will need to be submitted and reviewed as a separate prior authorization request for review with drug-specific criteria.
2. The prior authorization review is requested for an oncology drug or biologic.
3. The member is eligible for regimen review.
4. The indication is for a cancer that is eligible for regimen review. Currently, the cancer types in scope for regimen review include the following:
   - o Ampullary Adenocarcinoma
   - o Anal Carcinoma
   - o B-Cell Lymphomas

- Basal Cell Skin Cancer
- Biliary Tract Cancers
- Bone Cancer
- Breast Cancer
- Bladder Cancer
- Central Nervous System Cancers
- Cervical Cancer
- Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma
- Chronic Myeloid leukemia
- Colon Cancer
- Dermatofibrosarcoma Protuberans
- Esophageal Cancer
- Gastric Cancer
- Gastrointestinal Stromal Tumors
- Gestational Trophoblastic Neoplasms
- Hairy Cell Leukemia
- Head and Neck Cancers
- Hodgkin Lymphoma
- Hepatocellular Carcinoma
- Kaposi Sarcoma
- Kidney Cancer
- Melanoma: Cutaneous
- Melanoma: Uveal
- Merkel Cell Carcinoma
- Mesothelioma: Peritoneal
- Mesothelioma: Pleural
- Myelodysplastic Syndromes
- Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Gene Fusions
- Myeloproliferative Neoplasms
- Neuroendocrine and Adrenal Tumors
- Non-Small Cell Lung Cancer
- Occult Primary
- Ovarian Cancer
- Pancreatic Cancer
- Penile Cancer
- Prostate Cancer
- Rectal Cancer
- Small Bowl Adenocarcinoma
- Small Cell Lung Cancer
- Soft Tissue Sarcoma
- Squamous Cell Skin Cancer
- Systemic Mastocytosis
- Systemic Light Chain Amyloidosis
- Testicular Cancer
- Thymomas and Thymic Carcinomas
- Thyroid Carcinoma
- Uterine Neoplasms
- Vulvar Cancer
- Waldenström Macroglobulinemia / Lymphoplasmacytic Lymphoma

In addition, the following criteria must be met for approval:

1. The requested regimen for the drug(s) or biologic(s) and indication is consistent with an NCCN recommendation with a level of evidence category of 1 or 2A.
2. The NCCN template must be accepted by the provider without modification.

Further review may be indicated when the above criteria are not met.

Authorizations may be granted for 12 months or as medically required, based on the member's condition and provider's assessment.

Supportive Care: Myeloid Growth Factor Therapy
Granulocyte colony stimulating factors are recommended for primary prophylaxis based on the febrile neutropenia risk of the chemotherapy regimen. Febrile neutropenia risk levels vary by NCCN Chemotherapy Order template and are listed at the top of the template. Regimens associated with a high or intermediate risk of febrile neutropenia may include a granulocyte colony stimulating factor as part of the prior authorization.

Continuation of Therapy
To submit a request for continuation of therapy, a new regimen prior authorization review must be requested. Upon template selection, the template must be modified to include the appropriate therapies being used for maintenance treatment. The regimen request will be submitted for further review.

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

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POLICY Document for ZELBORAF (vemurafenib)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, and overall, clinically appropriate use. This document provides specific information to both sections of the overall policy.

Section 1: Clinical Criteria

- Policy information specific to the clinical appropriateness for the medication

Section 2: Oncology Clinical Policy

- Policy information specific to regimen review per NCCN Guidelines.

Section 1: Clinical Criteria

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.

Section 2: Oncology Clinical Policy

Oncology Clinical Policy

Program Description

The National Comprehensive Care Network® (NCCN®) is an alliance of leading cancer centers devoted to patient care, research and education dedicated to improving the quality, effectiveness and efficiency of cancer care so patients can live better lives.[1] It is comprised of oncology experts who convene regularly to establish the best treatments for patients. NCCN develops various resources for use by stakeholders in the health care delivery system. These resources include, but are not limited to, the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®), the NCCN Drugs & Biologics Compendium (NCCN Compendium®) and the NCCN Chemotherapy Order Templates (NCCN Templates®).

NCCN templates are based on NCCN Clinical Practice Guidelines and NCCN Compendium. The NCCN Compendium lists the appropriate drugs and biologics for specific cancers using U.S. Food and Drug Administration (FDA)-approved disease indications and specific NCCN panel recommendations. Each recommendation is supported by a level of evidence category.

NCCN Categories of Evidence and Consensus

Category 1: Based on high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2A: Based on lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2B: Based on lower-level evidence, there is NCCN consensus that the intervention is appropriate.
Category 3: Based any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

Policy for Regimen Prior Authorization

A regimen prior authorization allows submission of a single prior authorization request for all oncology drugs or biologics within an NCCN template that require prior authorization.

This policy provides coverage of a regimen review when *all* of the following criteria are met:

a. Regimen prior authorization reviews, based on NCCN templates, are initiated through the provider portal: https://provider.carefirst.com/providers/home.page
b. If the prior authorization request is submitted via phone or fax, each drug or biologic will need to be submitted and reviewed as a separate prior authorization request for review with drug-specific criteria.
c. 2. The prior authorization review is requested for an oncology drug or biologic that requires prior authorization on the medical benefit.
d. The indication is for a cancer that is eligible for regimen review. Currently, the cancer types in scope for regimen review include breast, lung, colon and rectal cancer.
e. The member is eligible for regimen review.

In addition, the following criteria must be met for approval:

a. The requested regimen for the drug(s) or biologic(s) and indication is consistent with an NCCN recommendation with a level of evidence category of 1 or 2A.
b. The NCCN template must be accepted by the provider without modification.

Authorizations may be granted for 12 months.
Further review may be indicated where the above criteria are not met.

