Clinical Policy: Amifampridine (Firdapse)

Reference Number: CP.PHAR.411
Effective Date: 01.22.19
Last Review Date: 02.22
Line of Business: Commercial, HIM, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Amifampridine (Firdapse®) is potassium channel blocker.

FDA Approved Indication(s)

Firdapse is indicated for the treatment of Lambert-Eaton myasthenic syndrome (LEMS) in adults.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Firdapse is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Lambert-Eaton Myasthenic Syndrome (must meet all)**:**

1. Diagnosis of LEMS;
2. Documentation of confirmatory diagnostic test results from one of the following (a or b):
   a. Repetitive Nerve Stimulation (RNS) testing showing reproducible post-exercise increase in compound muscle action potential (CMAP) amplitude of at least 60 percent compared with pre-exercise baseline value or a similar increment on high-frequency repetitive nerve stimulation without exercise;
   b. If member is unable to complete RNS testing, positive anti-P/Q type voltage-gated calcium channel (VGCC) antibody blood test;
3. Prescribed by or in consultation with a neurologist;
4. Age ≥ 18 years;
5. Documentation of a baseline clinical muscle strength assessment (examples may include but are not limited to the Quantitative Myasthenia Gravis (QMG) score, triple-timed up-and-go test (3TUG), Timed 25-foot Walk test (T25FW)) (see *Appendix D)*;
6. Dose does not exceed 80 mg (8 tablets) per day.

Approval duration: 6 months

B. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is

NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Lambert-Eaton Myasthenic Syndrome (must meet all)**:**

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy as evidenced by clinical muscle strength assessments (examples may include but are not limited to the QMG score, 3TUG test, T25FW test) (see *Appendix D)*;
3. If request is for a dose increase, new dose does not exceed 80 mg (8 tablets per day).

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CMAP: compound muscle action potential
FDA: Food and Drug Administration
LEMS: Lambert-Eaton myasthenic syndrome
QMG: Quantitative Myasthenia Gravis
3TUG: triple-timed up-and-go test
RNS: repetitive nerve stimulation
T25FW: Timed 25-foot Walk test
VGCC: voltage-gated calcium channel

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): history of seizures; hypersensitivity to amifampridine or another aminopyridine
- Boxed warning(s): none reported

Appendix D: General Information

- QMG is a physician-rated evaluation consisting of 13 assessments of muscle function (e.g., swallowing, speech, forced vital capacity, movement of arms and legs). Each assessment is rated 0 to 3, where 0 indicates "no weakness" and 3 indicates "severe weakness" (lower scores reflect better muscle strength).
- The 3TUG is a functional mobility test that requires a patient to stand up from a straight-backed armchair, walk 3 meters, turn around, walk back, and sit down in the chair. Based upon literature reports that a significant change in gait for a similar walk-test is an increase in time of more than 20%, this was incorporated into the secondary endpoint used in the NCT02970162 clinical trial.
- The T25FW test, a component of the Multiple Sclerosis Functional Composite, is a quantitative mobility and leg function performance test based on a timed 25-foot walk. The patient was directed to walk a clearly marked 25-foot course as quickly and safely as possible. Following a period of rest, the timed 25-foot walk is repeated to determine an average score.
- During RNS testing, an increase in the CMAP amplitude >100% after exercise or with high-frequency RNS is considered diagnostic of a presynaptic neuromuscular junction disorder, and the increase is frequently even greater. However, some studies have found that a significant number of patients have increments with RNS below 100%; thus, increments of 60 to 99% are strongly supportive of a presynaptic neuromuscular junction disorder.
- P/Q-type VGCC antibody result is strongly suggestive of LEMS. However, P/Q-type VGCC antibodies are present in a variety of clinical situations where LEMS is not present. While the anti-P/Q-type VGCC antibody test is confirmatory in patients who otherwise have clinical and electrophysiologic features of LEMS, the antibody test alone is not diagnostic, especially in the presence of a malignancy or amyotrophic lateral sclerosis.
- On February 1, 2022 the FDA converted the final approval of Ruzurgi to a tentative approval. Due to the 7-year orphan-drug exclusivity for Catalyst's product Firdapse, the application for Ruzurgi for the treatment of LEMS in patients 6 to less than 17 years of age may not be finally approved for marketing until the period of exclusivity has expired. As a result Ruzurgi is no longer commercially available.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
LEMS	15 mg to 30 mg PO in 3 to 4 divided doses daily. Dose can be increased by 5 mg daily every 3 to 4 days. The maximum single dose is 20 mg.	80 mg/day

VI. Product Availability

Tablet: 10 mg

VII. References

1. Firdapse Prescribing Information. Coral Gables, FL: Catalyst Pharmaceuticals, Inc.; February 2021. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/208078s007lbl.pdf. Accessed September 21, 2021.
2. Weinberg DH. Lambert-Eaton myasthenic syndrome: Clinical features and diagnosis. In: UpToDate, Waltham, MA. Updated July 15, 2021. Accessed September 21, 2021.
3. American Association of Electrodiagnostic Medicing (AAEM) Quality Assurance Committee. Practice Parameter for Repetitive Nerve Stimulation and Single Fiber EMG Evaluation of Adults with Suspected Myasthenia Gravis or Lambert–Eaton Myasthenic Syndrome: Summary Statement. Muscle Nerve 24: 1236-1238, 2001.
4. Oh SJ, Kurokawa K, Claussen GC, Ryan HF Jr. Electrophysiological diagnostic criteria of Lambert-Eaton myasthenic syndrome. Muscle Nerve 2005;32:515–520.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	01.22.19	02.19
No significant changes; finalized line of business to apply to HIM.	04.23.19	
Added new FDA-approved agent: Ruzurgi, in line with previously approved clinical guidance for amifampridine; references reviewed and updated.	08.12.19	
1Q 2020 annual review: no significant changes; added quantities associated with dosing requirements; for Ruzurgi requests added reference to HIM non-formulary policy in approval durations for each criteria set; references reviewed and updated.	10.29.19	02.20
Added redirection to Ruzurgi for Firdapse requests per SDC and prior clinical guidance.	01.14.20	
1Q 2021 annual review: added requirement for diagnostic testing to confirm diagnosis; references to HIM.PHAR.21 revised to HIM.PA.154; references reviewed and updated.	10.27.20	02.21
1Q 2022 annual review: no significant changes; for Ruzurgi redirection modified from medical justification to member must use language per template; references reviewed and updated.	09.21.21	02.22
Ruzurgi redirection and references to Ruzurgi removed as the product is no longer commercially available.	02.23.22	

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical

practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.