amifampridine (Firdapse®, Ruzurgi®)
EOCCO POLICY

Policy Type: PA/SP Pharmacy Coverage Policy: EOCCO004

Description
Amifampridine (Firdapse, Ruzurgi) are orally administered, broad-spectrum potassium channel blockers.

Length of Authorization
- Initial: Three months
- Renewal: 12 months

Quantity limits

Product Name	Indication	Dosage Form	Quantity Limit
amifampridine (Firdapse)	Lambert-Eaton myasthenic syndrome	10 mg tablets	240 tablets/30 days
amifampridine (Ruzurgi)*		10 mg tablets	240 tablets/30 days

**In a January 2022 court ruling, the FDA converted the final approval of the Ruzurgi new drug application to a tentative approval. Therefore, Ruzurgi may not be legally marketed or distributed in the United States at this time*

Initial Evaluation

I. Amifampridine (Firdapse, Ruzurgi) may be considered medically necessary when the following criteria are met:
   A. Prescribed by, or in consultation with, a neurologist; **AND**
   B. A diagnosis of **Lambert-Eaton Myasthenic Syndrome (LEMS)**; **AND**
      a. Documentation of a confirmatory diagnostic test:
         i. Repetitive Nerve Stimulation (RNS); **OR**
         ii. Positive anti-P/Q type voltage-gated calcium channel (VGCC) antibody test; **AND**
      b. Member is experiencing moderate to severe weakness that interferes with function

II. Amifampridine (Firdapse, Ruzurgi) is considered investigational when used for all other conditions, including but not limited to the diagnosis of:
   A. Inflammatory muscle disease
   B. Limb-girdle muscular dystrophy
   C. Myasthenia gravis

D. Congenital myasthenic syndrome
E. Motor neuron disease (i.e. amyotrophic lateral sclerosis, multifocal motor neuropathy)

Renewal Evaluation

I. Member has received a previous prior authorization approval for this agent through this health plan or has been established on therapy from a previous health plan; **AND**
II. Member is not continuing therapy based off being established on therapy through samples, manufacturer coupons, or otherwise. If they have, initial policy criteria must be met for the member to qualify for renewal evaluation through this health plan; **AND**
III. Member has exhibited improvement or stability of disease symptoms [e.g., improved muscle strength

Supporting Evidence

I. LEMS is a rare presynaptic disorder of neuromuscular transmission in which the release of acetylcholine is impaired. Disruption of a subset of P/Q-type CA2+ channels causes proximal muscle weakness, depressed tendon reflexes, post-tetanic potentiation, and autonomic dysfunction. Major clinical presentation is progressive proximal muscle weakness. Forty to 60% of LEMs cases are paraneoplastic, involving and correlated with a [usually new] cancer diagnosis. Remaining patients with autonomic LEMS and without cancer, expect normal longevity.
II. Patients with LEMS who have mild weakness that does not interfere with function can be monitored without the use of symptomatic or immunologic therapy. Amifampridine (also known as 3,4-diaminopyridine) is the recommended therapy in patients with moderate or severe weakness that interferes with functions of daily living. Guanidine is approved for the treatment of LEMS, however, is associated with a high-level of toxicity and adverse effects, limiting its use. Pyridostigmine is known to be less toxic overall and is sometimes taken as in conjunction with guanidine. Use of pyridostigmine is generally accepted if amifampridine is not accessible, however its use is not supported by high-quality data. When used as monotherapy it has been shown to be only mildly effective with no effect on muscle strength. Immunoglobulin is often used in patients specifically for refractory weakness, which may or may not be associated with the underlying cancer in paraneoplastic LEMS. Alternative immunotherapies used include prednisone, azathioprine, plasma exchange, mycophenolate, rituximab.
III. In trials LMS-002, LMS-003, and DAPPER, subjects were confirmed of diagnosis of LEMS by nerve conduction findings OR positive anti-P/Q type voltage-gated calcium channel (VGCC) antibody test. This appears to be aligned with practice as the diagnosis is made via clinical features (e.g., muscle weakness, autonomic dysfunction, ptosis and diplopia) and electrodiagnostic studies (e.g., VGCC or repetitive nerve stimulation) as confirmatory evidence.

IV. The clinical presentation of LEMS that of slowly progressive, symmetric and proximal weakness, among other clinical symptoms, indicates a need of specific diagnosis by an experienced specialist.

V. There is a lack of strong scientific evidence to support the safety and efficacy for an increased dosing frequency or doses above the recommended. Trials were too small to indicate a dose-related trend of improvement or indicate a variation in effectiveness among subgroup populations.

Investigational or Not Medically Necessary Uses

I. Diagnosis of LEMS is largely based on clinical assessment and rule-out of other symptomatically similar disease. The following disease states have a similar presentation or relatedness to LEMS, however, randomized controlled trials to support the efficacy and safety of amifampridine (Firdapse, Ruzurgi) have yet to be completed.
   A. Inflammatory muscle disease
   B. Limb-girdle muscular dystrophy
   C. Myasthenia gravis
   D. Congenital myasthenic syndrome
   E. Motor neuron disease (i.e. amyotrophic lateral sclerosis, multifocal motor neuropathy)

References

1. Firdapse [prescribing information]. Coral Gables, FL: Catalyst Pharmaceuticals; February 2021.
2. Ruzurgi [prescribing information]. Plainsboro, NJ: Jacobson Pharmaceutical Company; May 2019.
3. FDA. Center for Drug Evaluation and Research. Application number: 208078Orig1s000 Summary Review. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/nda/2018/208078Orig1s000SumR.pdf. Accessed December 21, 2018.
4. FDA. Center for Drug Evaluation and Research. Application number: 209321Orig1s000 Summary Review.
5. UpToDate, Inc. Lambert-Eaton myasthenic syndrome: Clinical features and diagnosis. UpToDate [Online Database]. Waltham, MA. Last updated July 15, 2021. Available from: http://uptodate.com/home/index.html. Accessed March 21, 2022.
6. UpToDate, Inc. Lambert-Eaton myasthenic syndrome: Treatment and prognosis. UpToDate [Online Database]. Waltham, MA. Last updated January 07, 2021. Available from: http://uptodate.com/home/index.html. Accessed March 21, 2022.
7. GuaTitulaer MJ, Lang B, Verschuuren J. Lambert–Eaton myasthenic syndrome: from clinical characteristics to therapeutic strategies. Lancet Neurol. 2011;10:1098-107.
8. Guanidine [prescribing information]. Whitehouse Station, NJ: Merck Sharp & Dohme; November 2017.
9. FDA. Letter to Jacobus Pharmaceutical Company, Inc: Conversion to NDA Tentative Approval. February 01, 2022. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2022/209321Orig1s000TA_ltr.pdf

Related Policies

Currently there are no related policies.

Policy Implementation/Update:

Action and Summary of Changes	Date
Removal of requirement to trail Ruzurgi prior to Firdapse due to removal of Ruzurgi from market. In a January 2022 court ruling, the FDA converted the final approval of the Ruzurgi new drug application to a tentative approval. Therefore, Ruzurgi may not be legally marketed or distributed in the United States at this time. Addition of criteria requiring symptomatic disease. Removal of initial criteria requiring trial of pyridostigmine or IVIG. Updated renewal section to include samples language and previous approvals.	04/2022
Addition of Ruzurgi to policy	07/2019
Policy created	02/2019