Continuation of Therapy

To submit a request for continuation of therapy, a new regimen prior authorization review must be requested. Upon template selection, the template must be modified to include the appropriate therapies being used for maintenance treatment. The regimen request will be submitted for further review.

Dosage and Administration

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

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SECTION 1

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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.

SECTION 2

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2. National Comprehensive Cancer Network. NCCN Categories of Evidence and Consensus website. https://www.nccn.org/professionals/physician_gls/categories_of_consensus.aspx, accessed September 16, 2019.
3. National Comprehensive Cancer Network. NCCN Guidelines website. http://www.nccn.org/professionals/physician_gls/f_guidelines.asp, accessed September 16, 2019. *(Note: An account may be required.)*
4. National Comprehensive Cancer Network. NCCN Drugs and Biologics Compendium® website. http://www.nccn.org/professionals/drug_compendium/content/contents.asp, accessed September 16, 2019. *(Note: A subscription may be required.)*
5. National Comprehensive Cancer Network. NCCN Chemotherapy Order Templates (NCCN Templates) website. https://www.nccn.org/professionals/OrderTemplates/Default.aspx, accessed September 16, 2019. *(Note: A subscription may be required.)*

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)
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. Zeposia 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.
B. Zeposia is indicated for the 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:

Ulcerative colitis (UC):

A. 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.
B. Continuation requests: Chart notes or medical record documentation supporting positive clinical response to therapy or remission.

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) when Zeposia will not be used concomitantly with other disease modifying multiple sclerosis agents (Note: Ampyra and Nuedexta are not disease modifying).

B. Clinically Isolated Syndrome

Authorization of 12 months may be granted to members for the treatment of clinically isolated syndrome of multiple sclerosis when Zeposia will not be used concomitantly with other disease modifying multiple sclerosis agents (Note: Ampyra and Nuedexta are not disease modifying).

C. Moderately to Severely Active Ulcerative Colitis

Authorization of 12 months may be granted for the treatment of moderately severely active ulcerative colitis when both of the following are met:

1. The member meets one of the following:

a. Member has previously received a biologic or targeted synthetic drug (e.g., Xeljanz) indicated for moderately to severely active ulcerative colitis.
b. Member has had an inadequate response, intolerance or contraindication to at least one conventional therapy option (See Appendix).

2. Zeposia will not be used concomitantly with immunomodulators, biologic therapy, or targeted synthetic drugs.

IV. CONTINUATION OF THERAPY

A. Relapsing Forms of Multiple Sclerosis and Clinically Isolated Syndrome

Authorization of 12 months may be granted when both of the following are met:

1. The member is experiencing disease stability or improvement while receiving Zeposia.
2. Zeposia will not be used concomitantly with other disease modifying multiple sclerosis agents (Note: Ampyra and Nuedexta are not disease modifying).

B. Moderately to Severely Active Ulcerative Colitis

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 when both of the following are met:

1. The member meets one of the following:
   a. The member has achieved or maintained remission.
   b. The member has achieved or maintained 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)
2. Zeposia will not be used concomitantly with immunomodulators, biologic therapy, or targeted synthetic drugs.

V. APPENDIX

Examples of Conventional Therapy Options for Ulcerative Colitis

1. Mild to moderate disease – induction of remission:
   a. Oral mesalamine (e.g., Asacol, Asacol HD, Lialda, Pentasa), balsalazide, olsalazine
   b. Rectal mesalamine (e.g., Canasa, Rowasa)
   c. Rectal hydrocortisone (e.g., Colocort, Cortifoam)
   d. Alternatives: prednisone, azathioprine, mercaptopurine, sulfasalazine
2. Mild to moderate disease – maintenance of remission:
   a. Oral mesalamine, balsalazide, olsalazine, rectal mesalamine
   b. Alternatives: azathioprine, mercaptopurine, sulfasalazine
3. Severe disease – induction of remission:
   a. Prednisone, hydrocortisone IV, methylprednisolone IV
   b. Alternatives: cyclosporine IV, tacrolimus, sulfasalazine
4. Severe disease – maintenance of remission:

a. Azathioprine, mercaptopurine
b. Alternative: sulfasalazine

VI. REFERENCES

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POLICY Document for ZOLADEX (goserelin acetate)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, and overall, clinically appropriate use. This document provides specific information to both sections of the overall policy.

Section 1: Preferred Product
- Policy information specific to preferred medications

Section 2: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 3: Oncology Clinical Policy
- Policy information specific to regimen review per NCCN Guidelines.

Section 1: Preferred Product

EXCEPTIONS CRITERIA
GONADOTROPIN RELEASING HORMONE AGONISTS

PREFERRED PRODUCT: ELIGARD

POLICY
This policy informs prescribers of preferred products and provides an exception process for targeted products through prior authorization.

I. PLAN DESIGN SUMMARY

This program applies to the gonadotropin releasing hormone agonist products specified in this policy. Coverage for targeted products is provided based on clinical circumstances that would exclude the use of the preferred product and may be based on previous use of a product. The coverage review process will ascertain situations where a clinical exception can be made. This program applies to all members requesting treatment with Camcevi and Lupron Depot. This program also applies to members who are new to treatment with Firmagon, Trelstar, or Zoladex for the first time.

Each referral is reviewed based on all utilization management (UM) programs implemented for the client.

Table. Gonadotropin releasing hormone agonists

	Product(s)
Preferred*	• **Eligard** (leuprolide acetate)
Targeted	• **Camcevi** (leuprolide mesylate) • **Firmagon** (degarelix) • **Lupron Depot** (leuprolide acetate for depot suspension) • **Trelstar** (triptorelin) • **Zoladex** (goserelin acetate)

*: Medications considered formulary or preferred on your plan may still require a clinical prior authorization review.

II. EXCEPTION CRITERIA

This program applies to members requesting treatment for prostate cancer.

