BlueCross BlueShield of Alabama

Lyrica® (pregabalin CR) Prior Authorization with Quantity Limit Program Summary

This prior authorization applies to Commercial, NetResults A series, SourceRx and Health Insurance Marketplace formularies.

OBJECTIVE

The intent of the Lyrica CR Prior Authorization is to appropriately select patients for therapy according to product labeling and/or clinical guidelines and/or clinical studies and according to dosing recommended in product labeling. The program also encourages the use of generic duloxetine, amitriptyline, nortriptyline, desipramine, imipramine, gabapentin, venlafaxine, or tramadol; as well as pregabalin immediate release prior to therapy with the target agent. The program will accommodate for use of the target agent when the member has a documented intolerance, FDA labeled contraindication, or hypersensitivity to a generic listed above in addition to pregabalin immediate release. The program will not allow approval for patients who have an FDA contraindication to the target agent. The program will approve for doses within the set limit. Doses above the set limit will be approved if the requested quantity is below the FDA limit and cannot be dose optimized or when the quantity is above the FDA limit and the prescriber has submitted documentation in support of therapy with a higher dose for the intended diagnosis. Requests will be reviewed when patient specific documentation is provided.

TARGET AGENT

Lyrica® CR (pregabalin ER)

Prior Authorization and Quantity Limit Target

Agent	GPI	MSC	Daily Quantity Limit
Lyrica CR (pregabalin ER)			
82.5 mg tablet	62540060007520	M, N, O, Y	1 tablet
165 mg tablet	62540060007530	M, N, O, Y	1 tablet
330 mg tablet	62540060007540	M, N, O, Y	2 tablets

PRIOR AUTHORIZATION CRITERIA FOR APPROVAL

TARGET AGENT will be approved when ALL of the following are met:

1. The patient has ONE of the following diagnosis:
    a. Neuropathic pain associated with diabetic peripheral neuropathy (DPN)
    OR
    b. Postherpetic neuralgia (PHN)

    AND
2. BOTH of the following:
    a. ONE of the following:
        i. The patient has tried and failed generic duloxetine, amitriptyline, nortriptyline, imipramine, desipramine, venlafaxine, gabapentin, or tramadol
        OR
        ii. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to the prerequisite agents listed above

    AND
    b. ONE of the following:
        i. The patient has tried and failed pregabalin immediate release
        OR

ii. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to pregabalin immediate release that is not expected to occur with the requested agent

AND

3. The patient does NOT have any FDA labeled contraindication(s) to the requested agent
   AND
4. ONE of the following:
   a. The requested quantity (dose) is NOT greater than the program quantity limit
      OR
   b. ALL of the following:
      i. The requested quantity (dose) is greater than the program quantity limit
         AND
      ii. The requested quantity (dose) is less than or equal to the FDA labeled dose
         AND
      iii. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does not exceed the limit

      OR
   c. ALL of the following:
      i. The requested quantity (dose) is greater than the program quantity limit
         AND
      ii. The requested quantity (dose) is greater than the FDA labeled dose
         AND
      iii. The prescriber has submitted documentation in support of therapy with a higher dose for the intended diagnosis (must be reviewed by the Clinical Review pharmacist)

Length of Approval: 12 months

FDA APPROVED INDICATIONS AND DOSAGE[1]

<table>
<tr><th>Agents</th><th>Indications</th><th>Dosing and Administration</th></tr>
<tr>
<td>Lyrica CR®
(pregabalin ER)

tablets</td>
<td>Management of:
• Neuropathic pain associated with diabetic peripheral neuropathy (DPN)
• Postherpetic neuralgia (PHN)

Efficacy of Lyrica CR has not been established for the management of fibromyalgia or as adjunctive therapy for adult patients with partial onset seizures</td>
<td>
<table>
<tr><th>Indication</th><th>Initial Dose</th><th>Maximum Daily Dose</th></tr>
<tr><td>DPN Pain</td><td>165 mg/day as a single dose</td><td>330 mg/day as a single dose within 1 week.</td></tr>
<tr><td>PHN</td><td>165 mg/day as a single dose</td><td>330 mg/day as a single dose within 1 week. Maximum dose of 660 mg/day once daily.</td></tr>
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CLINICAL RATIONALE

