Clinical Policy: Gabapentin ER (Gralise, Horizant)

Reference Number: ERX.NPA.49
Effective Date: 06.01.15
Last Review Date: 08.22
Line of Business: Commercial, Medicaid

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 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.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

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 ≥ 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: 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 gabapentin immediate release (IR) and generic pregabalin 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: 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 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: 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

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

Drug Name	Indication	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).	3,600 mg/day
	RLS	300 mg PO daily. The dose can be titrated up by 300 mg every week as needed up to 3600 mg/day. Doses should be spaced at least 2 hours apart.	
Pregabalin (Lyrica®)	RLS	75 mg PO daily. The dose can be titrated up by 75 mg every week as needed up to 450 mg daily.	450 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 15, 2022.
2. Horizant Prescribing Information. Atlanta, GA; Arbor Pharmaceuticals, LLC; April 2020. Available at: https://horizant.com/. Accessed April 15, 2022.
3. Clinical Pharmacology [database online]. Elsevier; 2022. Available at: https://www.clinicalkey.com/pharmacology/. Accessed April 15, 2022.
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. 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. Silber MH, Buchfuhrer MJ, Earley CJ, et al. The management of restless legs syndrome: an updated algorithm. Mayo Clinic July 2021: 96(7): 1921-1937. https://doi.org/10.1016/j.mayocp.2020.12.026.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
3Q 2018 annual review: no significant changes; references reviewed and updated.	04.23.18	08.18
3Q 2019 annual review: no significant changes; references reviewed and updated.	05.19.19	08.19
3Q 2020 annual review: no significant changes; added quantity associated with dosing limits; references reviewed and updated.	04.27.20	08.20
3Q 2021 annual review: no significant changes; references reviewed and updated.	05.03.21	08.21

Reviews, Revisions, and Approvals	Date	P&T Approval Date
3Q 2022 annual review: updated RLS approval criteria – removed trial of ropinirole and pramipexole, added trial of gabapentin IR and generic pregabalin to align with RLS Foundation clinical guidelines, updated Appendix B: therapeutic alternative table to include; references reviewed and updated.	04.22.22	08.22

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.