A. Firmagon, Trelstar, and Zoladex

Coverage for the Firmagon, Trelstar, and Zoladex is provided when any of the following criteria is met:

1. Member is currently receiving treatment with the requested targeted product, excluding when the requested targeted product is obtained as samples or via manufacturer's patient assistance programs.
2. Member has a documented hypersensitivity to the preferred product.

B. Camcevi and Lupron Depot

Coverage for Camcevi and Lupron Depot is provided when the member has a documented hypersensitivity to the preferred product.

Section 2: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

ZOLADEX (goserelin 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 Indications
   1. Prostate cancer
      a. For use in combination with flutamide for the management of locally confined stage T2b-T4 (Stage B2-C) carcinoma of the prostate. Treatment with Zoladex and flutamide should start 8 weeks prior to initiating radiation therapy and continue during radiation therapy.
      b. In the palliative treatment of advanced carcinoma of the prostate.
   2. Endometriosis
      For the management of endometriosis, including pain relief and reduction of endometriotic lesions for the duration of therapy. Experience with Zoladex for the management of endometriosis has been limited to women 18 years of age and older treated for 6 months. (Zoladex 3.6 mg strength only)
   3. Endometrial thinning
      For use as an endometrial-thinning agent prior to endometrial ablation for dysfunctional uterine bleeding. (Zoladex 3.6 mg strength only)
   4. Advanced breast cancer
      For use in the palliative treatment of advanced breast cancer in pre-and perimenopausal women.

B. Compendial Uses
   1. Breast cancer
   2. Prostate cancer
   3. Gender dysphoria (also known as gender non-conforming or transgender persons)
   4. Preservation of ovarian function
   5. Prevention of recurrent menstrual related attacks in acute porphyria
   6. Uterine leiomyomata (fibroids)
   7. Treatment of chronic anovulatory uterine bleeding with severe anemia

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: Use of the 10.8 mg strength for diagnoses other than prostate cancer, breast cancer, and gender dysphoria.

III. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: Hormone receptor status testing results (where applicable).

IV. PRESCRIBER SPECIALTIES

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 patients less than 18 years of age.

V. CRITERIA FOR INITIAL APPROVAL

A. Breast Cancer
Authorization of 12 months may be granted for the treatment of hormone receptor-positive breast cancer.

B. Prostate Cancer
Authorization of 12 months may be granted for treatment of prostate cancer.

C. Endometriosis
Authorization of a total of 6 months may be granted to members for treatment of endometriosis.

D. Endometrial-thinning agent
1. Authorization of 2 doses may be granted for endometrial thinning prior to endometrial ablation or resection for dysfunctional uterine bleeding.
2. Authorization of a total of 6 months may be granted for treatment of chronic anovulatory uterine bleeding with severe anemia.

E. Gender Dysphoria
1. Authorization of 12 months may be granted for pubertal hormonal suppression in an adolescent member when all of the following criteria are met:
   i. The member has a diagnosis of gender dysphoria.
   ii. The member has reached Tanner stage 2 of puberty or greater.
   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 transition when all of the following criteria are met:
   i. The member has a diagnosis of gender dysphoria.
   ii. The member will receive the requested medication concomitantly with gender-affirming hormones.
   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.

F. Preservation of ovarian function
Authorization of 3 months may be granted for preservation of ovarian function when the member is premenopausal and undergoing chemotherapy.

G. Prevention of recurrent menstrual related attacks in acute porphyria
Authorization of 12 months may be granted for prevention of recurrent menstrual related attacks in members with acute porphyria when the requested medication is prescribed by or in consultation with a physician experienced in the management of porphyrias.

H. Uterine leiomyomata (fibroids)
Authorization of a total of 3 months may be granted for treatment of uterine leiomyomata (fibroids) prior to surgery.

VI. CONTINUATION OF THERAPY

A. Breast cancer
Authorization of 12 months may be granted for continued treatment in members requesting reauthorization who are experiencing clinical benefit to therapy and who have not experienced an unacceptable toxicity.

B. Prostate cancer
Authorization of 12 months may be granted for continued treatment in members requesting reauthorization who are experiencing clinical benefit to therapy (e.g., serum testosterone less than 50 ng/dL) and who have not experienced an unacceptable toxicity.

C. Gender dysphoria
1. Authorization of 12 months may be granted for continued treatment for pubertal hormonal suppression 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 has previously reached Tanner stage 2 of puberty or greater.
   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 transition in members requesting reauthorization when all of the following criteria are met:
   i. The member has a diagnosis of gender dysphoria.
   ii. The member will receive the requested medication concomitantly with gender-affirming hormones.
   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.

D. All members (including new members) requesting authorization for continuation of therapy for the specified indications below must meet all initial authorization criteria:
1. Endometriosis
2. Endometrial-thinning agent
3. Preservation of ovarian function
4. Prevention of recurrent menstrual related attacks in acute porphyria
5. Uterine leiomyomata (fibroids)

Section 3: Oncology Clinical Policy

Oncology Clinical Policy

Program Description

The National Comprehensive Care Network® (NCCN®) is an alliance of leading cancer centers devoted to patient care, research and education dedicated to improving the quality, effectiveness and efficiency of cancer care so patients can live better lives.[1] It is comprised of oncology experts who convene regularly to establish the best treatments for patients. NCCN develops various resources for use by stakeholders in the health care delivery system. These resources include, but are not limited to, the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®), the NCCN Drugs & Biologics Compendium (NCCN Compendium®) and the NCCN Chemotherapy Order Templates (NCCN Templates®).

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NCCN Categories of Evidence and Consensus[2]

Category 1: Based on high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2A: Based on lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2B: Based on lower-level evidence, there is NCCN consensus that the intervention is appropriate.
Category 3: Based any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

Policy for Regimen Prior Authorization

A regimen prior authorization allows submission of a single prior authorization request for all oncology drugs or biologics within an NCCN template that require prior authorization.

