### FDA APPROVED INDICATIONS AND DOSAGE

<table>
<thead>
<tr>
<th>Available Products**</th>
<th>Indications</th>
<th>Dosing and Administration*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Horizant</strong> <em>(gabapentin enacarbil)</em> extended-release tablet 300 mg, 600 mg</td>
<td>Treatment of moderate-to-severe primary Restless Legs Syndrome (RLS) in adults Management of postherpetic Neuralgia (PHN)</td>
<td>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 &lt;60 mL/min.</td>
</tr>
<tr>
<td><strong>Gralise</strong> <em>(gabapentin)</em> extended-release tablet 300 mg, 600 mg starter pack 300 mg (9), 600 mg (69)</td>
<td>Management of Postherpetic Neuralgia (PHN)</td>
<td>Once daily at evening meal, titrated (schedule below).</td>
</tr>
</tbody>
</table>

<table>
<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>
<th>Dose (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>300</td>
<td>600</td>
<td>900</td>
<td>1200</td>
<td>1500</td>
<td>1800</td>
<td></td>
</tr>
</tbody>
</table>

**Horizant and Gralise are not interchangeable with other gabapentin products due to differing pharmacokinetic profiles.**

### 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). 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, impulse control disorder, comorbid anxiety, or Parkinson disease. 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
harm 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

AAN recommendations for treatment of painful diabetic neuropathy include pregabalin (level A
evidence, established as effective); and gabapentin, sodium valproate, venlafaxine, duloxetine,
amitriptyline, dextromethorphan, maprotiline, tramadol, oxycodone, capsaicin, isosorbide
dinitrate, electrical stimulation, percutaneous nerve stimulation (level B evidence, considered
probably effective).10

A review (2010) suggests primary agents for treatment of painful diabetic neuropathy include
TCAs, anticonvulsants, SNRIs, opiates, and topical medications. Although complete relief is
ideal, pain reduction of only 30 to 50 percent can be expected in most patients taking maximal
doses of medication. TCAs (amitriptyline, nortriptyline) are recommended as first-line therapy
for painful diabetic neuropathy in appropriate patients. If TCAs are contraindicated, newer
anticonvulsants (gabapentin, pregabalin) are considered. SNRIs may be used if first line agents
are unsuccessful.11

Guidelines5,12 consider TCAs, gabapentin, pregabalin, or tramadol, as effective first-line
medications for treatment of neuropathic pain associated with spinal cord injury; lamotrigine
and opioids may be effective in some patients.5,12 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.12-14 The guidelines
consider both gabapentin and pregabalin to be equal in efficacy and one is not preferred over
the other.12,14

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

REFERENCES


**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. The program allows continuation of therapy when there is documentation that the patient is receiving the requested agent. 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. There is documentation that the patient is currently receiving the requested agent
   **OR**
3. The prescriber states the patient is using the requested agent AND is at risk if therapy is changed
   **OR**
4. 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.