PRIOR AUTHORIZATION POLICY

POLICY: Amifampridine Products Prior Authorization Policy
- Firdapse® (amifampridine tablets – Catalyst Pharmaceuticals)
- Ruzurgi® (amifampridine tablets – Jacobus Pharmaceutical)

REVIEW DATE: 06/24/2020

OVERVIEW

Amifampridine is a broad spectrum potassium channel blocker.[1,2] The mechanism by which amifampridine exerts its therapeutic effect in patients with Lambert-Eaton myasthenic syndrome (LEMS) has not been fully elucidated.

- Firdapse is indicated for the treatment of LEMS in adults.[1]
- Ruzurgi is indicated for the treatment of LEMS in patients 6 years to < 17 years of age.[2]

Disease Overview

LEMS is a rare autoimmune disorder affecting the connection between nerves and muscles and causing proximal muscle weakness, autonomic dysfunction, and areflexia.[3,4] LEMS can occur at any age. The prevalence of LEMS specifically in pediatric patients is not known, but the overall prevalence of LEMS is estimated to be three per million individuals worldwide.[3] The characteristic weakness is thought to be caused by antibodies generated against the P/Q-type voltage-gated calcium channels (VGCC) present on presynaptic nerve terminals and by diminished release of acetylcholine (ACh).[4] More than half of LEMS cases are associated with small cell lung carcinoma (SCLC), which expresses functional VGCC. The diagnosis of LEMS is confirmed by electrodiagnostic studies, including repetitive nerve stimulation (RNS), or anti-P/Q-type VGCC antibody testing to confirm the diagnosis.

Clinical Efficacy

Firdapse was approved based on two pivotal trials.[1,5] One pivotal trial enrolled both amifampridine-naïve and treatment-experienced patients; patients were initially entered into an open-label run-in phase lasting 90 days.[5] During the open-label run-in phase, Firdapse was titrated for each individual patient to a dose that produced optimal neuromuscular benefit and tolerability in the opinion of the investigator. In order to continue in the study, treatment-naïve patients were required to have an improvement of at least three points in the quantitative myasthenia gravis score from the initial evaluation.

Although Ruzurgi is indicated for use in children, the efficacy of Ruzurgi for the treatment of LEMS was established in one randomized, double-blind, placebo-controlled, withdrawal study in adults with an established diagnosis of LEMS (n = 32).[2] Patients were required to be on an adequate and stable dosage for ≥ 3 months of Ruzurgi prior to entering the study. The efficacy of Ruzurgi in patients 6 to < 17 years of age is supported by evidence from adequate and well-controlled studies of Ruzurgi in adults with LEMS, pharmacokinetic data in adult patients, pharmacokinetic modeling and simulation to identify the dosing regimen in pediatric patients, and safety data from pediatric patients 6 to < 17 years of age.

Safety

Firdapse and Ruzurgi are contraindicated in patients with a history of seizures.[1,2] There is also a Warning/Precaution in the prescribing information for these medications because seizures have been observed in patients with and without a history of seizures taking amifampridine at the recommended doses. Many of these patients were taking medications or had comorbidities that may have lowered their seizure threshold. Seizures may be dose-dependent.

POLICY STATEMENT

Prior authorization is recommended for prescription benefit coverage of amifampridine. Because of the specialized skills required for evaluation and diagnosis of patients treated with amifampridine as well as the monitoring required for adverse events and long-term efficacy, initial approval requires amifampridine to be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

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

FDA-Approved Indications

1. **Lambert-Eaton Myasthenic Syndrome (LEMS).** Approve amifampridine for the duration noted if the patient meets ONE of the following criteria (A or B):
   - **A)** Initial therapy. Approve amifampridine for 3 months if the patient meets the following criteria (i, ii, iii, and iv):
     - **i.** Patient is ≥ 6 years of age; AND
     - **ii.** Patient has confirmed LEMS based on at least one electrodiagnostic study (e.g., repetitive nerve stimulation) or anti-P/Q-type voltage-gated calcium channels antibody testing, according to the prescriber; AND
     - **iii.** Patient does not have a history of seizures; AND
     - **iv.** Amifampridine is being prescribed by or in consultation with a neurologist or a neuromuscular specialist; OR
   - **B)** Patient is Currently Receiving amifampridine. Approve amifampridine for 1 year if the patient is continuing to derive benefit from amifampridine, according to the prescriber.
     Note: Examples of continued benefit include improved muscle strength and improvements in mobility.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of amifampridine is not recommended in the following situations:

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

REFERENCES

1. Firdapse® tablets [prescribing information]. Coral Gables, FL: Catalyst Pharmaceuticals, Inc.; November 2018.
2. Ruzurgi® tablets [prescribing information]. Princeton, NJ: Jacobus Pharmaceutical Company, Inc.; May 2019.
3. FDA news release. FDA approves first treatment for children with Lambert-Eaton myasthenic syndrome, a rare autoimmune disorder. Issued on: May 6, 2019. Available at: https://www.fda.gov/news-events/press-announcements/fda-approves-first-treatment-children-lambert-eaton-myasthenic-syndrome-rare-autoimmune-disorder. Accessed on May 23, 2019.
4. Kesner VG, Oh SJ, Dimachkie MM, et al. Lambert-Eaton Myasthenic Syndrome. *Neurol Clin*. 2018;36(2):379-394.
5. Oh S, Shcherbakova N, Kostera-Pruszczyk A, et al. Amifampridine phosphate (Firdapse®) is effective and safe in a phase 3 clinical trial in LEMS. *Muscle Nerve*. 2016;53(5):717-25.