This policy provides coverage of a regimen review when *all* the following criteria are met:

a. Regimen prior authorization reviews, based on NCCN templates, are initiated through the provider portal: https://provider.carefirst.com/providers/home.page
b. If the prior authorization request is submitted via phone or fax, each drug or biologic will need to be submitted and reviewed as a separate prior authorization request for review with drug-specific criteria.
c. The prior authorization review is requested for an oncology drug or biologic that requires prior authorization on the medical benefit.
d. The indication is for a cancer that is eligible for regimen review. Currently, the cancer types in scope for regimen review include breast, lung, colon and rectal cancer.
e. The member is eligible for regimen review.

In addition, the following criteria must be met for approval:

a. The requested regimen for the drug(s) or biologic(s) and indication is consistent with an NCCN recommendation with a level of evidence category of 1 or 2A.
b. The NCCN template must be accepted by the provider without modification.

Authorizations may be granted for 12 months.
Further review may be indicated where the above criteria are not met.

Continuation of Therapy

To submit a request for continuation of therapy, a new regimen prior authorization review must be requested. Upon template selection, the template must be modified to include the appropriate therapies being used for maintenance

treatment. The regimen request will be submitted for further review.

Dosage and Administration

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

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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

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POLICY Document for XOLAIR (omalizumab)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, lower cost site of care and overall, clinically appropriate use. This document provides specific information to each of the three sections of the overall policy.

Section 1: Site of Care

- Policy information specific to site of care (outpatient, hospital outpatient, home infusion)

Section 2: Clinical Criteria

- Policy information specific to the clinical appropriateness for the medication

Section 1: Site of Care

CareFirst Site of Care Criteria
Administration of Subcutaneous Xolair

POLICY

I. CRITERIA FOR APPROVAL FOR ADMINISTRATION IN OUTPATIENT HOSPITAL SETTING

This policy provides coverage for administration of Xolair* in an outpatient hospital setting for up to 60 days when a member is new to therapy or is reinitiating therapy after not being on therapy for 3 months or more. .

This policy provides coverage for administration of Xolair in an outpatient hospital setting for a longer course of treatment when ANY of the following criteria are met:

A. The member has experienced an adverse reaction to the medication that did not respond to conventional interventions (eg, acetaminophen, steroids, diphenhydramine, fluids or other pre-medications) or a severe adverse event (anaphylaxis, anaphylactoid reactions, myocardial infarction, thromboembolism, or seizures) during or immediately after administration.
B. The member is medically unstable (eg respiratory, cardiovascular, or renal conditions).
C. The member has significant behavioral issues and/or physical or cognitive impairment that would impact the safety of the administration AND the patient does not have access to a caregiver.
D. The member is less than 14 years of age.

For situations where administration of Xolair does not meet the criteria for outpatient hospital administration, coverage for Xolair is provided when administered in alternative specially certified sites such as; physician office or ambulatory care. Xolair reconstituted solution is not indicated for home administration.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the site of care prior authorization review (where applicable):

A. Medical records supporting the member has experienced an adverse reaction that did not respond to conventional interventions or a severe adverse event during or immediately after administration
B. Medical records supporting the member is medically unstable
C. interventions only available in the outpatient hospital setting

D. Medical records supporting the member has behavioral issues and/or physical or cognitive impairment and no access to a caregiver

Section 2: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

XOLAIR (omalizumab)

POLICY

III. INDICATIONS

The indications below including FDA-approved indications and compendial 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. Allergic asthma
      Xolair is indicated for patients 6 years of age and older with moderate to severe persistent asthma who have a positive skin test or in vitro reactivity to a perennial aeroallergen and whose symptoms are inadequately controlled with inhaled corticosteroids.

      Limitations of use: Xolair is not indicated for the relief of acute bronchospasm or status asthmaticus, or for treatment of other allergic conditions.

   2. Chronic spontaneous urticaria (CSU)
      Xolair is indicated for the treatment of adults and adolescents 12 years of age and older with chronic spontaneous urticaria (CSU) who remain symptomatic despite H1 antihistamine treatment.

      Limitations of use: Xolair is not indicated for treatment of other forms of urticaria.

   3. Nasal polyps
      Xolair is indicated for add-on maintenance treatment of nasal polyps in adult patients 18 years of age and older with inadequate response to nasal corticosteroids.

B. Compendial Uses
   1. Immune checkpoint inhibitor-related toxicities
   2. Systemic mastocytosis

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

IV. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
A. Asthma:
   1. Initial Requests:
      i. Member's chart or medical record showing pre-treatment IgE level
      ii. Chart notes, medical record documentation, or claims history supporting previous medications tried

2. Continuation requests: Chart notes or medical record documentation supporting improvement in asthma control.

B. CSU:
   1. Initial Requests: Member's chart or medical record documentation, or claims history supporting previous medications tried showing an inadequate treatment response to a second-generation H1 antihistamine
   2. Continuation Requests: Chart notes or medical record documentation supporting response to therapy

C. Nasal polyps:
   1. 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. Continuation Requests: Chart notes or medical record documentation supporting response to therapy

D. Immune checkpoint inhibitor-related toxicity (initial requests): Member's chart or medical record showing pre-treatment IgE level

E. Systemic mastocytosis (initial requests):
   1. Chart notes or medical record documentation supporting diagnosis of systemic mastocytosis
   2. Chart notes, medical record documentation, or claims history of prerequisite therapies (if applicable)

V. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with one of the following:

A. Asthma: allergist/immunologist or pulmonologist
B. Chronic spontaneous urticaria: allergist/immunologist or dermatologist
C. Nasal polyps: allergist/immunologist or otolaryngologist

VI. CRITERIA FOR INITIAL APPROVAL

A. Asthma

Authorization of 6 months may be granted for treatment of asthma when all of the following criteria are met:

1. Member is 6 years of age or older.
2. Member has a positive skin test or in vitro reactivity to at least one perennial aeroallergen.
3. Member has a pre-treatment IgE level greater than or equal to 30 IU/mL.
4. 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).
5. Member has inadequate asthma control despite current treatment with both of the following medications at optimized doses:
   i. Medium-to-high-dose inhaled corticosteroid
   ii. Additional controller (i.e., long acting beta$_2$-agonist, long acting muscarinic antagonist, leukotriene modifier, or sustained-release theophylline)
6. Member will continue to use maintenance asthma treatments (e.g., inhaled corticosteroid, additional controller) in combination with Xolair.
7. Member will not use Xolair concomitantly with other biologics indicated for asthma (e.g., Cinqair, Dupixent, Fasenra, Nucala, Tezspire).

