

Clinical Policy: Pregabalin (Lyrica, Lyrica CR)

Reference Number: CP.PMN.33

Effective Date: 01.01.07

Last Review Date: 05.25

Line of Business: Commercial, HIM, Medicaid

[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

Description

Pregabalin (Lyrica[®], Lyrica[®] CR), a structural derivative of the inhibitory neurotransmitter gamma-aminobutyric acid (GABA), is a calcium channel alpha 2-delta ligand with anti-nociceptive and anti-seizure effects.

FDA Approved Indication(s)

Lyrica is indicated for:

- Neuropathic pain associated with diabetic peripheral neuropathy (DPN)
- Postherpetic neuralgia (PHN)
- Adjunctive therapy for the treatment of partial-onset seizures in patients 1 month of age and older
- Fibromyalgia
- Neuropathic pain associated with spinal cord injury

Lyrica CR is indicated for the treatment of:

- Neuropathic pain associated with DPN
- PHN

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

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation[®] that Lyrica, Lyrica CR, pregabalin, and pregabalin CR are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Neuropathic Pain (must meet all):

1. Diagnosis of neuropathic pain associated with one of the following (a, b, c, or d):
 - a. DPN;
 - b. PHN;
 - c. Treatment of cancer (*immediate-release only*);
 - d. Spinal cord injury (*immediate-release only*);
2. Age \geq 18 years;

3. Failure of a 30-day trial of gabapentin at $\geq 1,800$ mg/day, unless contraindicated or clinically significant adverse effects are experienced;*
**For Illinois HIM requests, the step therapy requirements above do not apply as of 1/1/2026 per IL HB 5395*
4. Failure of a 30-day trial of a tricyclic antidepressant (TCA) (e.g., amitriptyline, nortriptyline, imipramine) at up to maximally indicated doses, unless clinically significant adverse effects are experienced, member's age is ≥ 65 , or all are contraindicated;*
** For Illinois HIM requests, the step therapy requirements above do not apply as of 1/1/2026 per IL HB 5395*
5. For all requests except neuropathic pain associated with PHN, failure of a 30-day trial of a formulary serotonin/norepinephrine reuptake inhibitor (SNRI) (e.g., duloxetine, venlafaxine) at up to maximally indicated doses, unless clinically significant adverse effects are experienced or all are contraindicated;*
** For Illinois HIM requests, the step therapy requirements above do not apply as of 1/1/2026 per IL HB 5395*
6. If request is for controlled-release formulation, member must use immediate-release pregabalin, unless contraindicated or clinically significant adverse effects are experienced;*
** For Illinois HIM requests, the step therapy requirements above do not apply as of 1/1/2026 per IL HB 5395*
7. If request is for brand Lyrica, member must use generic pregabalin, unless contraindicated or clinically significant adverse effects are experienced;
8. Dose does not exceed one of the following (a, b, or c):
 - a. DPN (i or ii):
 - i. Pregabalin: 300 mg per day;
 - ii. Pregabalin CR: 330 mg per day;
 - b. Neuropathic pain associated with treatment of cancer or spinal cord injury:
pregabalin – 600 mg per day;
 - c. PHN (i or ii):
 - i. Pregabalin: 600 mg per day;
 - ii. Pregabalin CR: 660 mg per day.

Approval duration:

Medicaid/HIM – 12 months

Commercial – 12 months or duration of request, whichever is less

B. Partial Onset Seizures (must meet all):

1. Diagnosis of partial onset seizures;
2. Prescribed by or in consultation with a neurologist;
3. Age ≥ 1 month;
4. Request is for immediate-release formulation;
5. Member meets one of the following (a or b):
 - a. Request is for the treatment of a member in a State with limitations on step therapy in certain settings (*see Appendix E*);
 - b. All the following (i, ii, and iii):
 - i. Failure of gabapentin used as adjunctive therapy to other anticonvulsants, unless contraindicated or clinically significant adverse effects are experienced;*

