

QUANTITY LIMIT CRITERIA

BRAND NAME*
(generic)

LYRICA
(pregabalin)

LYRICA CR
(pregabalin extended-release)

Status: CVS Caremark Criteria

Type: Quantity Limit

Ref # 134-H

* Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated

FDA-APPROVED INDICATIONS

Lyrice

Lyrice is indicated for:

- Management of neuropathic pain associated with diabetic peripheral neuropathy
- Management of postherpetic neuralgia
- Adjunctive therapy for the treatment of partial onset seizures in patients 4 years of age and older
- Management of fibromyalgia
- Management of neuropathic pain associated with spinal cord injury

Compendial Uses

- Cancer-Related Neuropathic Pain⁴
- Cancer Treatment Related Neuropathic Pain^{4,5}

Lyrice CR

Lyrice CR is indicated for the management of:

- Neuropathic pain associated with diabetic peripheral neuropathy
- Postherpetic neuralgia

Efficacy of Lyrice CR has not been established for the management of fibromyalgia or as adjunctive therapy for adult patients with partial onset seizures.

RATIONALE

Lyrice (pregabalin) is indicated for management of neuropathic pain associated with diabetic peripheral neuropathy (DPN), management of postherpetic neuralgia (PHN), adjunctive therapy for the treatment of partial onset seizures in patients 4 years of age and older, management of fibromyalgia (FM), and management of neuropathic pain associated with spinal cord injury. Lyrice CR (pregabalin extended-release) is indicated for the management of neuropathic pain associated with diabetic peripheral neuropathy (DPN) and management of postherpetic neuralgia (PHN).

Neuropathic pain associated with diabetic peripheral neuropathy

The maximum recommended dose of Lyrice (pregabalin) is 100 mg three times a day (300 mg/day) in patients with creatinine clearance of at least 60 mL/min. Begin dosing at 50 mg three times a day (150 mg/day). The dose may be increased to 300 mg/day within 1 week based on efficacy and tolerability. Although Lyrice was also studied at 600 mg/day, there is no evidence that this dose confers additional significant benefit and this dose was less well tolerated. In view of the dose-dependent adverse reactions, treatment with doses above 300 mg/day is not recommended.

The maximum recommended dose of Lyrice CR (pregabalin extended-release) is 330 mg once daily. Begin dosing at 165 mg once daily and increase to 330 mg once daily within 1 week based on individual patient response and tolerability.

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Although Lyrica was studied at 600 mg/day, there was no evidence that this dose conferred additional significant benefit and this dose was less well tolerated. In view of the dose-dependent adverse reactions with Lyrica, treatment with doses above 330 mg/day is not recommended for Lyrica CR.

Postherpetic neuralgia

The recommended dose of Lyrica (pregabalin) is 75 to 150 mg two times a day, or 50 to 100 mg three times a day (150 to 300 mg/day) in patients with creatinine clearance of at least 60 mL/min. Begin dosing at 75 mg two times a day, or 50 mg three times a day (150 mg/day). The dose may be increased to 300 mg/day within 1 week based on efficacy and tolerability. Patients who do not experience sufficient pain relief following 2 to 4 weeks of treatment with 300 mg/day, and who are able to tolerate Lyrica (pregabalin), may be treated with up to 300 mg two times a day, or 200 mg three times a day (600 mg/day). In view of the dose-dependent adverse reactions and the higher rate of treatment discontinuation due to adverse reactions, reserve dosing above 300 mg/day for those patients who have on-going pain and are tolerating 300 mg daily.

The maximum recommended dose of Lyrica CR is 660 mg once daily. Begin dosing at 165 mg once daily and increase to 330 mg once daily within 1 week based on individual patient response and tolerability. Patients who do not experience sufficient pain relief following 2 to 4 weeks of treatment with 330 mg once daily and who are able to tolerate Lyrica CR, may be treated with up to 660 mg once daily. In view of the dose-dependent adverse reactions and the higher rate of treatment discontinuation due to adverse reactions, dosing above 330 mg/day should be reserved only for those patients who have on-going pain and are tolerating 330 mg daily.

Adjunctive therapy for partial onset seizures in patients 4 years of age and older

The recommended dosage for adult and pediatric patients 4 years of age and older is included in the table below. Administer the total daily dosage orally in two or three divided doses. In pediatric patients 4 years of age and older, the recommended dosing regimen is dependent upon body weight. Based on clinical response and tolerability, dosage may be increased, approximately weekly.