B. Chronic spontaneous urticaria

Authorization of 6 months may be granted for treatment of chronic spontaneous urticaria when all of the following criteria are met:

1. Member is 12 years of age or older.
2. Member remains symptomatic despite treatment with up-dosing (in accordance with EAACI/GA^{2}LEN/EDF/WAO guidelines) of a second-generation H_1 antihistamine (e.g., cetirizine, fexofenadine, levocetirizine, loratadine) for at least 2 weeks.
3. Member has been evaluated for other causes of urticaria, including bradykinin-related angioedema and interleukin-1-associated urticarial syndromes (auto-inflammatory disorders, urticarial vasculitis).
4. Member has experienced a spontaneous onset of wheals, angioedema, or both, for at least 6 weeks.

C. Nasal polyps

Authorization of 6 months may be granted for treatment of nasal polyps when all of the following criteria are met:

1. Member is 18 years of age or older.
2. Member has bilateral nasal polyps and chronic symptoms of sinusitis despite intranasal corticosteroid treatment for at least 2 months unless contraindicated or not tolerated.
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 Xolair, unless contraindicated or not tolerated.
6. Member will not use Xolair concomitantly with other biologics indicated for nasal polyps (e.g., Dupixent, Nucala).

D. Immune checkpoint inhibitor-related toxicity

Authorization of 1 month may be granted for treatment of immune checkpoint inhibitor-related toxicity when both of the following are met:

1. The member has a refractory case of immune-therapy related severe (G3) pruritus
2. The member has elevated IgE levels

E. Systemic mastocytosis

Authorization of 12 months may be granted for the treatment of systemic mastocytosis when both of the following are met:

1. The major and at least one minor diagnostic criterion for systemic mastocytosis are present or three or more minor diagnostic criteria are present (see Appendix)
2. Xolair will be used in any of the following treatment settings:
   i. Used as stepwise prophylactic treatment for chronic mast cell mediator-related cardiovascular and pulmonary symptoms when the member has tried both of the following:
      a. H1 blockers and H2 blockers
      b. Corticosteroids
   ii. Used for prevention of recurrent unprovoked anaphylaxis
   iii. Used for prevention of hymenoptera or food-induced anaphylaxis, with negative specific IgE or negative skin test
   iv. Used to improve tolerability of venom immunotherapy

VII. CONTINUATION OF THERAPY

A. Asthma

Authorization of 12 months may be granted for continuation of treatment of asthma when all of the following criteria are met:

1. Member is 6 years of age or older.
2. Asthma control has improved on Xolair 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[9]
3. Member will continue to use maintenance asthma treatments (e.g., inhaled corticosteroid, additional controller) in combination with Xolair.
4. Member will not use Xolair concomitantly with other biologics indicated for asthma (e.g., Cinqair, Dupixent, Fasenra, Tezspire, Nucala).

B. Chronic spontaneous urticaria

Authorization of 12 months may be granted for continuation of treatment of chronic spontaneous urticaria when all of the following criteria are met:

1. Member is 12 years of age or older.
2. Member has experienced a response (e.g., improved symptoms, decrease in weekly urticaria activity score [UAS7]) since initiation of therapy.

C. Nasal polyps

Authorization of 12 months may be granted for continuation of treatment of nasal polyps when all of the following criteria are met:

1. Member is 18 years of age or older.
2. Member has experienced a response as evidenced by improvement in signs and symptoms (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).
3. Member will not use Xolair concomitantly with other biologics indicated for nasal polyps (e.g., Dupixent, Nucala).

D. Immune checkpoint inhibitor-related toxicities and systemic mastocytosis

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

VIII. OTHER

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.

IX. APPENDIX

2017 WHO Diagnostic Criteria for Systemic Mastocytosis

A. Major Criteria: multifocal, dense infiltrates of mast cells (at least 15 mast cells in aggregates) detected in sections of bone marrow and/or other extracutaneous organs
B. Minor Criteria
   1. In biopsy sections of bone marrow or other extracutaneous organs, greater than 25% of mast cells in the infiltrate are spindle-shaped or have atypical morphology, or greater than 25% of all mast cells in bone marrow aspirate smears are immature or atypical
   2. Detection of an activating point mutation at codon 816 of *KIT* in the bone marrow, blood, or another extracutaneous organ

3. Mast cells in bone marrow, blood, or other extracutaneous organs express CD25, with or without CD2, in addition to normal mast cell markers
4. Serum total tryptase persistently greater than 20 ng/mL (unless there is an associated myeloid neoplasm, in which case this parameter is not valid)

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POLICY Document for ZEPZELCA (lurbinectedin)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, and overall, clinically appropriate use. This document provides specific information to both sections of the overall policy.

Section 1: Clinical Criteria

- Policy information specific to the clinical appropriateness for the medication

Section 2: Oncology Clinical Policy

- Policy information specific to regimen review per NCCN Guidelines.

Section 1: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

ZEPZELCA (lurbinectedin)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Zepzelca is indicated for the treatment of adult patients with metastatic small cell lung cancer (SCLC) with disease progression on or after platinum-based chemotherapy.