** For Illinois HIM requests, the step therapy requirements above do not apply as of 1/1/2026 per IL HB 5395*

- ii. Failure of TWO anticonvulsants indicated for partial seizures (e.g., carbamazepine, phenytoin, valproic acid, oxcarbazepine, phenobarbital, lamotrigine, levetiracetam, topiramate, zonisamide, tiagabine, felbamate) unless clinically significant adverse effects are experienced or all are contraindicated;
** For Illinois HIM requests, the step therapy requirements above do not apply as of 1/1/2026 per IL HB 5395*
 - iii. If request is for brand Lyrica, member must use generic pregabalin, unless contraindicated or clinically significant adverse effects are experienced;
6. Pregabalin will be used as adjunctive therapy to other anticonvulsants;
 7. Request meets one of the following (a or b):
 - a. For members weighing < 30 kg: Dose does not exceed 14 mg/kg per day;
 - b. For members weighing ≥ 30 kg: Dose does not exceed 600 mg per day.

Approval duration:

Medicaid/HIM – 12 months

Commercial – 12 months or duration of request, whichever is less

C. Fibromyalgia (must meet all):

1. Diagnosis of fibromyalgia;
2. Age ≥ 18 years;
3. Request is for immediate-release formulation;
4. Failure of a 30-day trial of gabapentin at ≥ 1,800 mg/day, unless contraindicated or clinically significant adverse effects are experienced;
** For Illinois HIM requests, the step therapy requirements above do not apply as of 1/1/2026 per IL HB 5395*
5. Failure of a 30-day trial of duloxetine at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
** For Illinois HIM requests, the step therapy requirements above do not apply as of 1/1/2026 per IL HB 5395*
6. Failure of a 30-day trial of cyclobenzaprine or a TCA at up to maximally indicated doses, unless clinically significant adverse effects are experienced, member's age is ≥ 65, or all are contraindicated;
** For Illinois HIM requests, the step therapy requirements above do not apply as of 1/1/2026 per IL HB 5395*
7. If request is for brand Lyrica, member must use generic pregabalin, unless contraindicated or clinically significant adverse effects are experienced;
8. Dose does not exceed 450 mg per day.

Approval duration:

Medicaid/HIM – 12 months

Commercial – 12 months or duration of request, whichever is less

D. Generalized Anxiety Disorder (off-label) (must meet all):

1. Diagnosis of generalized anxiety disorder (GAD);
2. Age ≥ 18 years;
3. Request is for immediate-release formulation;
4. Failure of TWO of the following alternatives, unless clinically significant adverse effects are experienced or all are contraindicated: escitalopram, paroxetine, venlafaxine

ER, duloxetine, buspirone;*

** For Illinois HIM requests, the step therapy requirements do not apply as of 1/1/2026 per IL HB 5395*

5. If request is for brand Lyrica, member must use generic pregabalin, unless contraindicated or clinically significant adverse effects are experienced;
6. Dose does not exceed 600 mg per day.

Approval duration:

Medicaid/HIM – 12 months

Commercial – 12 months or duration of request, whichever is less

E. Restless Leg Syndrome (off-label) (must meet all):

1. Diagnosis of restless leg syndrome (RLS);
2. Age \geq 18 years;
3. If request is for controlled-release formulation, member must use immediate-release pregabalin, unless contraindicated or clinically significant adverse effects are experienced;*

** For Illinois HIM requests, the step therapy requirements do not apply as of 1/1/2026 per IL HB 5395*

4. If request is for brand Lyrica, member must use generic pregabalin, unless contraindicated or clinically significant adverse effects are experienced;
5. Dose does not exceed one of the following (a or b):
 - a. Pregabalin: 450 mg per day;
 - b. Pregabalin CR: 495 mg per day.

