Clinical Policy: Pregabalin (Lyrica)
Reference Number: CP.PMN.33
Effective Date: 01/07
Last Review Date: 052/17
Line of Business: Medicaid

Coding Implications
Revision Log

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
Pregabalin is indicated ~~for~~:

- For the treatment of n~~N~~europathic pain associated with diabetic peripheral neuropathy
- For the treatment of p~~P~~ostherpetic neuralgia
- For the treatment of ~~Adjunctive therapy for~~ adult patients with partial onset seizures as adjunctive therapy
- For the treatment of ~~F~~fibromyalgia
- For the treatment of n~~N~~europathic pain associated with spinal cord injury

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

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It is the policy of health plans affiliated with Centene Corporation® that Lyrica is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Neuropathic Pain – Not Associated with Diabetic Peripheral Neuropathy (must meet all)**:**

1. Diagnosis of neuropathic pain (not associated with diabetic peripheral neuropathy);
2. Failure of a 30 day trial of ~~≥ 30 day trial of~~ gabapentin at ≥ 1800 mg/day ~~at doses ≥ 1800 mg/day, unless~~ unless contraindicated or clinically significant adverse effects are experienced~~member experiences clinically significant adverse effects or has contraindication(s) to gabapentin~~;
3. Failure of a 30 day trial ~~≥ 30 day trial~~ of one PDL TCA ~~at maximum indicated doses, unless member experiences clinically significant adverse effects or has contraindication~~at up to maximally indicated doses unless contraindicated or clinically significant adverse effects are experienced~~(s) to all PDL TCAs~~;
4. Failure of a 30 day trial ~~≥ 30 day trial~~ of one PDL SNRI ~~at maximum indicated doses~~at up to maximally indicated doses unless contraindicated or clinically significant adverse effects are experienced~~, unless member experiences clinically significant adverse effects or has contraindication(s) to all PDL SNRIs~~;

5. DoseRequest does not exceed 600 mg per/ day and health plan approved daily quantity limit.

Approval duration: 6 months

B. Diabetic Peripheral Neuropathy (must meet all)**:**
1. Diagnosis of diabetic peripheral neuropathy;
2. Failure of a 30 day trial of gabapentin at ≥ 1800 mg/day unless contraindicated or clinically significant adverse effects are experiencedFailure of ≥ 30 day trial of gabapentin at doses ≥ 1800 mg/day, unless member experiences clinically significant adverse effects or has contraindication(s) to gabapentin;
3. Failure of a 30 day trial of one PDL TCA or SNRI at up to maximally indicated doses unless contraindicated or clinically significant adverse effects are experiencedFailure of ≥ 30 day trial of one PDL TCA or SNRI at maximum indicated doses, unless member experiences clinically significant adverse effects or has contraindication(s) to all PDL TCAs and SNRIs;
4. DoseRequest does not exceed 300 mg per /day and health plan approved daily quantity limit.

Approval duration: 6 months

C. Postherpetic Neuralgia (must meet all)**:**
1. Diagnosis of postherpetic neuralgia;
2. Failure of a 30 day trial of gabapentin at ≥ 1800 mg/day unless contraindicated or clinically significant adverse effects are experiencedFailure of ≥ 30 day trial of gabapentin at doses ≥ 1800 mg/day, unless member experiences clinically significant adverse effects or has contraindication(s) to gabapentin;
3. Failure of a 30 day trial of one PDL TCA at up to maximally indicated doses unless contraindicated or clinically significant adverse effects are experiencedFailure of ≥ 30 day trial of one PDL TCA at maximum indicated doses, unless member experiences clinically significant adverse effects or has contraindication(s) to all PDL TCAs;
4. DoseRequest does not exceed 600 mg per /day and health plan approved daily quantity limit.

Approval duration: 6 months

D. Partial Onset Seizures (must meet all)**:**
1. Diagnosis of partial onset seizures;
2. Prescribed by or in consultation with a neurologist;
3. Age ≥ 12 years;
4. 3. Failure of gabapentin used as adjunctive therapy to other anticonvulsants, unless contraindicated or clinically significant adverse effects are experiencedunless member has contraindication(s) to gabapentin;
5. 4. Failure of 2 PDL anticonvulsants indicated for partial seizures (carbamazepine, phenytoin, valproic acid, oxcarbazepine, phenobarbital, lamotrigine, levetiracetam, topiramate, zonisamide, tiagabine, felbamate), unless contraindicated or clinically significant adverse effects are experiencedunless member has contraindication(s) to these agents;

6.5. Lyrica will be used as adjunctive therapy to other anticonvulsants;
7.6. Dose~~Request~~ does not exceed 600 mg per ~~/~~day ~~and health plan approved daily quantity limit~~.

