VENTURA COUNTY
HEALTH CARE PLAN

PRIOR AUTHORIZATION POLICY

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- Ruzurgi® (amifampridine tablets – Jacobus Pharmaceutical [approval withdrawn])

REVIEW DATE: 07/06/2022

OVERVIEW

Amifampridine, a broad spectrum potassium channel blocker, indicated for the **treatment of Lambert-Eaton myasthenic syndrome** (LEMS).[1,2]

- Firdapse is indicated in **adults and pediatric patients ≥ 6 years of age**.[1]
- Ruzurgi was indicated in **patients 6 years to < 17 years of age** (prior to withdrawal of FDA approval).[2]

As of February 01, 2022, the FDA has withdrawn approval for Ruzurgi. Firdapse was approved by the FDA on November 28, 2018, for the treatment of LEMS in adults, with 7 years of orphan-drug exclusivity (ODE). On May 6, 2019, Ruzurgi was approved by the FDA for the treatment of LEMS in patients 6 to < 17 years of age. On June 12, 2019, Catalyst brought suit against the FDA, challenging the FDA's approval of Ruzurgi stating that it violated the ODE for Firdapse. In 2022, the Court of Appeals for the Eleventh Circuit sided with Catalyst; therefore, the FDA had to withdraw approval for Ruzurgi. Due to the 7-year ODE for Firdapse, Ruzurgi may not be approved for marketing until ODE has expired on November 28, 2025.

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] The characteristic weakness is thought to be caused by antibodies generated against the P/Q-type voltage-gated calcium channels present on presynaptic nerve terminals and by diminished release of acetylcholine.[4] The diagnosis of LEMS is confirmed by electrodiagnostic studies, including repetitive nerve stimulation, or anti-P/Q-type voltage-gated calcium channels antibody testing.

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. For its pediatric indication, use is supported by evidence from studies of Firdapse in adults with LEMS, pharmacokinetic data in adults, pharmacokinetic modeling and simulation to identify the dosing regimen in pediatric patients, and safety data from pediatric patients ≥ 6 years of age.

Although Ruzurgi was 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 was 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 of the following, according to the prescriber:
       - **a)** Electrodiagnostic study (e.g., repetitive nerve stimulation); OR
       - **b)** Anti-P/Q-type voltage-gated calcium channels antibody testing; 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; September 2022.
2. Ruzurgi® tablets [prescribing information]. Princeton, NJ: Jacobus Pharmaceutical; April 2020.
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 July 5, 2022.
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.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	06/23/2021
Update	02/10/2022: Information on the FDA's withdrawal of marketing approval for Ruzurgi was included in the policy Overview.	--
Annual Revision	No criteria changes.	07/06/2022
Update	02/28/2023: Overview section updated to include pediatric indication for Firdapse.	--