Clinical Policy: Pregabalin (Lyrica)
Reference Number: HIM.PA.64
Effective Date: 12/14
Last Review Date: 08/17 Revision Log
Line of Business: Health Insurance Marketplace

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Pregabalin (Lyrica®), 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
Lyrica is indicated:
- For the treatment of neuropathic pain associated with diabetic peripheral neuropathy
- For the treatment of postherpetic neuralgia
- For the treatment of adult patients with partial-onset seizures as adjunctive therapy
- For the treatment of fibromyalgia
- For the treatment of neuropathic pain associated spinal cord injury

Policy/Criteria
** Provider must submit documentation (including office chart notes and lab results) supporting that member has met all approval criteria **

I. Initial Approval Criteria

A. Diabetic Peripheral Neuropathy (must meet all)**:**
1. Diagnosis of diabetic peripheral neuropathy;
2. Failure of a 30 day trial of gabapentin at ≥ 1,800 mg/day unless contraindicated or clinically significant adverse effects are experienced;
3. Failure of a 30 day trial of a formulary TCA (e.g., amitriptyline, nortriptyline, imipramine) at up to maximally indicated doses unless contraindicated or clinically significant adverse effects are experienced;
4. Failure of a 30 day trial of a formulary SNRI (e.g., venlafaxine) at up to maximally indicated doses unless contraindicated or clinically significant adverse effects are experienced;
5. Dose does not exceed 300 mg/day (3 capsules/day).

Approval duration: 12 months

B. Postherpetic Neuralgia (must meet all)**:**
1. Diagnosis of postherpetic neuralgia;
2. Failure of a 30 day trial gabapentin at ≥ 1,800 mg/day unless contraindicated or clinically significant adverse effects are experienced;
3. Failure of a 30 day trial of a formulary TCA (e.g., amitriptyline, nortriptyline, imipramine) at up to maximally indicated doses unless contraindicated or clinically significant adverse effects are experienced;

4. Failure of a 30 day trial of a formulary SNRI (e.g., venlafaxine) at up to maximally indicated doses unless contraindicated or clinically significant adverse effects are experienced;
5. Dose does not exceed 600 mg/day (3 capsules/day).

Approval duration: 12 months

C. Partial-Onset Seizures (must meet all)**:**

1. Diagnosis of partial onset seizures;
2. Prescribed by or in consultation with a neurologist;
3. Failure of gabapentin used as adjunctive therapy to other anticonvulsants unless contraindicated or clinically significant adverse effects are experienced;
4. Failure of 2 formulary anticonvulsants indicated for partial seizures (e.g., carbamazepine, phenytoin, valproic acid, oxcarbazepine, phenobarbital, lamotrigine, levetiracetam, topiramate, zonisamide, tiagabine, felbamate) unless contraindicated or clinically significant adverse effects are experienced;
5. Lyrica will be used as adjunctive therapy to other anticonvulsants;
6. Dose does not exceed 600 mg/day (3 capsules/day).

Approval duration: 12 months

D. Fibromyalgia (must meet all)**:**

1. Diagnosis of fibromyalgia with symptoms present for at least 3 months;
2. Failure of a 30 day trial of gabapentin at ≥ 1,800 mg/day unless contraindicated or clinically significant adverse effects are experienced;
3. Failure of a 30 day trial of cyclobenzaprine or a formulary TCA at up to maximally indicated doses unless contraindicated or clinically significant adverse effects are experienced;
4. Failure of a 30 day trial of duloxetine at up to maximally indicated doses unless contraindicated or clinically significant adverse effects are experienced;
5. One of the aforementioned trials occurred within the past 90 days, unless member was unable to complete any trial due to clinically significant adverse effects or contraindication(s) to all of the agents;
6. Dose does not exceed 450 mg/day (3 capsules/day).