For patients with diabetic neuropathy, an antidepressant (e.g., amitriptyline, duloxetine, venlafaxine) or anticonvulsant (e.g., pregabalin) is recommend as initial therapy. Available evidence suggests these agents have similar modest benefit, though few high-quality comparative trials have been done. Among these options, the preference is to start with amitriptyline, particularly in younger healthier patients. Patients who fail to improve with a reasonable trial of one of these agents can be switched to monotherapy with another agent. For patients who do not improve on one drug, suggest combination therapy employing two drugs from different medication classes as the next step in the treatment paradigm. For patients who are unable to tolerate any of these drugs, alternative treatments include capsaicin cream, lidocaine patch, alpha-lipoic acid, isosorbide dinitrate topical spray, and transcutaneous electrical nerve stimulation.[3]

A meta-analysis (2015; 225 RCTs) evaluated pharmacotherapy for treatment of neuropathic pain (including peripheral diabetic neuropathy). Studies published in peer-reviewed journals reported greater effects than did unpublished studies. Trial outcomes were generally modest: combined NNTs (50% pain relief) were 6.4 for SNRIs, mainly including duloxetine (9 of 14 studies); 7.7 for pregabalin; 7.2 for gabapentin, and 10.6 for capsaicin high-concentration patches. NNTs were lower for tricyclic antidepressants (TCA), strong opioids, tramadol, and botulinum toxin A, and undetermined for lidocaine patches. Based on grade, final quality of evidence was moderate or high for all treatments apart from lidocaine patches; tolerability and safety, and values and preferences were higher for topical drugs; and cost was lower for TCAs and tramadol.[4]

These findings permitted a strong recommendation for use and proposal as first-line treatment in neuropathic pain for TCAs, SNRIs, pregabalin, and gabapentin; a weak recommendation for use and proposal as second line for lidocaine patches, capsaicin high-concentration patches, and tramadol; and a weak recommendation for use and proposal as third line for strong opioids and botulinum toxin A. Topical agents and botulinum toxin A are recommended for peripheral neuropathic pain only.[4]

Several societies and associations have strong recommendations for TCAs, gabapentin, pregabalin, and SNRI antidepressants (duloxetine [most studied], venlafaxine) as first-line therapies.[5]

Dworkin et al. states that most randomized controlled trials of chronic neuropathic pain have examined only two pain syndromes, diabetic peripheral neuropathy and postherpetic neuralgia. 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.[6]

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 [off-label] as first- or second-line treatment. Carbamazepine and lamotrigine [both off-label] have been considered second- or third-line treatments for neuropathic pain. TCAs (e.g. amitriptyline) are often recommended as a first-line treatment for neuropathic pain.[7-21]

American Academy of Neurology (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).[22]

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.[23]

Guidelines 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.[16,20] 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.[2,24,25] The guidelines consider both gabapentin and pregabalin to be equal in efficacy and one is not preferred over the other.[20,25]

Pregabalin is indicated for use in neuropathic pain associated with diabetic peripheral neuropathy (DPN), postherpetic neuralgia (PHN), adjunctive therapy for adult patients with partial onset seizures, fibromyalgia, and neuropathic pain associated with spinal cord injury.[2] Pregabalin ER is only indicated in two of pregabalin's approved indications: neuropathic pain associated with DPN, and PHN.[1]

Safety

Pregabalin ER has the following contraindication:[1]

- Known hypersensitivity to pregabalin or any of its components

REFERENCES

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This pharmacy policy is not an authorization, certification, explanation of benefits or a contract. Eligibility and benefits are determined on a case-by-case basis according to the terms of the member's plan in effect as of the date services are rendered. All pharmacy policies are based on (i) information in FDA approved package inserts (and black box warning, alerts, or other information disseminated by the FDA as applicable); (ii) research of current medical and pharmacy literature; and/or (iii) review of common medical practices in the treatment and diagnosis of disease as of the date hereof. Physicians and other providers are solely responsible for all aspects of medical care and treatment, including the type, quality, and levels of care and treatment.

The purpose of Blue Cross and Blue Shield of Alabama's pharmacy policies are to provide a guide to coverage. Pharmacy policies are not intended to dictate to physicians how to practice medicine. Physicians should exercise their medical judgment in providing the care they feel is most appropriate for their patients.