Approval duration:

Medicaid/HIM – 12 months

Commercial – 12 months or duration of request, whichever is less

F. Other diagnoses/indications (must meet 1 or 2):

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
 - a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
 - b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. All Indications in Section I (must meet all):

1. Member meets one of the following (a or b):

- a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
 - b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B*);
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed (a or b):
- a. Immediate-release pregabalin (i, ii, iii, or iv):
 - i. DPN: 300 mg per day;
 - ii. PHN, neuropathic pain associated with treatment of cancer or spinal cord injury, GAD: 600 mg per day;
 - iii. For partial-onset seizures (1 or 2):
 - 1) For members weighing < 30 kg: dose does not exceed 14 mg/kg per day;
 - 2) For members weighing ≥ 30 kg: dose does not exceed 600 mg per day;
 - iv. Fibromyalgia, RLS: 450 mg per day;
 - b. Controlled-release pregabalin (i, ii, or iii):
 - i. DPN: 330 mg per day;
 - ii. PHN: 660 mg per day;
 - iii. RLS: 495 mg per day.

Approval duration:

Medicaid/HIM – 12 months

Commercial – 12 months or duration of request, whichever is less

B. Other diagnoses/indications (must meet 1 or 2):

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
 - a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
 - b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

- A. Dental pain;
- B. Essential tremor;
- C. Social phobia (i.e., social anxiety disorder);

D. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid, or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

DPN: diabetic peripheral neuropathy
 FDA: Food and Drug Administration
 GABA: gamma-aminobutyric acid
 PHN: postherpetic neuralgia
 SNRI: serotonin/norepinephrine reuptake inhibitor
 TCA: tricyclic antidepressant

*Appendix B: Therapeutic Alternatives**

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
TCAs		
amitriptyline (Elavil [®])	Fibromyalgia** 10 mg to 50 mg PO QD Neuropathic Pain** 25 to 150 mg PO QHS	150 mg/day [†]
desipramine (Norpramin [®])	DPN** Initially 25 mg PO QHS, then titrate as tolerated to efficacy (usual range: 75 mg to 150 mg PO QHS) PHN**, Neuropathic Pain associated with Cancer Treatment ** 10 to 25 mg PO QHS and titrate to pain relief as tolerated (in one study, mean dose was 167 mg/day)	200 mg/day [†]
imipramine (Tofranil [®] , Tofranil PM [®])	DPN** 50 mg to 150 mg PO QHS	150 mg/day
nortriptyline (Pamelor [®])	DPN** 50 mg to 75 mg PO daily PHN ** 75 mg to 150 mg PO daily Neuropathic Pain associated with Cancer Treatment** 50 to 150 mg PO QHS	150 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Serotonin/Norepinephrine Reuptake Inhibitors		
duloxetine (Cymbalta [®])	Fibromyalgia 30 to 60 mg PO QD Neuropathic pain** 60 to 120 mg PO QD GAD 30 to 60 mg PO QD	120 mg/day
venlafaxine extended-release (Effexor XR [®])	Neuropathic pain** 75 mg to 225 mg PO QD GAD 37.5 to 225 mg PO QD	225 mg/day
escitalopram (Lexapro [®])	GAD 10 to 20 mg PO QD	20 mg/day
paroxetine (Paxil [®])	GAD 20 to 50 mg PO QD	50 mg/day
Miscellaneous		
gabapentin (immediate-release: Neurontin [®] ; extended-release: Horizant [®] , Gralise [®])	DPN**, Neuropathic Pain associated with Cancer Treatment** <i>Immediate-release:</i> 300 mg PO TID titrated based on clinical response Fibromyalgia** 300 mg PO QHS then increased to target dosage of 2,400 mg/day PHN <i>Immediate-release:</i> 300 mg PO QD on day 1, 300 mg PO BID on day 2, 300 mg PO TID on day 3, then titrate as needed to 1800 mg/day <i>Extended-release (Gralise):</i> 300 mg PO on day 1, 600 mg on day 2, 900 mg on days 3-6, 1200 mg on days 7-10, 1500 mg on days 11-14, and 1800 mg on day 15 and thereafter <i>Extended-release (Horizant):</i> 600 mg/day PO for 3 days, 600 mg PO BID on day 4 and thereafter Partial Seizures <i>Immediate-release:</i>	Immediate release: 3,600 mg/day [†] Gralise: 1,800 mg/day [†] Horizant: 1,200 mg/day [†]