Approval duration: 6 months

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

1. Diagnosis of fibromyalgia;
2. Failure of a 30 day trial of gabapentin at ≥ 1800 mg/day unless contraindicated or clinically significant adverse effects are experienced~~Failure of ≥ 30 day trial of gabapentin at doses ≥ 1800 mg/day, unless member experiences clinically significant adverse effects or has contraindication(s) to gabapentin~~;
3. Failure of a 30 day trial of~~≥ 30 day trial of~~ duloxetine ~~at maximum indicated doses~~at up to maximally indicated doses unless contraindicated or clinically significant adverse effects are experienced~~, unless member experiences clinically significant adverse effects or has contraindication(s) to duloxetine~~;
4. Failure of a 30 day trial of ~~≥ 30 day trial of~~ cyclobenzaprine~~,~~ or a PDL TCA at up to maximally indicated doses unless contraindicated or clinically significant adverse effects are experienced~~at maximum indicated doses, unless member experiences clinically significant adverse effects or has contraindication(s) to these agents~~;
5. One of the abovementioned 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 listed in criteria 2, 3, and 4;
6. ~~Request~~ Dose does not exceed 450 mg per ~~/~~ day ~~and health plan approved daily quantity limit~~.

Approval duration: 6 months

F. Other diagnoses/indications –

1. Refer to CP.PMN.53 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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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;
   ~~1.~~b. ~~or d~~Documentation supports that member is currently ~~on this medication~~receiving Lyrica for partial onset seizures and~~,~~ has received this medication for at least 30 days~~, and is responding positively to therapy~~;
2. Documentation of positive response to therapy;
~~2.~~3. If request is for a dose increase, new dose does not exceed FDA approved maximum recommended dose for the relevant indication ~~and health plan approved daily quantity limit~~.

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Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy; or
2. Refer to CP.PMN.53 if requested indication is NOT listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

Approval duration: 12 months

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 - CP.PMN.53 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. Dosage and Administration

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.

Indication	~~Recommended~~ Dosing Regimen	Maximum Dose
Diabetic peripheral neuropathy	3 divided doses per day	300 mg/day
Postherpetic neuralgia	2 or 3 divided doses per day	600 mg/day
Partial onset seizures	2 or 3 divided doses per day	600 mg/day
Fibromyalgia	2 divided doses per day	450 mg/day
Spinal cord injury neuropathic pain	2 divided doses per day	600 mg/day

VI. Product Availability

- Capsules: 25 mg, 50 mg, 75 mg, 100 mg, 150 mg, 200 mg, 225 mg, and 300 mg
- Oral solution: 20 mg/mL

VII. Workflow Document


CP.PMN.33
Pregablin (Lyrica) wc

VIII. References

1. Lyrica Prescribing Information. New York, NY: Pfizer Inc.; March 2016. Available at: www.lyrica.com. Accessed ~~September 7, 2016~~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
Separated diagnosis and criteria for diabetic neuropathy and neuropathic pain. Added carbamazepine as a PDL option for treatment of neuropathic pain. Added a Savella trial for treatment of fibromyalgia as a criteria point. Treatment for fibromyalgia criteria were changed to require trials on each. Update the "References" section to reflect the most current literature search.	8/12	8/12
Added the "Spinal Cord Nerve Pain due to injury" to the Indications and "Criteria for Approval" sections. Revised Criteria for Approval "Diabetic Neuropathy": Took out requirement of "2 PDL agents one of which must be" and "plus NSAIDs or antidepressants" from Criteria D. Added Criteria "Patient has failure, or intolerance to 2 PDL agents in these drug classes: TCAs (eg. amitriptyline, nortriptyine, Imipramine), SSRIs/SNRIs (paroxetine, citalopram, venlafaxine), Anticonvulsants (eg. Carbamazepine, topiramate, valproic Acid), opioids /tramadol. Revised Criteria for Approval for "Postherpetic Neuralgia": Took out requirement of "2 PDL agents one of which must be" "plus NSAIDs or antidepressants" from Criteria D. Added Criteria "E. Patient has failure, or intolerance to 2 of these PDL agents: TCAs (eg. amitriptyline, nortriptyine, imipramine), opioids (eg. morphine, methadone), tramadol, capsaisin cream based on treatment guideline	8/13	8/13