B. Compendial Uses
1. Relapsed small cell lung cancer
2. Primary progressive small cell lung cancer

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

II. CRITERIA FOR INITIAL APPROVAL

Small Cell Lung Cancer
Authorization of 12 months may be granted for subsequent treatment of small cell lung cancer as a single agent in any of the following settings:
A. Relapse following complete or partial response or stable disease with initial treatment
B. Primary progressive disease
C. Metastatic disease following disease progression on or after platinum-based 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.

Section 2: Oncology Clinical Policy

PROGRAM DESCRIPTION

The National Comprehensive Care Network® (NCCN®) is an alliance of leading cancer centers devoted to patient care, research and education dedicated to improving the quality, effectiveness, and efficiency of cancer care so patients can live better lives.[1] It is comprised of oncology experts who convene regularly to establish the best treatments for patients. NCCN develops various resources for use by stakeholders in the health care delivery system. These resources include, but are not limited to, the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®), the NCCN Drugs & Biologics Compendium (NCCN Compendium®) and the NCCN Chemotherapy Order Templates (NCCN Templates®).

NCCN Templates® are based on NCCN Guidelines® and NCCN Compendium®. The NCCN Compendium lists the appropriate drugs and biologics as treatment options for specific cancers using U.S. Food and Drug Administration (FDA)-approved disease indications and specific NCCN panel recommendations. Each recommendation is supported by a level of evidence category.

NCCN Categories of Evidence and Consensus[2]

- Category 1: Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
- Category 2A: Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
- Category 2B: Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.
- Category 3: Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

POLICY

Policy for Regimen Prior Authorization
A regimen prior authorization allows submission of a single prior authorization request for all oncology drugs or biologics within an NCCN template that require prior authorization.

PROCEDURE

This policy provides coverage of a regimen review when all of the following criteria are met:
1. Regimen prior authorization reviews, based on NCCN templates, are initiated through the provider portal.
   - If the prior authorization request is submitted via phone or fax, each drug or biologic will need to be submitted and reviewed as a separate prior authorization request for review with drug-specific criteria.
2. The prior authorization review is requested for an oncology drug or biologic.
3. The member is eligible for regimen review.
4. The indication is for a cancer that is eligible for regimen review. Currently, the cancer types in scope for regimen review include the following:
   - Ampullary Adenocarcinoma
   - Anal Carcinoma
   - B-Cell Lymphomas
   - Basal Cell Skin Cancer
   - Biliary Tract Cancers

- Bone Cancer
- Breast Cancer
- Bladder Cancer
- Central Nervous System Cancers
- Cervical Cancer
- Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma
- Chronic Myeloid leukemia
- Colon Cancer
- Dermatofibrosarcoma Protuberans
- Esophageal Cancer
- Gastric Cancer
- Gastrointestinal Stromal Tumors
- Gestational Trophoblastic Neoplasms
- Hairy Cell Leukemia
- Head and Neck Cancers
- Hodgkin Lymphoma
- Hepatocellular Carcinoma
- Kaposi Sarcoma
- Kidney Cancer
- Melanoma: Cutaneous
- Melanoma: Uveal
- Merkel Cell Carcinoma
- Mesothelioma: Peritoneal
- Mesothelioma: Pleural
- Myelodysplastic Syndromes
- Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Gene Fusions
- Myeloproliferative Neoplasms
- Neuroendocrine and Adrenal Tumors
- Non-Small Cell Lung Cancer
- Occult Primary
- Ovarian Cancer
- Pancreatic Cancer
- Penile Cancer
- Prostate Cancer
- Rectal Cancer
- Small Bowl Adenocarcinoma
- Small Cell Lung Cancer
- Soft Tissue Sarcoma
- Squamous Cell Skin Cancer
- Systemic Mastocytosis
- Systemic Light Chain Amyloidosis
- Testicular Cancer
- Thymomas and Thymic Carcinomas
- Thyroid Carcinoma
- Uterine Neoplasms
- Vulvar Cancer
- Waldenström Macroglobulinemia / Lymphoplasmacytic Lymphoma

In addition, the following criteria must be met for approval:

1. The requested regimen for the drug(s) or biologic(s) and indication is consistent with an NCCN recommendation with a level of evidence category of 1 or 2A.
2. The NCCN template must be accepted by the provider without modification.

Further review may be indicated when the above criteria are not met.

Authorizations may be granted for 12 months or as medically required, based on the member's condition and provider's assessment.

Supportive Care: Myeloid Growth Factor Therapy
Granulocyte colony stimulating factors are recommended for primary prophylaxis based on the febrile neutropenia risk of the chemotherapy regimen. Febrile neutropenia risk levels vary by NCCN Chemotherapy Order template and are listed at the top of the template. Regimens associated with a high or intermediate risk of febrile neutropenia may include a granulocyte colony stimulating factor as part of the prior authorization.

Continuation of Therapy
To submit a request for continuation of therapy, a new regimen prior authorization review must be requested. Upon template selection, the template must be modified to include the appropriate therapies being used for maintenance treatment. The regimen request will be submitted for further review.

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

REFERENCES:

SECTION 1

1. Zepzelca [package insert]. Palo Alto, CA: Jazz Pharmaceuticals, Inc.; April 2022.
2. The NCCN Drugs & Biologics Compendium® © 2023 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed July 12, 2023.

SECTION 2

1. National Comprehensive Cancer Network. About NCCN website. https://www.nccn.org/home/about, accessed June 6, 2023.
2. National Comprehensive Cancer Network. NCCN Categories of Evidence and Consensus website, https://www.nccn.org/guidelines/guidelines-process/development-and-update-of-guidelines, accessed June 6, 2023.
3. National Comprehensive Cancer Network. NCCN Guidelines website. https://www.nccn.org/guidelines/category_1, accessed June 6, 2023. (Note: An account may be required.)
4. National Comprehensive Cancer Network. NCCN Drugs and Biologics Compendium website https://www.nccn.org/compendia-templates/compendia/drugs-and-biologics-compendia, accessed June 6, 2023. (Note: A subscription may be required.)
5. National Comprehensive Cancer Network. NCCN Chemotherapy Order Templates (NCCN Templates) website. https://www.nccn.org/compendia-templates/nccn-templates-main/browse-by-cancer-type, accessed June 6, 2023. (Note: A subscription may be required.)

