Drug Coverage Policy

Effective Date..... 10/15/2025
Coverage Policy Number IP0290
Policy Title.... Amifampridine Products

Amifampridine Products

- Firdapse® (amifampridine tablets – Catalyst)
- Ruzurgi® (amifampridine tablets – Jacobus [approval withdrawn])

INSTRUCTIONS FOR USE

The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment where appropriate and have discretion in making individual coverage determinations. Where coverage for care or services does not depend on specific circumstances, reimbursement will only be provided if a requested service(s) is submitted in accordance with the relevant criteria outlined in the applicable Coverage Policy, including covered diagnosis and/or procedure code(s). Reimbursement is not allowed for services when billed for conditions or diagnoses that are not covered under this Coverage Policy (see "Coding Information" below). When billing, providers must use the most appropriate codes as of the effective date of the submission. Claims submitted for services that are not accompanied by covered code(s) under the applicable Coverage Policy will be denied as not covered. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

OVERVIEW

Amifampridine, a broad spectrum potassium channel blocker, is 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 (manufacturer of Firdapse) 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] 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. 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.[1,4] 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.[4] 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.

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.

Coverage Policy

POLICY STATEMENT

Prior Authorization is required for benefit coverage of amifampridine. 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. 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.

Documentation: Documentation is required where noted in the criteria as **[documentation required]**. Documentation may include, but is not limited to, chart notes, laboratory tests, claims records, and/or other information.

Amifampridine is considered medically necessary when the following are met:

FDA-Approved Indications

1. **Lambert-Eaton Myasthenic Syndrome (LEMS).** Approve for the duration noted if the patient meets ONE of the following (A or B):
   - **A)** Initial therapy. Approve amifampridine for 3 months if the patient meets ALL of the following (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 (a or b);
       - **a)** Electrodiagnostic study (e.g., repetitive nerve stimulation) **[documentation required]**; OR
       - **b)** Anti-P/Q-type voltage-gated calcium channels antibody testing **[documentation required]**; AND
     - **iii.** Patient does not have a history of seizures; AND
     - **iv.** The medication is being prescribed by or in consultation with a neurologist or a neuromuscular specialist; OR
   - **B)** Patient is Currently Receiving amifampridine. Approve for 1 year if according to the prescriber, the patient is continuing to derive benefit from amifampridine.
     Note: Examples of continued benefit include improved muscle strength and improvements in mobility.

Conditions Not Covered

Amifampridine for any other use is considered not medically necessary. Criteria will be updated as new published data are available.

References

1. Firdapse® tablets [prescribing information]. Coral Gables, FL: Catalyst; May 2024.
2. Ruzurgi® tablets [prescribing information]. Princeton, NJ: Jacobus; April 2020.
3. Kesner VG, Oh SJ, Dimachkie MM, et al. Lambert-Eaton Myasthenic Syndrome. *Neurol Clin*. 2018;36(2):379-394.
4. 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):717-725.

Revision Details

Type of Revision	Summary of Changes	Date
Annual Revision	**Updated** coverage policy title from "Amifampridine" to "Amifampridine Products." **Lambert-Eaton Myasthenic Syndrome (LEMS).**	11/1/2024

	Updated criteria for confirmation of diagnosis from "neurophysiology studies" to "Electrodiagnostic study (e.g., repetitive nerve stimulation)."	
Annual Revision	**Lambert-Eaton Myasthenic Syndrome (LEMS). Added "[Documentation Required]"** to criteria.	10/15/2025

The policy effective date is in force until updated or retired.