Clinical Policy: Gabapentin ER (Gralise, Horizant)

Reference Number: ERX.NPA.49
Effective Date: 06.01.15
Last Review Date: 11.17 Revision Log

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

Description
Gabapentin ER [extended-release] (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 is indicated for the management of postherpetic neuralgia (PHN).

Horizant is indicated:
- For the treatment of moderate-to-severe primary restless legs syndrome (RLS) in adults
  - Horizant is not recommended for patients who are required to sleep during the daytime and remain awake at night.
- For the management of PHN in adults

Limitation(s) of use: Gralise and Horizant are not interchangeable with other gabapentin products because of differing pharmacokinetic profiles.

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

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ 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 ≥ 1800 mg/day unless contraindicated to its excipients or clinically significant adverse effects are experienced;
4. Dose does not exceed:
   a. Gralise: 1800 mg/day;
   b. Horizant: 1200 mg/day.

Approval duration: 12 months

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 contraindicated or clinically significant adverse effects are experienced;
5. Dose does not exceed 600 mg/day.

Approval duration: 12 months

C. Other diagnoses/indications
1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

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

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions 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. PHN: 1800 mg/day (Gralise) or 1200 mg/day (Horizant);
   b. RLS: 600 mg/day (Horizant).

Approval duration: 12 months

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

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 12 months (whichever is less); or
2. Refer to ERX.PA.01 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 – ERX.PA.01 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

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

Appendix B: Therapeutic Alternatives

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
gabapentin IR (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).	3600 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.

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: 1200 mg PO QD Days 11 to 14: 1500 mg PO QD Days ≥15: 1800 mg PO QD	1800 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	1200 mg/day
	RLS	600 mg PO QD at about 5 PM (A daily dose of 1200 mg provided no additional benefit compared with the 600-mg dose, but caused an increase in adverse reactions)	600 mg/day

VI. Product Availability

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

VII. References

1. Gralise Prescribing Information. Newark, CA: Depomed, Inc.; December 2012. Available at: https://www.gralise.com/. Accessed September 8, 2017.
2. Horizant Prescribing Information. Atlanta, GA; Arbor Pharmaceuticals, LLC; October 2016. Available at: https://horizant.com/. Accessed September 8, 2017.
3. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2017. Available at: http://www.clinicalpharmacology-ip.com/. .
4. 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.
5. 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	06.15	06.15
Converted to new template in written format; Updated references to show most current literature search; Created a BACKGROUND to include description, mechanism of action, and FDA approved indications for Gralise and Horizant; Added table to show maximum dose of Gralise and Horizant for each FDA approved indication; Modified diagnosis of PHN to include trial and failure of gabapentin ≥ 1800mg/day for both Gralise and Horizant; Added bullet point to include intolerant of gabapentin at maximum dose. Modified workflow document and separated by indication.	02.16	06.16
4Q17 Annual Review Converted to new template. PHN: Modified requirement related to failure of immediate-release gabapentin to include contraindications to its excipients as an option.	09.08.17	11.17

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Added a requirement that member is responding positively to therapy on re-auth. 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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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.

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