Clinical Policy: Gabapentin ER (Gralise, Horizant)

Reference Number: CP.PMN.240
Effective Date: 09.01.20
Last Review Date: 08.20
Line of Business: Commercial, HIM, Medicaid Revision Log

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

Description

Gabapentin (Gralise®) is an analog of gamma-aminobutyric acid (GABA) that has GABA agonist activity.

Gabapentin enacarbil ER (Horizant®) is a prodrug of gabapentin.

FDA Approved Indication(s)

Gralise and Horizant are indicated for the management of postherpetic neuralgia (PHN).

Horizant is also indicated for the treatment of moderate-to-severe primary restless legs syndrome (RLS) in adults.

Limitation(s) of use:

- Horizant is not recommended for patients who are required to sleep during the daytime and remain awake at night.
- Gralise and Horizant are not interchangeable with other gabapentin products because of differing pharmacokinetic profiles that affect the frequency of administration.

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 Gralise and Horizant are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Postherpetic Neuralgia (must meet all)**:**

1. Diagnosis of PHN;
2. Age ≥ 18 years;
3. Failure of a ≥ 30 day trial of immediate-release gabapentin at ≥ 1,800 mg per day, unless contraindicated to its excipients or clinically significant adverse effects are experienced;
4. Dose does not exceed (a or b):
   a. Gralise: 1,800 mg (3 tablets) per day;
   b. Horizant: 1,200 mg (2 tablets) per day.

Approval duration:
Medicaid/HIM – 12 months

Commercial – Length of Benefit

B. Restless Leg Syndrome (must meet all)**:**
1. Diagnosis of RLS;
2. Request is for Horizant;
3. Age ≥ 18 years;
4. Failure of ropinirole and pramipexole at up to maximally indicated doses, each used for ≥ 30 days, unless both are contraindicated or clinically significant adverse effects are experienced;
5. Dose does not exceed 600 mg (1 tablet) per day.

Approval duration:
Medicaid/HIM – 12 months
Commercial – Length of Benefit

C. Other diagnoses/indications
1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**
1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed (a or b):
   a. PHN: 1,800 mg (3 tablets) per day (Gralise) or 1,200 mg (2 tablets) per day (Horizant);
   b. RLS: 600 mg (1 tablet) per day (Horizant).

Approval duration:
Medicaid/HIM – 12 months
Commercial – Length of Benefit

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 12 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid.

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 policies –

CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

FDA: Food and Drug Administration
GABA: gamma-aminobutyric acid
PHN: post herpetic neuralgia
RLS: restless legs syndrome

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
gabapentin (Neurontin®)	PHN 300 mg PO as a single dose on day 1, then 600 mg/day (300 mg PO BID) on day 2, and 900 mg/day (300 mg PO TID) on day 3. The dose can then be titrated up as needed for pain relief to a dose of 1800 mg/day (600 mg PO TID).	3,600 mg/day
ropinirole (Requip®)	RLS Initially, 0.25 mg PO QD given 1 to 3 hours before bedtime. During days 3 through 7, the dosage may be increased to 0.5 mg PO QD. At the beginning of week 2 (day 8) the dose may be increased to 1 mg PO QD for 7 days. In weeks 3 through 6, the dose may be titrated up by 0.5 mg PO weekly (from 1.5 mg to 3 mg PO over the 5 week period), as needed to achieve desired effect. In week 7, may increase dose to 4 mg PO QD.	4 mg/day
pramipexole (Mirapex®)	RLS 0.125 mg PO QD 2 to 3 hours before bedtime. If necessary, dosage may be increased after 4 to 7 days to 0.25 mg PO QD. If additional upward titration is necessary, dosage may be increased after 4 to 7 days to 0.5 mg PO QD 2 to 3 hours before bedtime. Dosages higher than 0.5 mg do not appear to provide additional benefits.	0.5 mg/day

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.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): hypersensitivity (Gralise)
- Boxed warning(s): none reported

V. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
Gabapentin ER (Gralise)	PHN	Gralise should be initiated and titrated as follows: Day 1: 300 mg PO Day 2: 600 mg PO Days 3 to 6: 900 mg PO QD Days 7 to 10: 1,200 mg PO QD Days 11 to 14: 1,500 mg PO QD Days ≥ 15: 1,800 mg PO QD	1,800 mg/day
Gabapentin enacarbil ER (Horizant)	PHN	600 mg PO QAM for 3 days, then increase to 600 mg PO BID beginning on day 4	1,200 mg/day
	RLS	600 mg PO QD at about 5 PM	600 mg/day

VI. Product Availability

Drug Name	Availability
Gabapentin ER (Gralise)	ER tablets: 300 mg, 600 mg
Gabapentin enacarbil ER (Horizant)	ER tablets: 300 mg, 600 mg

VII. References

1. Gralise Prescribing Information. Morristown, NJ: Almatica Pharma, Inc.; April 2020. Available at: https://www.gralise.com/. Accessed April 27, 2020.
2. Horizant Prescribing Information. Atlanta, GA; Arbor Pharmaceuticals, LLC; April 2020. Available at: https://horizant.com/. Accessed April 27, 2020.
3. 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. Neurology September 28, 2004 vol. 63 no. 6 959-965.
4. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2020. Available at: http://www.clinicalpharmacology-ip.com/. Accessed April 27, 2020.
5. Finnerup NB, Attal N, Haroutounian S, et al. Pharmacotherapy for neuropathic pain in adults: a systematic review and meta-analysis. Lancet Neurology February 2015; 14(2): 162-173.
6. Winkelman JW, Armstrong MJ, Allen RP, et al. Practice guideline summary: Treatment of restless legs syndrome in adults: Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. Neurology. 2016;87(24):2585.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created: adapted from previously approved policy CP.CPA.38 (now retired); added HIM and Medicaid line of business; added Horizant to policy with new criteria set for RLS; added quantity associated with dosing limits; references reviewed and updated.	04.27.20	08.20

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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