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	<p><u>Adults</u>: initially 300 mg PO TID; effective range 900-1,800 mg/day but up to 2400 mg/day has been used long term</p> <p><u>Children 3-12 years</u>: 10-15 mg/kg/day PO in 3 divided doses; effective dose 25-35 mg/kg/day if > 5 years and 40 mg/kg/day if 3-4 years</p>	
cyclobenzaprine (Flexeril [®])	Fibromyalgia** 10 mg to 20 mg PO QHS	20 mg/day
bupirone (BuSpar [®])	GAD 7.5 mg to 60 mg PO BID	60 mg/day
Anticonvulsants		
carbamazepine (Carbatrol [®] , Epitol [®] , Equetro [®] , Tegretol [®] , Tegretol XR [®])	Refer to prescribing information	Refer to prescribing information
felbamate (Felbatol [®])		
lamotrigine (Lamictal [®] , Lamictal CD [®] , Lamictal ODT [®] , Lamictal XR [®])		
levetiracetam (Elepsia XR [®] , Keppra [®] , Keppra XR [®] , Rowcepra [®] , Spritam [®])		
oxcarbazepine (Oxtellar XR [®] , Trileptal [®])		
phenobarbital (Luminal [®])		
phenytoin (Dilantin [®] , Phenytek [®])		
tiagabine (Gabitril [®])		
topiramate (Qudexy XR [®] , Topamax [®] , Topamax Sprinkle [®] , Topiragen [®] , Trokendi XR [®])		
valproic acid (divalproex sodium, Depakote Sprinkle [®] , Depakote ER [®] , Depakote [®] , Depakene [®])		
zonisamide (Zonegran [®])		

Therapeutic alternatives are listed as Brand name[®] (generic) when the drug is available by brand name only and generic (Brand name[®]) when the drug is available by both brand and generic.

*Agents not included in this list may not have evidence supporting their use in the indications covered by this policy

**Off-label use

†Maximum dose for drug, not necessarily indication

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): known hypersensitivity to pregabalin or any of its components
- Boxed warning(s): none reported

Appendix D: General Information

- Class IIb recommendation in Micromedex for GAD is supported by 5 randomized, double blind, placebo-controlled studies. It is also considered a second-line agent by the Canadian Psychiatric Association.

Appendix E: States with Limitations against Redirections in Certain Settings

State	Step Therapy Prohibited?	Notes
NV	No	<p><i>*Applies to Medicaid requests only*</i></p> <p>Partial onset seizures: Failure of ONE of the following, unless clinically significant adverse effects are experienced or all are contraindicated: generic pregabalin, gabapentin (used as adjunctive therapy to other anticonvulsants), alternative anticonvulsants indicated for partial seizures (e.g., carbamazepine, phenytoin, valproic acid, oxcarbazepine, phenobarbital, lamotrigine, levetiracetam, topiramate, zonisamide, tiagabine, felbamate).</p>

V. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
Pregabalin (Lyrica)*	DPN	3 divided doses PO per day	300 mg/day
	Neuropathic pain associated with treatment of cancer**	2 or 3 divided doses PO per day	600 mg/day
	PHN	2 or 3 divided doses PO per day	600 mg/day
	Partial onset seizures	<p>Adults: 2 or 3 divided doses PO per day</p> <p>Pediatric patients weighing > 30 kg: 2.5 mg/kg/day in 2 or 3 divided doses</p> <p>Pediatric patients weighing < 30 kg: 3.5 mg/kg/day</p> <ul style="list-style-type: none"> • 1 month to < 4 years old: 3 divided doses 	<p>Adults: 600 mg/day</p> <p>Pediatrics < 30 kg: 14 mg/kg/day</p>

