Gabapentin ER (extended-release) [Horizant, Gralise] Step Therapy with Quantity Limit Program Summary

Program applies to FlexRx Open, FocusRx, GenRx Open, Health Insurance Marketplace, and KeyRx.

This is a FlexRx standard and GenRx standard step therapy program.

The BCBS MN Step Therapy Supplement also applies to this program for all Commercial/HIM lines of business.

POLICY REVIEW CYCLE

Effective Date	Date of Origin
07-01-2024	06-01-2012

FDA APPROVED INDICATIONS AND DOSAGE

Agent(s)	FDA Indication(s)	Notes	Ref#
Gralise® (gabapentin)* Extended-release tablet	Management of postherpetic neuralgia (PHN)	*generic available	2
Horizant® (gabapentin) Extended-release tablet	Treatment of moderate-to-severe primary Restless Legs Syndrome (RLS) in adults Management of postherpetic neuralgia (PHN) in adults		1

See package insert for FDA prescribing information: https://dailymed.nlm.nih.gov/dailymed/index.cfm

CLINICAL RATIONALE

Restless Legs Syndrome (RLS)	Restless legs syndrome (RLS) is a movement disorder characterized by an urge to move the legs or arms, commonly in response to uncomfortable dysesthesia.(5) Pramipexole, ropinirole, and rotigotine transdermal system are recommended by the American Academy of Sleep Medicine (AASM) and the European Federation of Neurological Societies/European Neurological Society/European Sleep Research Society as first-line treatment for RLS.(3,4) The non-ergot dopamine agonists, pramipexole and ropinirole, are effective in the treatment of RLS and are less likely to cause side effects than other dopamine agonists (e.g., cabergoline and pergolide) and levodopa. Gabapentin and pregabalin may be useful in RLS in patients with comorbid pain.(3) The American Academy of Neurology recommends that the choice of agent for the treatment of primary RLS be based on goal of treatment and patient comorbidities. The level of evidence for use of pramipexole, rotigotine, cabergoline, gabapentin, IV ferric carboxymaltose, levodopa, and pregabalin in RLS varies depending on those goals and comorbidities.(5)
Postherpetic Neuralgia (PHN)	Postherpetic neuralgia (PHN) is the most common complication of herpes zoster. PHN is defined as pain in the dermatomal distribution that is sustained for at least 90 days after the rash. PHN is caused by nerve damage secondary to an inflammatory response induced by viral replication within a nerve. Pain-management strategies

	should focus on symptom control. Some patients have complete resolution of symptoms at several years while others continue medications indefinitely.(7) Both topical (capsaicin and lidocaine) and systemic treatments can be effective in the management of PHN. The anticonvulsants gabapentin and pregabalin are approved for treatment of PHN. Tricyclic antidepressants are also effective in treating PHN, but up to one-fourth of patients discontinue treatment due to adverse reactions. Opioids are considered third-line treatment with two systematic reviews finding tramadol provided significant pain relief in patients with PHN.(6,7) Acetaminophen and nonsteroidal anti-inflammatory drugs (NSAIDs) are generally considered to be ineffective for neuropathic pain.(7)
Safety	Gralise is contraindicated in patients who have demonstrated hypersensitivity to the drug or its ingredients. Horizant has no FDA labeled contraindications for use.

REFERENCES

Number	Reference
1	Horizant prescribing information. Azurity Pharmaceuticals, Inc. August 2022.
2	Gralise prescribing information. Almatica Pharma LLC. March 2023.
3	Aurora RN, Kristo DA, Bista SR, et al. The Treatment of Restless Legs Syndrome and Periodic Limb Movement Disorder in Adults - An Update for 2012: Practice Parameters with an Evidence-Based Systematic Review and Meta-Analyses. An American Academy of Sleep Medicine Clinical Practice Guideline. *Sleep.* 2012;35(8):1039-1062. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3397811/
4	Garcia-Borreguero D, Ferini-Strambi L, Kohnen R, et al. European guidelines on management of restless legs syndrome: report of a joint task force by the European Federation of Neurological Societies, the European Neurological Society and the European Sleep Research Society. *European Journal of Neurology.* 2012, 19(11):1385-1396. Available at: https://onlinelibrary.wiley.com/doi/full/10.1111/j.1468-1331.2012.03853.x
5	Winkelman WJ, Armstrong MJ, Chaudhuri KR. Practice guideline summary: Treatment of restless legs syndrome in adults. Neurology. December 13, 2016;87(24). Reaffirmed October 2022.
6	Johnson, RW, Rice AS. Postherpetic Neuralgia. *N Engl J Med.* 2014;371:1526-1533. Available at: https://www.nejm.org/action/showPdf?downloadfile=showPdf&doi=10.1056/NEJMcp1403062&loaded=true
7	Saguil AS, Kane S, Mercado M, et al. Herpes Zoster and Postherpetic Neuralgia: Prevention and Management. *Am Fam Physician.* 2017;96(10):656-663. Available at: https://www.aafp.org/afp/2017/1115/p656.pdf