Reference number(s)
2380-A

SPECIALTY GUIDELINE MANAGEMENT

RECLAST (zoledronic acid)
zoledronic 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

A. Treatment and prevention of osteoporosis in postmenopausal women
B. Treatment to increase bone mass in men with osteoporosis
C. Treatment and prevention of glucocorticoid-induced osteoporosis in patients expected to be on glucocorticoids for at least 12 months
D. Treatment of Paget's disease of bone in men and women

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, treatment and prevention

Authorization of 12 months may be granted to postmenopausal members for treatment or prevention of 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
3. Member has osteopenia (i.e., pre-treatment T-score greater than -2.5 and less than -1)

B. Osteoporosis in men

Authorization 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 has a pre-treatment T-score less than or equal to -2.5
3. 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 A)

C. Glucocorticoid-induced osteoporosis

Authorization of 12 months may be granted for members with glucocorticoid-induced osteoporosis when BOTH of the following criteria are met:

1. Member is currently receiving or will be initiating glucocorticoid therapy at an equivalent prednisone dose of greater than or equal to 2.5 mg/day for at least 3 months
2. Member meets ANY of the following criteria:
   a. Member has a history of a fragility fracture
   b. Member has a pre-treatment T-score of 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 A)

D. Paget's disease of bone

Authorization of one dose (5 mg) may be granted for treatment of Paget's disease of bone.

IV. CONTINUATION OF THERAPY

A. Paget's disease of bone

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

B. All other indications

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:

1. Member has received less than 24 months of therapy and has not experienced clinically significant adverse events during therapy
2. Member has received 24 months of therapy or more and meets both of the following:
   a. Member has experienced clinical benefit (i.e., improvement or stabilization in T-score since the previous bone mass measurement)
   b. Member has not experienced any adverse effects

V. APPENDIX

Appendix A. 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.

VI. REFERENCES

1. Reclast [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; April 2020.
2. Zoledronic acid injection [package insert]. Schaumburg, IL: Sagent Pharmaceuticals, Inc.; August 2021.
3. Bisphosphonates. *Drug Facts and Comparisons.* Facts & Comparisons [database online]. St. Louis, MO: Wolters Kluwer Health Inc; March 21, 2019. Accessed October 10, 2022.
4. 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.*

5. Jeremiah MP, Unwin BK, Greenwald MH, et al. Diagnosis and management of osteoporosis. *Am Fam Physician*. 2015;92(4):261-268.
6. 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.
7. ACOG Practice Bulletin Number 129: Osteoporosis. *Obstet Gynecol*. 2012;120(3):718-734.
8. National Institute for Health and Care Excellence. Osteoporosis Overview. Last updated October 13, 2021. Available at: http://pathways.nice.org.uk/pathways/osteoporosis. Accessed October 13, 2021.
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. Singer FR, Bone HG, Hosking DJ, et al. Paget's Disease of Bone: An Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab.* 2014; 99(12): 4408-22.
13. FRAX® Fracture Risk Assessment Tool. © Centre for Metabolic Bone Diseases, University of Sheffield, UK. Available at: https://www.shef.ac.uk/FRAX. Accessed October 13,2021.
14. Ensrud KE, Crandall CJ. Osteoporosis. *Ann Intern Med*. 2017;167(03):ITC17–ITC32.

Reference number(s)
C16942-A

CAREFIRST: ZOLGENSMA

Client Requested: The intent of the criteria is to ensure that patients follow selection elements as established by CareFirst.

COVERAGE CRITERIA

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

- Diagnosis of spinal muscular atrophy confirmed by genetic testing demonstrating bi-allelic mutations in the survival motor neuron 1 (SMN1) gene as stated below:
  - deletion of both copies of the SMN1 gene
    OR
  - compound heterozygous mutations of the SMN1 gene (defined below):
    - pathogenic variant(s) in both copies of the SMN1 gene.
    - pathogenic variant in 1 copy and deletion of the second copy of the SMN1 gene.

  AND
- Documentation of a genetic test confirms no more than 4 copies of the SMN2 gene.
  AND
- The patient is less than 2 years of age at the time of infusion of onasemnogene abeparvovec- xioi
  AND
- Documentation of baseline laboratory assessments such as AST, ALT, total bilirubin, and prothrombin time.
  AND
- The patient does not have advanced spinal muscular atrophy (e.g., complete paralysis of limbs, permanent ventilator dependence).
  AND
- Baseline anti-adeno-associated virus serotype 9 (AAV9) antibody titers < 1:50.
  AND
- Prescribed by a neurologist with expertise in treating spinal muscular atrophy.
  AND
- Dosing Limits: 1 injection per lifetime

  Repeat treatment or ante-partum use of onasemnogene abeparvovec-xioi is considered **investigational**.
  Onasemnogene abeparvovec-xioi is considered **investigational** for all other indications.
  Concurrent use of onasemnogene abeparvovec-xioi with nusinersen and/or risdiplam is considered **investigational.**
  Use of nusinersen and/or risdiplam after administration of onasemnogene abeparvovec-xioi is considered **investigational.**

DOCUMENT HISTORY

Created:	Specialty Clinical Development (KF) 06/2019
Revised:	KF 07/2019; KF 12/2019 (implement for CareFirst only), JL 02/2020, 09/2020, AS 07/2022, AM 10/2022, JS 07/2023
Reviewed:	CDPR/ CT 03/2020, 09/2020, DC 08/2022, RR 10/2022, DC 08/2023

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)
2917-A

SPECIALTY GUIDELINE MANAGEMENT

ZULRESSO (brexanolone)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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 postpartum depression (PPD) in patients 15 years and older.

