PRIOR AUTHORIZATION POLICY

POLICY: Lyrica® CR (pregabalin extended-release tablets – Pfizer)

DATE REVIEWED: 03/04/2020

OVERVIEW

Lyrica CR is indicated for the management of neuropathic pain associated with diabetic peripheral neuropathy (DPN) and postherpetic neuralgia (PHN).[1] The efficacy of Lyrica CR has not been established for the management of fibromyalgia or as adjunctive therapy for adults with partial onset seizures. Lyrica CR is an analog of the neurotransmitter gamma-aminobutyric acid (GABA). Lyrica CR is dosed once daily (QD), and it is a Schedule V controlled substance.

Gabapentin immediate-release (IR) [Neurontin, generics] is also a GABA analog.[2] Gabapentin is indicated for the management of PHN in adults and as adjunctive therapy in the treatment of partial onset seizures, with and without secondary generalization, in adults and pediatric patients ≥ 3 years of age with epilepsy. Gabapentin IR has been used off-label extensively and is included as a treatment option in various guidelines. Pregabalin immediate-release capsules and oral solution are approved for neuropathic pain associated with DPN, PHN, adjunctive therapy for the treatment of partial onset seizures in patients ≥ 1 month of age, fibromyalgia, and neuropathic pain associated with spinal cord injury.[3] Like Lyrica CR, pregabalin immediate-release is a Schedule V controlled substance.

Disease Overview

These drugs exert their pharmacologic action by binding to the alpha-2-delta subunit of voltage-gated calcium channels.[4] The binding of this subunit reduces the release of several neurotransmitters including glutamate, noradrenaline, and substance P.

PHN is the persistence of the pain of herpes zoster > 3 months after resolution of the rash; it is relatively common, affecting 10 to 15% of those with herpes zoster.[5] The time interval used in the clinical case definition of PHN varies in the literature from 1 to 6 months after resolution of the rash. The incidence of PHN increases with age. The duration of PHN is highly variable; in one longitudinal study, only 48% of patients who developed PHN were symptomatic 1 year after onset. Thus, the natural history of resolution of PHN over time is a confounder in the evaluation of treatment efficacy and may limit the ability to generalize the results of controlled clinical trials in this population. Administration of antiviral agents within 72 hours of the onset of herpes zoster can reduce the intensity and duration of acute illness, and can prevent PHN. Efforts to prevent herpes zoster and PHN are important in that 40% to 50% of patients with PHN do not respond to any treatment.

The diabetic neuropathies are a heterogeneous group of disorders with diverse clinical manifestations.[6] The early recognition and appropriate management of neuropathy in the patient with diabetes is important. Diabetic neuropathy is a diagnosis of exclusion. Up to 50% of diabetic peripheral neuropathy (DPN) may be asymptomatic. Painful diabetic neuropathy (PDN) affects 16% of patients with diabetes, and it is frequently unreported (12.5%) and more frequently untreated (39%).[7] If not recognized and if preventive foot care is not implemented, patients are at risk for injuries to their insensate feet.[6] Recognition and treatment of autonomic neuropathy may improve symptoms, reduce sequelae, and improve quality of life. Glycemic control can effectively prevent DPN in type 1 diabetes and may modestly slow their progression in type 2 diabetes but does not reverse neuronal loss. Therapeutic strategies (pharmacologic and nonpharmacologic) for the relief of painful DPN can potentially reduce pain and improve quality of life.

Clinical Efficacy

Support for the efficacy of Lyrica CR for the management of PHN and DPN was based on the efficacy of IR Lyrica for these indications, along with one study of Lyrica CR in adults with PHN.[1] This 19-week, randomized, withdrawal study compared Lyrica CR 82.5 mg, 165 mg, 247.5 mg, 330 mg, 495 mg, or 660 mg QD with placebo. Those enrolled were required to have pain present for > 3 months after healing of the herpes zoster skin rash and a baseline pain score ≥ 4 on the numeric rating scale (NRS)-Pain (assessed over a 1 week recall period). Patients who responded to treatment in the single-blind phase of the study (≥ 50% reduction in pain) moved into the double-blind phase and were randomized to the Lyrica CR dose achieved in the single-blind phase or placebo. Patients were treated for ≤ 3 months following randomization. Lyrica CR demonstrated statistically significant improvement in the efficacy endpoint of change in mean pain score from baseline compared with placebo. In the Lyrica CR arm, 80% of patients achieved ≥ 30% improvement and 74% of patients achieved ≥ 50% improvement in pain intensity. In the placebo group, 65% of patients achieved ≥ 30% improvement and 55% of patients achieved ≥ 50% improvement in pain intensity.

Guidelines

Various guidelines for the treatment of DPN, neuropathic pain, PHN, and restless legs syndrome recommend gabapentin or pregabalin immediate-release as treatment options.[5-14] Guidelines have not been updated to address Lyrica CR.

POLICY STATEMENT

Prior authorization is recommended for prescription benefit coverage of Lyrica CR. All approvals are provided for the duration noted below.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Lyrica CR is recommended in those who meet the following criteria:

FDA-Approved Indications

A) Neuropathic Pain Associated with Diabetic Peripheral Neuropathy (DPN). Approve Lyrica CR for 1 year if the patient the patient meets ONE of the following criteria (A or B):
- **A)** Patient has tried gabapentin immediate-release (brand [Neurontin] or generic) or generic pregabalin; OR
- **B)** Patient is currently established on therapy with Lyrica CR.

B) Postherpetic Neuralgia. Approve Lyrica CR for 1 year if the patient meets ONE of the following criteria (A or B):
- **A)** Patient has tried gabapentin immediate-release (brand [Neurontin] or generic) or generic pregabalin; OR
- **B)** Patient is currently established on therapy with Lyrica CR.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Lyrica CR has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. Rationale for non-coverage for these specific conditions is provided below. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

1. **Fibromyalgia.** A double-blind, placebo-controlled, randomized withdrawal trial of Lyrica CR in adults with fibromyalgia failed to demonstrate efficacy.[1]

2. **Partial Onset Seizures.** A double-blind, placebo-controlled, randomized trial of Lyrica CR as adjunctive therapy in adults with partial onset seizures failed to demonstrate efficacy.[1]

3. **Restless Legs Syndrome.** No data are available for Lyrica CR for the treatment of restless legs at this time.

4. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

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