Gabapentin and Pregabalin
Prior Authorization/ Step Therapy Policy

**DRUGS AFFECTED:**
- pregabalin (Lyrica®)
- gabapentin (generics, Neurontin®)
- gabapentin extended release (Gralise™)
- gabapentin enacarbil (Horizant™)

**OVERVIEW:**
Pregabalin and gabapentin are analogs of the neurotransmitter gamma-aminobutyric acid (GABA) that have similar mechanisms of action. It has been postulated that pregabalin has a stronger receptor affinity and, therefore, may be more potent than gabapentin. The clinical relevance of this has yet to be established. There are no head-to-head clinical trials comparing pregabalin and gabapentin. The FDA has designated pregabalin as a schedule V controlled substance due to its potential for euphoric effects, abuse, and dependence. Gabapentin has not been designated as a controlled substance.

Despite their pharmacologic similarities, pregabalin and gabapentin do differ in some respects. For example, pregabalin can be dosed twice daily (BID) rather than three times daily (TID) for certain indications, it has a predictable dose-response relationship due to linear pharmacokinetics, a maximum effective dose has been established, and it may be able to be titrated to an effective dose faster than gabapentin.

Pregabalin is Food and Drug Administration (FDA)-approved for the management of postherpetic neuralgia (PHN), as adjunctive therapy in the treatment of partial onset seizures in adults, and for the management of pain associated with diabetic peripheral neuropathy (DPN), fibromyalgia, and neuropathic pain associated with spinal cord injury. Pregabalin and gabapentin differ in indication in that gabapentin is also indicated as adjunctive therapy for partial onset seizures in children but it is not FDA-approved for the management of painful DPN. Gabapentin extended release is FDA approved only for the treatment of PHN, gabapentin enacarbil is FDA approved only for the treatment of moderate to severe restless legs syndrome in adults. The listing below compares pregabalin, gabapentin, gabapentin extended release, and gabapentin enacarbil indications.
Table 1. Comparison of FDA-approved indications.

<table>
<thead>
<tr>
<th>Indication</th>
<th>pregabalin</th>
<th>gabapentin</th>
<th>gabapentin extended release</th>
<th>gabapentin enacarbil</th>
</tr>
</thead>
<tbody>
<tr>
<td>PHN</td>
<td></td>
<td>X</td>
<td>X</td>
<td>X</td>
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<tr>
<td>Adjunctive therapy in the treatment of partial onset seizures in adults</td>
<td>X</td>
<td></td>
<td></td>
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<tr>
<td>Adjunctive therapy in the treatment of partial onset seizures in children</td>
<td></td>
<td></td>
<td>X</td>
<td></td>
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<tr>
<td>Pain associated with DPN</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fibromyalgia</td>
<td></td>
<td></td>
<td>X</td>
<td></td>
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<tr>
<td>Restless Legs Syndrome (RLS)</td>
<td></td>
<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Neuropathic pain associated w/spinal cord injury</td>
<td>X</td>
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</tbody>
</table>

Although gabapentin is not FDA-approved for the management of pain associated with DPN, there are data supporting its use in this condition. Gabapentin was shown to be superior in efficacy to placebo and similar in efficacy to amitriptyline in three small placebo-controlled trials and one small comparative trial. Gabapentin is acknowledged as an effective therapeutic alternative in the management of pain associated with DPN in review articles as well as in several reputable clinical information resources (i.e., Micromedex, American Hospital Formulary Service [AHFS], The Medical Letter). The evidence available to support the use of pregabalin in the management of painful DPN is similar to gabapentin in that there are three placebo-controlled trials (albeit with a larger number of patients) but different in that pregabalin has no comparative data with any other agent used in this condition.

Prior Authorization/Step Therapy criteria for Lyrica (pregabalin), the following criteria must be met:

1. Patient has a seizure disorder. If anti-epileptic medications appear on the prescription claims history within the past 130 days, the Lyrica will process.

2. Patient has used gabapentin for ≥ 60 days for the same diagnosis as the diagnosis specified for the use of Lyrica within the past 130 days. If gabapentin appears on the member's prescription claims history for the specified number of days within the specified time period, the Lyrica will process. If the gabapentin does not appear on the prescription claims history within the past 130 days, the prior authorization request must be accompanied by physician's medical records documenting trial and failure and/or intolerance to gabapentin trial.

3. Patient has used gabapentin for any length of time at a dose ≥ 2400 mg/day for the same diagnosis as the diagnosis specified for the use of Lyrica. This use must be confirmed by gabapentin appearing on the prescription claims history with the specified dose.

4. Patient cannot tolerate gabapentin due to adverse events. The occurrence of these adverse effects must be documented by medical records accompanying the prior authorization form.

5. Pregabalin is being prescribed for the management of pain associated with DPN. If diabetic medications are present on the prescription claims history, the Lyrica will process without any intervention, otherwise this diagnosis must be documented by office notes accompanying the prior authorization request. Pregabalin is FDA-approved for the management of pain associated with DPN while gabapentin is not.

6. Patient has a documented diagnosis of fibromyalgia.

7. If the member is started on a 2nd step medication using "samples" without following the stated step criteria, authorization will not be given.
8. If you believe that the first-step drug requirement is inappropriate or it has failed to successfully treat your patient’s condition, you may submit a prior authorization request for consideration of approval of a second-step drug.

Lyrica has quantity limits restricting the dispensing to a total dose of 600 mg per day.

**Prior Authorization of Gralise will be approved for those members who meet the following criteria:**

Member must have a documented diagnosis of post-herpetic neuralgia (PHN) (ICD-10 B02.22) **AND** has used gabapentin for ≥ 60 days for the treatment of postherpetic neuralgia (PHN) within the past 130 days. Gabapentin must appear on the member’s prescription claims history for the specified time period, in addition medical records documenting the presence of PHN must be received for review. If the gabapentin does not appear on the prescription claims history within the past 130 days, the prior authorization request must be accompanied by physician’s medical records documenting trial and failure and/or intolerance to gabapentin trial.

Use of Gralise (gabapentin) in disease states outside of its FDA-approved indication will be denied based on the lack of clinical data to support its effectiveness and safety in other conditions.

Gralise should be titrated to an 1800 mg dose taken orally, once-daily, with the evening meal. Gralise is subject to quantity limits of 30 of the 300 mg tablets or 90 of the 600 mg tablets per 30 days.

**Prior Authorization of Horizant will be approved for those members who meet the following criteria:**

For RLS---the prescribing physician must submit medical records documenting the presence of Restless Legs Syndrome (RLS).

For PHN---patient must have used gabapentin for ≥ 60 days for the treatment of postherpetic neuralgia (PHN) within the past 130 days. Gabapentin must appear on the member’s prescription claims history for the specified time period, in addition medical records documenting the presence of PHN must be received for review. If the gabapentin does not appear on the prescription claims history within the past 130 days, the prior authorization request must be accompanied by physician’s medical records documenting trial and failure and/or intolerance to gabapentin trial.

Use of Horizant (gabapentin enacarbil) in disease states outside of its FDA-approved indication will be denied based on the lack of clinical data to support its effectiveness and safety in other conditions.

For the treatment of RLS, Horizant should be dosed as 600 mg once daily, taken with food at about 5 PM.

For the treatment of PHN, Horizant should be dosed as 600 mg once daily in the morning for 3 days, then 600 mg twice daily beginning on day 4.

The quantity limit will be set depending on diagnosis, when prior authorization is approved.