Drug Name	Indication	Dosing Regimen	Maximum Dose
		<ul style="list-style-type: none"> ≥ 4 years old: 2 or 3 divided doses 	
	Fibromyalgia	2 divided doses PO per day	450 mg/day
	Neuropathic pain associated with spinal cord injury	2 divided doses PO per day	600 mg/day
	GAD**	Initially, 75 mg PO BID. If tolerated after 1 week, the dose may be increased to 150 mg PO BID. Thereafter, the dose may be adjusted according to response and tolerability. Data from clinical trials indicate an effective dose range is 150 to 225 mg PO BID.	
	RLS**	75 mg PO daily. The dose can be titrated up by 75 mg every week as needed up to 450 mg daily.	450 mg/day
	DPN	165 mg PO QD. Dose may be increased to 330 mg PO QD within 1 week.	330 mg/day
Pregabalin extended-release (Lyrica CR)	PHN	165 mg PO QD. Dose may be increased to 330 mg PO QD within 1 week. After 2 to 4 weeks of treatment, dose may be increased to 660 mg PO QD in patients not experiencing adequate pain relief.	660 mg/day
	RLS**	82.5 mg PO daily. The dose can be titrated up by 82.5 mg every week as needed up to 495 mg daily.	495 mg/day

* Lyrica should be administered orally starting at 150 mg/day. It should be titrated up to 300 mg/day within 1 week for all indications except partial onset seizures and RLS.

**Off-label use

VI. Product Availability

Drug Name	Availability
Pregabalin (Lyrica)	<ul style="list-style-type: none"> Capsules: 25 mg, 50 mg, 75 mg, 100 mg, 150 mg, 200 mg, 225 mg, 300 mg Oral solution: 20 mg/mL
Pregabalin extended-release (Lyrica CR)	Tablets: 82.5 mg, 165 mg, 330 mg

VII. References

1. Lyrica Prescribing Information. New York, NY: Pfizer Inc.; December 2023. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/021446s041,022488s0181bl.pdf. Accessed January 16, 2025.
2. Lyrica CR Prescribing Information. New York, NY: Pfizer Inc.; December 2023. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/209501s0051bl.pdf. Accessed January 16, 2025.
3. Clinical Pharmacology [database online]. Philadelphia, PA: Elsevier. Updated periodically. Available at: <https://www.clinicalkey.com/pharmacology/>. Accessed January 27, 2025.
4. Micromedex[®] [Internet database]. Ann Arbor, Michigan: Merative[™]. Updated periodically. Accessed January 27, 2025.
5. Finnerup NB, Attal N, Haroutounian S, et al. Pharmacotherapy for Neuropathic Pain in Adults: Systematic Review, Meta-analysis, and Updated NeuPSIG Recommendations. *Lancet Neurol*. 2015 February; 14(2):162-173. doi:10.1016/S1474-4422(14)70251-0.
6. American Geriatrics Society 2019 Beers Criteria Update Expert Panel. American Geriatrics Society 2019 updated AGS Beers Criteria for potentially inappropriate medication use in older adults. *J Am Geriatr Soc*. 2019;00:1-21. DOI: 10.1111/jgs.15767.
7. Snedecor SJ, Sudharshan L, Cappelleri JC, et al. Systematic review and comparison of pharmacologic therapies for neuropathic pain associated with spinal cord injury. *J of Pain Research*. 2013;6:539-47.
8. Hagen EM, Rekan Tiina. Management of neuropathic pain associated with spinal cord injury. *Pain Ther*. 2015;4:51-65.