Recommended Dosage for Adults and Pediatric Patients 4 years and Older		
Age and Body Weight	Recommended Initial Dosage (administer in two to three divided doses)	Recommended Maximum Dosage (administer in two to three divided doses)
Adults (17 years and older)	150 mg/day	600 mg/day
Pediatric patients weighing 30 kg or more	2.5 mg/kg/day	10 mg/kg/day (not to exceed 600 mg/day)
Pediatric patients weighing 11 kg to less than 30 kg	3.5 mg/kg/day	14 mg/kg/day

Both the efficacy and adverse event profiles of Lyrica (pregabalin) have been shown to be dose-related. The effect of dose escalation on the tolerability of Lyrica (pregabalin) has not been formally studied. The efficacy of add-on Lyrica (pregabalin) in patients taking gabapentin has not been evaluated in controlled trials. Consequently, dosing recommendations for the use of Lyrica (pregabalin) with gabapentin cannot be offered.

Management of fibromyalgia

The recommended dose of Lyrica (pregabalin) for fibromyalgia is 300 to 450 mg/day. Begin dosing at 75 mg two times a day (150 mg/day). The dose may be increased to 150 mg two times a day (300 mg/day) within 1 week based on efficacy and tolerability. Patients who do not experience sufficient benefit with 300 mg/day may be further increased to 225 mg two times a day (450 mg/day). Although Lyrica (pregabalin) was also studied at 600 mg/day, there is no evidence that this dose confers additional benefit and this dose was less well tolerated. In view of the dose-dependent adverse reactions, treatment with doses above 450 mg/day is not recommended.

Neuropathic Pain Associated with Spinal Cord Injury

The recommended dose range of Lyrica (pregabalin) for the treatment of neuropathic pain associated with spinal cord injury is 150 to 600 mg/day. The recommended starting dose is 75 mg two times a day (150 mg/day). The dose may be increased to 150 mg two times a day (300 mg/day) within 1 week based on efficacy and tolerability. Patients who do not experience sufficient pain relief after 2 to 3 weeks of treatment with 150 mg two times a day and who tolerate Lyrica (pregabalin) may be treated with up to 300 mg two times a day.

Renal Impairment

In view of dose-dependent adverse reactions and since pregabalin is eliminated primarily by renal excretion, adjust the dose in patients with reduced renal function. The use of Lyrica (pregabalin) in pediatric patients with compromised renal function has not been studied. Base the dose adjustment in patients with renal impairment on creatinine clearance (CLcr), as indicated in Table 1 (Lyrica) and Table 2 (Lyrica CR). Next, determine the recommended total daily dose based on indication, for a patient with normal renal function (CLcr \geq 60mL/min). Then refer to Table 1 (Lyrica) or Table 2 (Lyrica CR) to determine the corresponding renal adjusted dose.

For patients undergoing hemodialysis, adjust the pregabalin daily dose based on renal function. In addition to the daily dose adjustment, administer a supplemental dose immediately following every 4-hour hemodialysis treatment (See Table 1).

Creatinine Clearance (CLcr) (mL/min)	Total Pregabalin Daily Dose (mg/day)*				Dose Regimen
	150	300	450	600	
\geq 60	150	300	450	600	BID or TID
30–60	75	150	225	300	BID or TID
15–30	25–50	75	100–150	150	QD or BID
<15	25	25–50	50–75	75	QD
Supplementary dosage following hemodialysis (mg)†					
Patients on the 25mg QD regimen: take one supplemental dose of 25mg or 50mg					
Patients on the 25–50mg QD regimen: take one supplemental dose of 50mg or 75mg					
Patients on the 50–75mg QD regimen: take one supplemental dose of 75mg or 100mg					
Patients on the 75mg QD regimen: take one supplemental dose of 100mg or 150mg					

TID= Three divided doses; BID = Two divided doses; QD = Single daily dose.

* Total daily dose (mg/day) should be divided as indicated by dose regimen to provide mg/dose.

† Supplementary dose is a single additional dose.