Approval duration: 12 months

E. Neuropathic Pain Associated with Spinal Cord Injury (must meet all)**:**

1. Diagnosis of neuropathy related to spinal cord injury;
2. Failure of a 30 day trial of gabapentin at ≥ 1,800 mg/day unless contraindicated or clinically significant adverse effects are experienced;
3. Failure of a 30 day trial of a formulary TCA (e.g., amitriptyline, nortriptyline, imipramine) at up to maximally indicated doses unless contraindicated or clinically significant adverse effects are experienced;
4. Failure of a 30 day trial of a formulary SNRI (e.g., venlafaxine) at up to maximally indicated doses unless contraindicated or clinically significant adverse effects are experienced;
5. Dose does not exceed 600 mg/day (3 capsules/day).

Approval duration: 12 months

F. Other diagnoses/indications
1. Refer to HIM.PHAR.21 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized)

II. Continued Therapy

A. All Indications (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. Documentation supports that member is currently receiving Lyrica for partial onset seizures and has received this medication for at least 30 days;
2. Documentation of positive response to therapy;
3. If request is for a dose increase, new dose does not exceed:
   a. Diabetic peripheral neuropathy: 300 mg/day (3 capsules/day);
   b. Postherpetic neuralgia, partial-onset seizures, and neuropathic pain associated with spinal cord injury: 600 mg/day (3 capsules/day);
   c. Fibromyalgia: 450 mg/day (3 capsules/day).

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via health plan benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 12 months (whichever is less); or
2. Refer to HIM.PA.21 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized)

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

A. 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 policy HIM.PA.21 or evidence of coverage documents

IV. Appendices/General Information

Appendix A: Abbreviation Key
FDA: Food and Drug Administration
PDL: preferred drug list
SNRI: serotonin/norepinephrine reuptake inhibitor
TCA: tricyclic antidepressant

V. References

1. Lyrica Prescribing Information. New York, NY: Pfizer Inc.; March 2016. Available at: www.lyrica.com. Accessed January 10, 2017.
2. O'Connor AB, Dworkin RH. Treatment of neuropathic pain: an overview of recent guidelines. Am J Med. 2009; 122(10): S22-S32.
3. 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.
4. Bouilton AJM, Vinik AI, Arezzo JC, et al. Diabetic neuropathies: a statement by the American Diabetes Association. Diabetes Care. 2005; 28(4): 956-962.
5. 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.
6. Clauw DJ. Fibromyalgia: a clinical review. JAMA. 2014; 311(15): 1547-1555.
7. 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.
8. Brodie MJ. Pregabalin as adjunctive therapy for partial seizures. Epilepsia. 2004; 45(S6): 19-27.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Changed guideline to new format	08/16	08/16
Converted to new template Diabetic peripheral neuropathy: removed anticonvulsants and tramadol from list of acceptable trials as they are not highly recommended first line agents Postherpetic neuralgia: removed opioids (e.g., morphine, methadone), tramadol, and capsaicin cream from list of acceptable trials to enforce the use of the most recommended first line agents and to avoid promoting opioid use Partial onset seizures: removed 3 month duration from gabapentin trial as anticonvulsant regimens are individualized based on patient response and patient concomitant therapy Fibromyalgia: removed fluoxetine as an accepted trial due to lack of sufficient evidence that it works. Replaced requirement for trial of Savella (tier 2 like Lyrica and requires PA) with duloxetine (tier 1) as duloxetine is generic, can be obtained without a PA, and is an SNRI that is FDA approved for fibromyalgia, similar to Savella Spinal cord nerve pain: removed tramadol and opioids from list of acceptable trials as these are second line agents and to avoid promoting opioid use For all indications except partial onset seizures: added 30-day trial durations of all agents at up to maximally indicated doses. Trial duration and maximum indicated dosing is not required for partial onset seizures as anticonvulsant dosing is individualized based on patient response and patient concomitant therapy Removed age restriction for all indications as they are not absolute contraindications per FDA labeling Partial seizures: added other formulary anticonvulsants indicated for	04/17	08/17

Reviews, Revisions, and Approvals	Date	P&T Approval Date
partial seizures to list of acceptable trials for partial. Added COC. Added max doses for all indications Updated references		

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.

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.