POLICY AGENT SUMMARY STEP THERAPY

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Targeted MSC	Available MSC	Final Age Limit	Preferred Status
Gralise	gabapentin (once-daily) tab ; gabapentin (once-daily) tab pack	300 (9) & 600(24) MG ; 300 MG ; 450 MG ; 600 MG ; 750 MG ; 900 MG	M ; N ; O ; Y	N ; O ; Y		
Horizant	gabapentin enacarbil tab er	300 MG ; 600 MG	M ; N ; O	N		

POLICY AGENT SUMMARY QUANTITY LIMIT

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	QL Amount	Dose Form	Day Supply	Duration	Addtl QL Info	Allowed Exceptions	Targeted NDCs When Exclusions Exist
Gralise	gabapentin (once-daily) tab	450 MG	30	Tablets	30	DAYS			
Gralise	gabapentin (once-daily) tab	750 MG	30	Tablets	30	DAYS			
Gralise	gabapentin (once-daily) tab	900 MG	60	Tablets	30	DAYS			
Gralise	Gabapentin (Once-Daily) Tab 300 MG	300 MG	30	Tablets	30	DAYS		The patient requires increased quantities of Gralise to accommodate a titration schedule. The increased quantity will be approved for 1 month only.	
Gralise	Gabapentin (Once-Daily) Tab 600 MG	600 MG	90	Tablets	30	DAYS		The patient requires increased quantities of Gralise to accommodate a titration schedule. The increased quantity will be approved for 1 month only.	
Horizant	gabapentin enacarbil tab er	300 MG ; 600 MG	60	Tablets	30	DAYS			

CLIENT SUMMARY – STEP THERAPY

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Gralise	gabapentin (once-daily) tab ; gabapentin (once-daily) tab pack	300 (9) & 600(24) MG ; 300 MG ; 450 MG ; 600 MG ; 750 MG ; 900 MG	FlexRx Open ; FocusRx ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Horizant	gabapentin enacarbil tab er	300 MG ; 600 MG	FlexRx Open ; FocusRx ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx

CLIENT SUMMARY – QUANTITY LIMITS

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Gralise	gabapentin (once-daily) tab	750 MG	FlexRx Open ; FocusRx ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Gralise	gabapentin (once-daily) tab	450 MG	FlexRx Open ; FocusRx ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Gralise	gabapentin (once-daily) tab	900 MG	FlexRx Open ; FocusRx ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Gralise	Gabapentin (Once-Daily) Tab 300 MG	300 MG	FlexRx Open ; FocusRx ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Gralise	Gabapentin (Once-Daily) Tab 600 MG	600 MG	FlexRx Open ; FocusRx ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Horizant	gabapentin enacarbil tab er	300 MG ; 600 MG	FlexRx Open ; FocusRx ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx

STEP THERAPY CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
	TARGET AGENT(S) **Gralise*** (gabapentin) **Horizant** (gabapentin enacarbil) * - generic available; included as a target in the step therapy program **Target Agent(s)** will be approved when ONE of the following is met: 1. The patient is currently being treated with the requested agent as indicated by ALL of the following: A. A statement by the prescriber that the patient is currently taking the requested agent **AND** B. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent **AND** C. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR** 2. The patient's medication history includes generic immediate release gabapentin agent use, intolerance, or hypersensitivity **OR** 3. BOTH of the following: A. The prescriber has stated that the patient has tried generic immediate release gabapentin **AND** B. Generic gabapentin was discontinued due to lack of effectiveness or an adverse event **OR** 4. The patient has an FDA labeled contraindication to ALL generic immediate release gabapentin agents **OR** 5. The prescriber has provided documentation that ALL generic immediate release gabapentin agents cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm **Length of Approval:** 12 months NOTE: If Quantity Limit program also applies, please refer to Quantity Limit Criteria.

QUANTITY LIMIT CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
	Quantity Limit for the Target Agent(s) will be approved when ONE of the following is met: 1. The requested quantity (dose) does NOT exceed the program quantity limit **OR** 2. The patient requires increased quantities of Gralise to accommodate a titration schedule. The increased quantity will be approved for 1 month only **OR** 3. The requested quantity (dose) exceeds the program quantity limit AND ONE of the following: A. BOTH of the following: 1. The requested agent does NOT have a maximum FDA labeled dose for the requested indication **AND** 2. There is support for therapy with a higher dose for the requested indication **OR** B. BOTH of the following: 1. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose for the requested indication **AND** 2. There is support for why the requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does NOT exceed the program quantity limit **OR** C. BOTH of the following: 1. The requested quantity (dose) exceeds the maximum FDA labeled dose for the requested indication **AND** 2. There is support for therapy with a higher dose for the requested indication **Length of Approval**: up to 12 months