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Reviews, Revisions, and Approvals	Date	P&T Approval Date
Revised Criteria for Approval for "Fibromyalgia": Deleted NSAIDs and as an accepted treatment option from criteria "C" due to lack of literature support for this indication in treatment guidelines. Added criteria D to ensure criteria for Savella use are met prior to referral for savella. Revised Criteria for Approval for "Neuropathic Pain": Took out requirement of "2 PDL agents one of which must be" and "plus NSAIDs or antidepressants" from Criteria D due to lack of literature support for NDAIS use Added Criteria "D. Patient has failure or intolerance to 2 of these PDL drugs/class: TCAs (eg. amitriptyline, nortriptyline, imipramine), SNRIs (eg. venlafaxine), opioids, tramadol. Included criteria for "Spinal Cord Nerve Injury": A. Patient > 18 yrs of age. B. Diagnosis of spinal cord injury nerve pain C. Patient has failure or intolerance to gabapentin at dosing of at least 1800mg. Patient has failure or intolerance to 1 PDL drugs: TCAs (eg. amitriptyline, nortriptyine, imipramine), SNRIs (eg. venlafaxine), opioids / tramadol. Update the "References" section to reflect the most current literature search.		
Updated criteria for Diabetic Neuropathy: removed SSRIs, topiramate and valproic acid as appropriate treatment failures	12/13	12/13
Updated age to be inclusive of 18 rather than greater. Clarified trial and failure for partial onset seizures.	05/15	05/15
Clarified that Lyrica should be used as an adjunctive therapy to other anticonvulsants Added that dose for each indication should be within FDA approved limit for the relevant indication.	08/15	08/15
Specified the maximum dose approvable for each diagnosis, Modified criteria for neuropathic and spinal cord injury pain to require the use of an SNRI and TCA for at least 30 days each; removed trial of opioid and tramadol from acceptable trials as these are second line agents and to avoid promoting opioid use; Modified criteria for diabetic neuropathy by removing the pain score requirement and removing capsaicin, opioid, tramadol and anticonvulsants from the list of acceptable trials to include only highly recommended first line agents. Criteria now requires the concurrent use of a TCA or an SNRI with gabapentin for at least 30 days;	10/15	11/15

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Reviews, Revisions, and Approvals	Date	P&T Approval Date
Modified criteria for post herpetic neuralgia by removing pain score requirement, requirement that pain must be present for > 3 months following the healing of zoster rash as these are subjective measures. Opioid, tramadol and capsaicin cream were also removed from list of acceptable trials to enforce the use of the most recommended first line agents. Criteria now requires the use of TCA for at least 30 days; Modified criteria for partial onset seizure to allow use in patient ≥ 12 years old as this use is supported by the literature, though not FDA approved; requirement that gabapentin must be used for up to 3 months was modified to only require trial and failure of gabapentin; Modified criteria for fibromyalgia by removing pain score requirements and the requirement for Savella trial was replaced with duloxetine because duloxetine is generic, can be obtained without a PA and is an SNRI FDA approved for fibromyalgia, similar to Savella; References updated		
Converted to new integrated template. Removed age restrictions for neuropathic pain, postherpetic neuralgia, and fibromyalgia as they are not absolute contraindications per FDA labeling; however, the age restriction for partial onset seizures is maintained since FDA labeling specifically indicates this use of Lyrica is for adults (note that Centene policy allows coverage of members ≥ 12 years as supported by literature). For all indications except partial onset seizures, added 30 day trial duration of gabapentin consistent with other required trial durations. Updated verbiage (including requirement for drug trials to be at maximum indicated doses) and references. -Neuropathic pain not associated with diabetic neuropathy: Combined general neuropathic pain with neuropathic pain related to spinal cord injury as approval criteria are the same. -Neuropathic pain associated with diabetic neuropathy: Removed requirement for T/F of concurrent gabapentin and SNRI/TCA as there is limited evidence to support. -Partial onset seizures: Modified T/F requirement to include additional PDL anticonvulsants with demonstrated efficacy in partial seizures per guidelines. Trial duration and maximum indicated dosing is not required as anticonvulsant dosing is individualized based on patient response and patient concomitant therapy.	09/16	11/16

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Reviews, Revisions, and Approvals	Date	P&T Approval Date
-Fibromyalgia: Added 30 day trial duration of cyclobenzaprine, fluoxetine, or TCA consistent with other required trial durations.		
~~-Clinical changes made to criteria~~ - Diagnosis of Fibromyalgia – line #4 – removed fluoxetine as an accepted trial due to lack of sufficient evidence that it works	12/16	02/17
~~No clinical changes made to criteria~~ Modified trial/failure verbiage and removed age restriction for partial seizures (Lyrica is not proven unsafe or ineffective in pediatric patients) per updated template Separated continued approval criterion II.A.1 into 2 sub-criteria (II.A.1.a and II.A.1.b) to delineate between continuity of care criteria for partial seizure indication and regular criteria for all other covered indications ~~Modified trial/failure verbiage and removed age restriction for partial seizures (Lyrica is not proven unsafe or ineffective in pediatric patients) per updated template~~ ~~Separated continued approval criterion II.A.1 into 2 sub-criteria (II.A.1.a and II.A.1.b) to delineate between continuity of care criteria for partial seizure indication and regular criteria for all other covered indications~~	03~~1~~/17	05/17

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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.

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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.