Diabetic Peripheral Neuropathy

9. Pop-Busui R, Boulton A, Feldman E, et al. Diabetic Neuropathy: A Position Statement by the American Diabetes Association. *Diabetes Care* Jan 2017, 40 (1) 136-154.
10. Bril V, England J, Franklin GM, et al. Evidence-based guideline: treatment of painful diabetic neuropathy, a report of the American Academy of Neurology, the American Association of Neuromuscular and Electrodiagnostic Medicine, and the American Academy of Physical Medicine and Rehabilitation. *Neurology*. 2011; 76(20): 1758-1765.
11. Price R, Smith D, Franklin G, et al. Oral and topical treatment of painful diabetic polyneuropathy: practice guideline update summary. *Neurology*. 2022;98:31-43.
12. Boulton AJM, Vinik AI, Arezzo JC, et al. Diabetic neuropathies: a statement by the American Diabetes Association. *Diabetes Care*. 2005; 28(4): 956-962.
13. ElSayed NA, Aleppo G, Aroda FM, et al. 12. Retinopathy, neuropathy, and foot care: standards of care in diabetes – 2023. *Diabetes Care* 2023;46(Suppl. 1):S203-S215.

Postherpetic Neuralgia, Fibromyalgia, Seizures

14. Dubinsky RM, Kabbani H, El-Chami Z, Boutwell C, Ali H. Practice parameter: treatment of postherpetic neuralgia, an evidence-based report of the Quality Standards Subcommittee of the American Academy of Neurology (*reaffirmed in 2008*). *Neurology*. 2004; 63(6): 969-965.
15. Clauw DJ. Fibromyalgia: a clinical review. *JAMA*. 2014; 311(15): 1547-1555.
16. Macfarlane GJ, Kronisch C, Dean LE, et al. EULAR revised recommendations for the management of fibromyalgia. *Ann Rheum Dis*. 2017;76:318-28.
17. Glauser T, Ben-Menachem E, Bourgeois B, et al. Updated ILAE evidence review of antiepileptic drug efficacy and effectiveness as initial monotherapy for epileptic seizures and syndromes. *Epilepsia*. 2013; 54(3): 551-563.

18. Brodie MJ. Pregabalin as adjunctive therapy for partial seizures. *Epilepsia*. 2004; 45(S6): 19-27.
19. Kanner AM, Ashman E, Gloss D, et al. Practice guidelines update summary: efficacy and tolerability of the new antiepileptic drugs II: treatment-resistant epilepsy. *Neurology*. 2018;91:82-90.

Generalized Anxiety Disorder

20. Rickels K, Pollack MH, Feltner DE, Et Al: Pregabalin for Treatment of Generalized Anxiety Disorder: A 4-Week, Multicenter, Double-Blind, Placebo-Controlled Trial of Pregabalin and Alprazolam. *Arch Gen Psychiatry*. 2005; 62(9):1022-1030.
21. Montgomery SA; Tobias K; Zornberg GL; Kasper S; Pande AC. Efficacy And Safety Of Pregabalin In The Treatment Of Generalized Anxiety Disorder: A 6-Week, Multicenter, Randomized, Double-Blind, Placebo-Controlled Comparison Of Pregabalin And Venlafaxine. *J Clin Psychiatry*. 2006;67: 771-782.
22. Pohl RB; Feltner DE; Fieve RR; Pande AC. Efficacy of Pregabalin in the Treatment Of Generalized Anxiety Disorder: Double-Blind, Placebo-Controlled Comparison Of Bid Versus Tid Dosing. *J Clin Psychopharmacol*. 2005;25:151-158.
23. Pande AC, et al. Pregabalin in generalized anxiety disorder: a placebo-controlled trial. *Am J Psychiatry*. 2003;160:533-540.
24. Canadian Psychiatric Association. Clinical practice guidelines management of anxiety disorders: Generalized Anxiety Disorder. *Can J Psychiatry*. 2006;51(suppl2):51S-55S.
25. Strawn JR, Geracioti L, Rajdev N, et al. Pharmacotherapy for generalized anxiety disorder in adults and pediatric patients: an evidence-based treatment review. *Expert Opin Pharmacother*. July 2018;19(10):1057-70.