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

II. CRITERIA FOR INITIAL APPROVAL

Authorization of 1 infusion may be granted for treatment of moderate to severe postpartum depression in members 15 years of age or older when all of the following criteria are met:

A. Member has moderate to severe postpartum depression and had a major depressive episode that began no earlier than the third trimester of pregnancy and no later than the first 4 weeks following delivery, 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], etc.)
B. Diagnosis is verified by a psychiatrist
C. Member is 6 months postpartum or less
D. Lactation has ceased or breastmilk produced will not be used for feedings during the infusion and up to 4 days following infusion completion
E. Member will not receive more than one infusion per pregnancy/childbirth

III. REFERENCES

1. Zulresso [package insert]. Cambridge, MA: Sage Therapeutics, Inc.; June 2022.

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® © 2022 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed June 2, 2022.

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 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 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.

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 2022 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed March 16, 2022.

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/

POLICY Document for ZYNYZ (retifanlimab-dlwr)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, lower cost site of care and overall, clinically appropriate use. This document provides specific information to each of the three sections of the overall policy.

Section 1: Site of Care

- Policy information specific to site of care (outpatient, hospital outpatient, home infusion)

Section 2: Clinical Criteria

- Policy information specific to the clinical appropriateness for the medication

Section 1: Site of Care

CareFirst Site of Care Criteria
Administration of Intravenous Checkpoint Inhibitors
Bavencio, Imfinzi, Jemperli, Keytruda, Libtayo, Opdivo, Opdualag, Tecentriq, Yervoy and Zynyz

POLICY

I. CRITERIA FOR APPROVAL FOR ADMINISTRATION IN OUTPATIENT HOSPITAL SETTING

This policy provides coverage for administration of a checkpoint inhibitor in an outpatient hospital setting for the initial 6 months approval and up to 45 days for renewal of therapy.

This policy provides coverage for administration of a checkpoint inhibitor in an outpatient hospital setting for a longer course of treatment when ANY of the following criteria are met:

A. The member has experienced an adverse reaction that did not respond to conventional interventions (eg, acetaminophen, steroids, diphenhydramine, fluids, other pre-medications or slowing of infusion rate) or a severe adverse event (anaphylaxis, anaphylactoid reactions, myocardial infarction, thromboembolism, or seizures) during or immediately after an infusion or has experienced severe toxicity requiring continuous monitoring (e.g. Grade 2-4 bullous dermatitis, transaminitis, pneumonitis, Stevens-Johnson syndrome, acute pancreatitis, primary adrenal insufficiency aseptic meningitis, encephalitis, transverse myelitis, myocarditis, pericarditis, arrhythmias, impaired ventricular function, conduction abnormalities).
B. The member is medically unstable (eg respiratory, cardiovascular, or renal conditions).
C. The member has severe venous access issues that require the use of a special interventions only available in the outpatient hospital setting.
D. The member has significant behavioral issues and/or physical or cognitive impairment that would impact the safety of the infusion therapy AND the patient does not have access to a caregiver.
E. The member is receiving provider administered combination chemotherapy.
F. The member is less than 14 years of age.

For situations where administration of a checkpoint inhibitor does not meet the criteria for outpatient hospital infusion, coverage for a checkpoint inhibitor is provided when administered in alternative sites such as physician office, home infusion or ambulatory care.

CVS/caremark

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the site of care prior authorization review (where applicable):

A. Medical records supporting the member has experienced an adverse reaction that did not respond to conventional interventions or a severe adverse event during or immediately after an infusion or a severe toxicity requiring continuous monitoring
B. Medical records supporting the member is medically unstable
C. Medical records supporting the member has severe venous access issues that require specialized interventions only available in the outpatient hospital setting
D. Medical records supporting the member has behavioral issues and/or physical or cognitive impairment and no access to a caregiver
E. Medical records supporting the member is receiving provider administered combination therapy.

Section 2: Clinical Criteria

PECIALTY GUIDELINE MANAGEMENT

ZYNYZ (retifanlimab-dlwr)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial 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
Merkel Cell Carcinoma
Zynyz is indicated for the treatment of adult patients with metastatic or recurrent locally advanced Merkel cell carcinoma (MCC).

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

II. EXCLUSIONS

Coverage will not be provided for members who have experienced disease progression while on PD-1 or PD-L1 inhibitor therapy.

III. CRITERIA FOR INITIAL APPROVAL

Merkel Cell Carcinoma (MCC)
Authorization of 6 months may be granted for treatment of metastatic or recurrent locally advanced MCC.

IV. CONTINUATION OF THERAPY

Authorization of 6 months may be granted (up to 24 months total) 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.

REFERENCES

SECTION 1

1. Opdivo [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; February 2023.
2. Bavencio [package insert]. Rockland, MA: EMD Serono, Inc; July 2020.
3. Imfinzi [prescribing information]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; November 2022.
4. Jemperli [prescribing information]. Philadelphia, PA: GlaxoSmithKline LLC; February 2023.
5. Keytruda [prescribing information]. Rahway, NJ: Merck Sharp & Dome LLC.; April 2023.
6. Libtayo [prescribing information]. Tarrytown, NY: Regeneron Pharmaceuticals, Inc.; April 2023.
7. Tecentriq [package insert]. South San Francisco, CA: Genentech, Inc.; December 2022.
8. Yervoy [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; February 2023.
9. Opdualag [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; March 2022.
10. Zynyz [package insert]. Wilmington, DE: Incyte Corporation; March 2023.

SECTION 2

1. Zynyz [package insert]. Wilmington, DE: Incyte Corporation; March 2023.