



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

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

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

FDA APPROVED INDICATIONS AND DOSAGE^{1,2}

Available Products**	Indications	Dosing and Administration*														
Gralise (gabapentin) extended-release tablet 300 mg, 600 mg starter pack 300 mg (9), 600 mg (69)	Management of Postherpetic Neuralgia (PHN)	Once daily at evening meal, titrated (schedule below). <table border="1" style="margin-left: 20px;"> <thead> <tr> <th>Day(s)</th> <th>1</th> <th>2</th> <th>3-6</th> <th>7-10</th> <th>11-14</th> <th>15</th> </tr> </thead> <tbody> <tr> <td>Dose (mg)</td> <td>300</td> <td>600</td> <td>900</td> <td>1200</td> <td>1500</td> <td>1800</td> </tr> </tbody> </table>	Day(s)	1	2	3-6	7-10	11-14	15	Dose (mg)	300	600	900	1200	1500	1800
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Discontinuation should be done gradually over a minimum of 1 week or longer (at the discretion of the prescriber).																
Horizant (gabapentin enacarbil) extended-release tablet 300 mg, 600 mg	Treatment of moderate-to-severe primary Restless Legs Syndrome (RLS) in adults	RLS: 600 mg once daily at 5 pm; PHN: 600 mg twice daily (initiate at 600 mg daily for 3 days, then increase to 600 mg twice daily) NOTE: 300 mg tablet to be used in patients with creatinine clearance <60 mL/min.														
	Management of postherpetic Neuralgia (PHN)															

** Gralise and Horizant are not interchangeable with other gabapentin products due to differing pharmacokinetic profiles.^{1,2}

CLINICAL RATIONALE

Restless Legs Syndrome (RLS)

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 restless leg syndrome (RLS).^{8,14} 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 (eg, cabergoline and pergolide) and levodopa. These agents, along with rotigotine, are considered to be the dopamine agonists of choice for RLS. Gabapentin and pregabalin may be useful in RLS in patients with painful peripheral neuropathy or an unrelated chronic pain syndrome, in patients with comorbid insomnia or sleep disturbance that is disproportionate to other RLS symptoms, impulse control disorder, comorbid anxiety, or Parkinson disease.¹⁵

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, pregabalin in RLS varies depending on those goals and comorbidities.¹⁰

An Agency for Healthcare Research and Quality (AHRQ, 2012) comparative effectiveness review concluded that evidence for RLS treatment is limited to short-term, placebo-controlled studies of dopamine agonists (ropinirole, pramipexole) and alpha-2-delta ligands (gabapentin enacarbil, gabapentin, and pregabalin) conducted in a highly selected population with high moderate to very severe primary RLS of long duration. Compared with placebo, dopamine agonists and alpha-2-delta ligands increase the percentage responders, reduce RLS symptom scores, and improve patient-reported sleep outcomes, quality of life, and overall RLS impact. Both short- and long-term adverse effects and treatment withdrawals due to adverse effects or lack of efficacy are common. There are no high-quality data on comparative effectiveness and harms of commonly used treatments, little data on nonpharmacologic interventions or the effect of patient or RLS characteristics on outcomes. Applicability is unknown for adults with less frequent or less severe RLS symptoms, children, or those with secondary RLS.⁹

Postherpetic Neuralgia (PHN)

Dworkin et al.⁵ states that most randomized controlled trials of chronic neuropathic pain have examined only two pain syndromes, diabetic peripheral neuropathy and PHN. These authors suggest that while the applicability of the results of clinical trials for one chronic neuropathic pain syndrome to others cannot be determined, most of the first-line therapies have been tested with multiple types of neuropathic pain and have shown similar results.⁵

Generally, guidelines and reviews on treatment of neuropathic pain have not been consistent regarding their placement of anticonvulsants as first-, second-, or third-line treatment. Some guidelines and reviews recommend pregabalin and gabapentin as first- or second-line treatment. Carbamazepine and lamotrigine have been considered second- or third-line treatments for neuropathic pain. Tricyclic antidepressants (e.g. amitriptyline) are often recommended as a first-line treatment for neuropathic pain.³⁻⁷

Guidelines from the European Federation of Neurological Societies (EFNS), American Association of Clinical Endocrinologists (AACE), and the AAN/Neuromuscular and Electrodiagnostic Medicine/Physical Medicine and Rehabilitation recommend both pregabalin and gabapentin as first line treatment for peripheral neuropathy (included diabetic peripheral neuropathy, and post herpetic neuralgia).¹¹⁻¹³ The guidelines consider both gabapentin and pregabalin to be equal in efficacy and one is not preferred over the other.^{11,13}

Safety

Gralise is contraindicated in patients who have demonstrated hypersensitivity to the drug or its ingredients. Horizant carries no FDA labeled contraindications.^{1,2}

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Gabapentin ER (extended-release) [Horizant[®], Gralise[®]] Step Therapy

OBJECTIVE

The intent of the Gabapentin ER (extended-release) [Horizant and Gralise] Step Therapy (ST) program is to encourage the use of cost-effective generic prerequisites over the more expensive target agents and to accommodate for use of target agents when the prerequisites cannot be used due to previous trial, documented intolerance, FDA labeled contraindication, or hypersensitivity. Requests for target agents will be reviewed when patient-specific documentation has been provided.

TARGET AGENTS

Gralise[®] (gabapentin)

Horizant[®] (gabapentin enacarbil)

PRIOR AUTHORIZATION CRITERIA FOR APPROVAL

Horizant (gabapentin enacarbil) or Gralise (gabapentin) will be approved when ONE of the following is met:

1. The patient's medication history includes use of generic gabapentin in the past 90 days
- OR**
2. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to generic gabapentin

Length of Approval: 12 months

NOTE: If Quantity Limit program also applies, please refer to Quantity Limit documents.