Cancer Treatment-related Neuropathic Pain

26. National Comprehensive Cancer Network. Adult Cancer Pain Version 3.2024. Available at https://www.nccn.org/professionals/physician_gls/pdf/pain.pdf. Accessed January 27, 2025.
27. Verma V, Singh N, Jaggi AS. Pregabalin in neuropathic pain: evidences and possible mechanisms. *Current Neuropharmacology*, 2014; 12:44-56.

Restless Leg Syndrome

28. Garcia-Borreguero D, Silber MH, Winkelman JW, et al. Guidelines for the first-line treatment of restless legs syndrome/Willis-Ekbom disease, prevention and treatment of dopaminergic augmentation: a combined task force of the IRLSSG, EURLSSG, and the RLS-foundation. *Sleep Med*. 2016 May;21:1-11. doi: 10.1016/j.sleep.2016.01.017.
29. Silber MH, Buchfuhrer MJ, Earley CJ, et al; Scientific and Medical Advisory Board of the Restless Legs Syndrome Foundation. The Management of Restless Legs Syndrome: An Updated Algorithm. *Mayo Clin Proc*. 2021 Jul;96(7):1921-1937. doi: 10.1016/j.mayocp.2020.12.026.
30. Winkelman JW, Berkowski JA, DelRosso LM, et al. Treatment of restless legs syndrome and periodic limb movement disorder: an American Academy of Sleep Medicine clinical practice guideline. *J Clin Sleep Med*. 2025 Jan 1;21(1):137-152. doi: 10.5664/jcsm.11390.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
2Q 2021 annual review: no significant changes; revised HIM.PHAR.21 to HIM.PA.154; references reviewed and updated.	02.24.21	05.21

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Added clarification that the policy applies to generic pregabalin, where applicable; clarified language for “Lyrica” to “pregabalin” where applicable to reduce confusion that policy also applies to generic pregabalin.	10.25.21	
2Q 2022 annual review: no significant changes; revised brand-to-generic redirection to “member must use” language; revised Commercial authorization duration from Length of Benefit to 12 months or duration of request, whichever is less; references reviewed and updated.	02.14.22	05.22
Revised SNRI redirection in neuropathic pain to apply for all requests except postherpetic neuralgia. Template changes applied to other diagnoses/indications and continued therapy section.	08.23.22	11.22
2Q 2023 annual review: no significant changes; references reviewed and updated.	02.14.23	05.23
For partial onset seizures, added redirection bypass for members in a State with limitations on step therapy in certain settings along with Appendix E, which includes Nevada with requirements for single drug redirection for Medicaid requests.	08.31.23	
2Q 2024 annual review: for partial onset seizures, revised maximum dose from 420 mg to 14 mg/kg/day for members weighing < 30 kg per PI; for neuropathic pain associated-with spinal cord injury, clarified usage of pregabalin immediate release only per PI; added GAD products and dosing regimen to Appendix B; references reviewed and updated.	01.19.24	05.24
2Q 2025 annual review: for neuropathic pain associated with treatment of cancer, revised maximum dosage from 300 mg/day to 600 mg/day per NCCN; references reviewed and updated. Added off-label criteria for RLS. Added step therapy bypass for IL HIM per IL HB 5395.	04.04.25	05.25

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:

For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

©2007 Centene Corporation. All rights reserved. All materials are exclusively owned by Centene Corporation and are protected by United States copyright law and international copyright law. No part of this publication may be reproduced, copied, modified, distributed, displayed, stored in a retrieval system, transmitted in any form or by any means, or otherwise published without the prior written permission of Centene Corporation. You may not alter or remove any trademark, copyright or other notice contained herein. Centene[®] and Centene Corporation[®] are registered trademarks exclusively owned by Centene Corporation.