Creatinine Clearance (CLcr) (mL/min)	Total Pregabalin Extended-Release Daily Dose (mg/day)*				Dose Regimen
	165	330	495 ^a	660 ^b	
\geq 60	165	330	495 ^a	660 ^b	Once a day
30–60	82.5	165	247.5 ^c	330	Once a day
Less than 30/hemodialysis	Dose with Lyrica				

a. 495 mg = 3 x 165 mg tablets taken once daily

b. 660 mg = 2 x 330 mg tablets taken once daily

c. 247.5 mg = 3 x 82.5 mg tablets taken once daily

Cancer-Related and Cancer Treatment Related Neuropathic Pain

Frequently used as an adjuvant to neuropathic pain, pregabalin starting dose is 50 mg three times a day increasing to 100 mg three times a day, and may increase to a maximum dose of 600 mg in divided doses two to three times a day.

Presently, there is limited clinical data regarding off-label uses and doses that exceed the FDA recommended maximum dose of 600 mg per day of Lyrica (pregabalin).¹⁻⁴ Lyrica (pregabalin) is available in several strengths and may be dosed two or three times daily. Therefore to allow for dosing intervals and dose titrations, the following limits have been established per 30 days: 120 capsules for 25 mg, 50 mg, 75 mg, 100 mg, and 150 mg strengths, a limit of 90 capsules for the 200 mg strength, a limit of 60 capsules for the 225 mg and 300 mg strengths, and a limit of 900 mL for the 20mg/mL oral solution. Lyrica CR (pregabalin extended-release) is available in 82.5 mg, 165 mg, and 330 mg tablets and is dosed once daily. Therefore to allow for dose titrations, a limit of 60 tablets per 30 days has been established for Lyrica CR 82.5 mg, 165 mg, and 330 mg.

If the patient is requesting more than the initial quantity limit the system will reject with a message indicating that quantity limits are exceeded.

REFERENCES

1. Lyrica [package insert]. New York, NY: Parke-Davis; May 2018.
2. Lyrica CR [package insert]. New York, NY: Parke-Davis; October 2017.
3. 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 May 2018.
4. Micromedex Healthcare Series [database online]. Greenwood Village, CO: Thomson Reuters (Healthcare) Inc. Updated periodically. <http://www.thomsonhc.com> [available with subscription]. Accessed May 2018.
5. NCCN Guidelines. Version 1.2018 Adult Cancer Pain. http://www.nccn.org/professionals/physician_gls/pdf/pain.pdf. Accessed May 2018.

Written by: UM Development (JG)
 Date Written: 08/2005
 Revised: UM Development (NB) 11/2006, 06/2007; (CT) 05/2008, 05/2009, 01/2010 (05/2009(2) Lyrica oral soln added), 05/2010, (TM) 06/2011, 03/2012, 06/2012 (update PI), 09/2012, (TM) 03/2013, (PL) 09/2013, 05/2014, (JH) 05/2015; (KM) 05/2016 (no clinical changes), 05/2017, 09/2017 (added cancer treatment pain), 10/2017 (added Lyrica CR); (DS) 05/2018 (no clinical changes) Medical Affairs 08/2005, 11/2006, 06/2007; (WF) 05/2008, 05/2009; (KP) 01/2010, 05/2010, 06/2011, 03/2012, 06/2012, (LB) 09/2012, (LS) 03/2013, (LCB) 05/2014, (DNC) 05/2015; (AN) 09/2017; (DNC) 10/2017
 Reviewed: External Review 12/2005, 12/2006, 10/2007, 08/2008, 10/2009, 01/2010, 12/2010, 10/2011, 08/2012, 10/2012, 06/2013, 10/2013, 02/2014, 10/2014, 10/2015, 02/2016, 10/2016, 10/2017, 12/2017, 10/2018

LIMIT CRITERIA

This quantity limit should not exceed a dose equivalent to a maximum of 600 mg per day of Lyrica or 660 mg per day of Lyrica CR.

	1 Month Limit*	3 Month Limit*
Lyrica (pregabalin) capsules 25 mg, 50 mg, 75 mg, 100 mg, 150 mg	120 capsules per 25 days	360 capsules per 75 days
Lyrica (pregabalin) capsules 200 mg	90 capsules per 25 days	270 capsules per 75 days
Lyrica (pregabalin) capsules 225 mg, 300 mg	60 capsules per 25 days	180 capsules per 75 days
Lyrica (pregabalin) oral solution 20 mg/mL	900 mL per 25 days	2700 mL per 75 days
Lyrica CR (pregabalin extended-release) 82.5 mg, 165 mg, 330 mg	60 tablets per 25 days	180 tablets per 75 days

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