

Title: Gabapentin (Gralise/Horizant)/pregabalin (Lyrica CR)

Policy #: Rx.01.112

Application of pharmacy policy is determined by benefits and contracts. Benefits may vary based on product line, group, or contract. Some medications may be subject to precertification, age, quantity, or formulary restrictions (ie limits on non-preferred drugs). Individual member benefits must be verified.

This pharmacy policy document describes the status of pharmaceutical information and/or technology at the time the document was developed. Since that time, new information relating to drug efficacy, interactions, contraindications, dosage, administration routes, safety, or FDA approval may have changed. This Pharmacy Policy will be regularly updated as scientific and medical literature becomes available. This information may include new FDA-approved indications, withdrawals, or other FDA alerts. This type of information is relevant not only when considering whether this policy should be updated, but also when applying it to current requests for coverage.

Members are advised to use participating pharmacies in order to receive the highest level of benefits.

Intent:

The intent of this policy is to communicate the medical necessity criteria for **gabapentin (Gralise®/Horizant®)** and **pregabalin (Lyrica CR®)** as provided under the member's prescription drug benefit.

Description:

Restless legs syndrome (RLS), also known as Willis-Ekbom disease, is a condition that is characterized by a constant urge to move the legs due to uncomfortable sensations. The symptoms are usually worse during the night and are relieved temporarily by movement of the legs. The risk of RLS has been linked to other conditions such as anemia, kidney disease, multiple sclerosis, and diabetes. Treatment drug classes for RLS included dopaminergic agents, alpha-2-delta calcium channel ligands, among others.

Post herpetic neuralgia (PHN) is a complication of herpes zoster that is classified by severe pain in the areas where the rash was located, even after it has cleared. The pain usually will resolve within a few weeks or months but it can last for years in some cases, which lead to an interference with daily life.

Gabapentin is structurally related to the neurotransmitter gamma aminobutyric acid (GABA). It has no effect on GABA binding, uptake, or degradation. The exact mechanism by which gabapentin exerts its effect in restless leg syndrome (RLS) and postherpetic neuralgia (PHN) is unknown. In vitro studies show that gabapentin binds with high affinity to the alpha-2-delta subunit of voltage activated calcium channels. The relationship of this binding and gabapentin's therapeutic effect is not known. Gabapentin enacarbil is a prodrug of gabapentin.

Gabapentin (Gralise®) is indicated for the management of postherpetic neuralgia (PHN).

Gabapentin enacarbil (Horizant®) is indicated for the treatment of moderate-to-severe primary RLS and PHN in adults.

Pregabalin is structurally related to the neurotransmitter gamma aminobutyric acid (GABA). It has no effect on GABA binding, uptake, or degradation. The exact mechanism by which pregabalin exerts its effects is unknown. Pregabalin binds with high affinity to the alpha-2-delta subunit of voltage activated calcium channels in central nervous system tissues. This binding may be involved in pregabalin's antinociceptive and antiseizure effects.

Pregabalin (Lyrica CR®) is indicated for the management of neuropathic pain associated with diabetic peripheral neuropathy and postherpetic neuralgia (PHN).

Policy:

INITIAL CRITERIA: Gabapentin (Gralise®) is approved when all of the following inclusion criteria are met:

1. Diagnosis of post-herpetic neuralgia, and
2. Inadequate response or inability to tolerate gabapentin or pregabalin

INITIAL CRITERIA: Gabapentin enacarbil (Horizant®) is approved when there is ONE of the following diagnoses:

1. Moderate-to-severe primary restless legs syndrome with inadequate response or inability to tolerate BOTH of the following:
 - a. Pramipexole; and
 - b. Ropinirole; or
2. Post-herpetic neuralgia with inadequate to tolerate ONE of the following:
 - a. gabapentin; or
 - b. pregabalin

INITIAL CRITERIA: Pregabalin (Lyrica CR®) is approved when ALL of the following inclusion criteria is met:

1. Diagnosis of ONE of the following:
 - a. Neuropathic pain associated with diabetic peripheral neuropathy; or
 - b. Post-herpetic neuralgia AND
2. Inadequate response or inability to tolerate gabapentin or pregabalin

Initial Authorization: 2 years

REAUTHORIZATION CRITERIA: Gabapentin (Gralise®), Gabapentin enacarbil (Horizant®), or Pregabalin (Lyrica CR®) is re-approved when there is positive clinical response to therapy.

Reauthorization: 2 years

Black Box Warning as shown in the drug Prescribing Information:

None

Guidelines:

Refer to the specific manufacturer's prescribing information for administration and dosage details and any applicable Black Box warnings.

BENEFIT APPLICATION

Subject to the terms and conditions of the applicable benefit contract, the applicable drug(s) identified in this policy is (are) covered under the prescription drug benefits of the Company's products when the medical necessity criteria listed in this pharmacy policy are met. Any services that are experimental/investigational or cosmetic are benefit contract exclusions for all products of the Company.

References:

Gabapentin. Available at: <http://www.micromedexsolutions.com>. Accessed March 25, 2021.

Gralise® (gabapentin) [package insert]. Newark, CA. Depomed, Inc. April 2020. Available at: https://www.gralise.com/static/Gralise_full_Prescribing_Information_-_Printed-b9a705a9011191f3f63f0a16e352cf4d.pdf . Accessed March 25, 2021.

Dopp JM, Phillips BG. Sleep–Wake Disorders. In: DiPiro JT, Talbert RL, Yee GC, Matzke GR, Wells BG, Posey L. eds. *Pharmacotherapy: A Pathophysiologic Approach, 10e* New York, NY: McGraw-Hill; .<http://accesspharmacy.mhmedical.com.libproxy.temple.edu/content.aspx?bookid=1861§ionid=134128126>. Accessed March 25, 2021.

Horizant® (gabapentin enacarbil) [package insert]. Santa Clara, CA. Xenoport, Inc. April 2020. Available at: https://www.horizant.com/pdf/Horizant_PrescribingInformation.pdf . Accessed March 25, 2021.

Pregabalin. Available at: <http://www.micromedexsolutions.com>. Accessed March 25, 2021.

Lyrica CR® (pregabalin hydrochloride) [package insert]. New York, NY. Pfizer. June 2020. Available from https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/209501s000lbl.pdf. Accessed March 25, 2021.

Shingles (Herpes Zoster). Centers for Disease Control and Prevention. <https://www.cdc.gov/shingles/about/complications.html>. Published January 19, 2018. Accessed March 25, 2021.

Applicable Drugs:

Inclusion of a drug in this table does not imply coverage. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

Brand Name

Gralise®
Horizant®
Lyrica CR®

Generic Name

gabapentin
Gabapentin enacarbil
pregabalin controlled-release

Cross References:

Off Label Use Rx.01.33

Policy Version Number:	13.00
P&T Approval Date:	March 18, 2021
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Next Required Review Date:	March 18, 2022

The Policy Bulletins on this web site were developed to assist the Company in administering the provisions of the respective benefit programs, and do not constitute a contract. If you have coverage through the Company, please refer to your specific benefit program for the terms, conditions, limitations and exclusions of your coverage. Company does not provide health care services, medical advice or treatment, or guarantee the outcome or results of any medical services/treatments. The facility and professional providers are responsible for providing medical advice and treatment. Facility and professional providers are independent contractors and are not employees or agents of the Company. If you have a specific medical condition, please consult with your doctor. The Company reserves the right at any time to change or update its Policy Bulletins.

