Drug Coverage Policy

Effective Date..... 11/1/2024
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- Ruzurgi® (amifampridine tablets – Jacobus [approval withdrawn])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 and have discretion in making individual coverage determinations. 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.

Cigna Healthcare Coverage Policy

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.[3,4] 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.

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.

Medical Necessity Criteria

Amifampridine is considered medically necessary when the following criteria are met:

FDA-Approved Indications

1. **Lambert-Eaton Myasthenic Syndrome (LEMS).** Approve amifampridine 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 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, 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.

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Receipt of sample product does not satisfy any criteria requirements for coverage.

Conditions Not Covered

Any other use is considered experimental, investigational, or unproven (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. 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 29, 2024.
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):717-725.

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).** **Updated** criteria for confirmation of diagnosis from "neurophysiology studies" to "Electrodiagnostic study (e.g., repetitive nerve stimulation)."	11/1/2024

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