Firdapse_Ruzurgi (amifampridine)
Policy Number: C15969-A

CRITERIA EFFECTIVE DATES:

ORIGINAL EFFECTIVE DATE	LAST REVIEWED DATE	NEXT REVIEW DUE BY OR BEFORE
4/1/2019	2/3/2021	4/2022
J CODE	**TYPE OF CRITERIA**	**LAST P&T APPROVAL/VERSION**
NA	RxPA	Q2 2021 20210428C15969-A

PRODUCTS AFFECTED:
Firdapse (amifampridine phosphate), Ruzurgi (amifampridine)

DRUG CLASS:
Antimyasthenic/Cholinergic Agent

ROUTE OF ADMINISTRATION:
Oral

PLACE OF SERVICE:
Specialty Pharmacy
The recommendation is that medications in this policy will be for pharmacy benefit coverage and patient self-administered

AVAILABLE DOSAGE FORMS:
Firdapse TABS 10MG (bottle of 240, blister pack of 10, box of 12 (10ct blister packs), Ruzurgi TABS 10mg (bottle of 100ct)

FDA-APPROVED USES:
Firdapse: For the treatment of Lambert-Eaton myasthenic syndrome (LEMS) in adults
Ruzurgi: for the treatment of Lambert-Eaton myasthenic syndrome (LEMS) in patients 6 to less than 17 years of age.

COMPENDIAL APPROVED OFF-LABELED USES:
None

COVERAGE CRITERIA: INITIAL AUTHORIZATION

DIAGNOSIS:
Lambert-Eaton myasthenic syndrome (LEMS)

REQUIRED MEDICAL INFORMATION:
A. LAMBERT-EATON MYASTHENIC SYNDROME:

1. Documentation of clinical symptoms suggestive of LEMS (i.e., proximal weakness affecting legs, eyes, face, throat)
   AND
2. (a) Documentation of confirmatory diagnostic test results including: 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
OR
(b) Positive anti-P/Q type voltage-gated calcium channel antibody test
AND

3. Documentation of a failed trial or labeled contraindication of pyridostigmine
AND
4. Prescriber attests to (or the clinical reviewer has found that) the member not having any FDA labeled contraindications that haven't been addressed by the prescriber within the documentation submitted for review [Contraindications to amifampridine include: A history of seizures, Hypersensitivity to amifampridine or another aminopyridine]

DURATION OF APPROVAL:
Initial authorization: 3 months, Continuation of Therapy: 12 months

QUANTITY:
FIRDAPSE: max of 80mg daily dose, max single dose of 20mg
RUZURGI: ≥45 kg: max of 100 mg daily dose, max single dose of 30 mg
<45 kg: max of 50 mg daily dose, max single dose of 15 mg

PRESCRIBER REQUIREMENTS:
Prescribed by or in consultation with a neurologist. NOTE: Consultation notes must be submitted for each the initial authorization and a new note for continuation of therapy authorization.

AGE RESTRICTIONS:
Firdapse: 18 years of age or older, Ruzurgi: age 6 years to less than 17 years

CONTINUATION OF THERAPY:
A. LAMBERT-EATON MYASTHENIC SYNDROME:

1. Documentation of clinical improvement in symptoms

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:
All other uses of amifampridine are considered experimental/investigational and therefore, will follow Molina's Off- Label policy. Contraindications of amifampridine include hypersensitivity to amifampridine phosphate, aminopyridines, or any component of the formulation, history of seizures.

OTHER SPECIAL CONSIDERATIONS:
None

BACKGROUND:
Lambert-Eaton myasthenic syndrome (LEMS) is a rare autoimmune disorder in which pre-synaptic release of acetylcholine from neurotransmitters is impaired. Antibodies directed against voltage-gated calcium channels (VGCCs) interfere with normal calcium flux required for release of acetylcholine. LEMS symptoms usually begin with leg weakness often followed by weakness in the muscles of the eyes, face, and throat. In some cases, weakness temporarily improves after exertion (post-tetanic potentiation). These symptoms affect patients' ability to perform daily activities and negatively impact quality of life. Unlike Myasthenia Gravis, LEMS does not have a severe an effect on vital muscles (i.e. those involved in respiration).
Approximately 50% of LEMS cases are associated with a malignancy, mainly Small Cell Lung Cancer. It is believed that in patients that have LEMS associated with a malignancy, cancer cells contain antigens that mimic VGCCs and induce production of VGCC antibodies. This is one reason

that when patients with LEMS and a malignancy are treated with chemotherapy, their LEMS symptoms often improve. Patients with LEMS and associated malignancy are older at age of onset (average onset 60 years old) and typically have a history of long-term smoking (all patients with SCLS). LEMS patients without a malignancy have a younger average age of onset (35 years). In these patients, VGCC antibodies are likely produced as part of the patient's general autoimmune state.

Current treatment strategies include initial therapy with medications that increase the amount of acetylcholine available at the post-synaptic membrane including pyridostigmine, 3,4-DAP (base form of amifampridine), and guanidine. Since pyridostigmine is more readily available and is well-tolerated, it is usually the first therapy tried although it is only mildly effective. Low-dose guanidine can also be used to treat LEMS in combination with pyridostigmine, but due to concerns about toxicity, it is a less-preferable option if 3,4-DAP (or amifampridine) is available. Pyridostigmine has also been used in combination with 3,4-DAP but benefit of the addition of pyridostigmine has not been proven.

For patients with inadequate response to initial therapies, immunosuppressive or immune-modulating therapies are usually the next step in treatment. These therapies often include IVIG, plasma exchange, prednisone, and azathioprine.

APPENDIX:

None

Documentation Requirements:

Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

REFERENCES:

1. Firdapse (amifampridine) [prescribing information]. Coral Gables, FL: Catalyst Pharmaceuticals, Inc;November 2018.
2. Lindquist S, Stangel M. Update on treatment options for Lambert-Eaton myasthenic syndrome: focus on use of amifampridine. Neuropsychiatr Dis Treat. 2011;7:341-349. doi: 10.2147/NDT.S10464. [PubMed 21822385]
3. Pelufo-Pellicer A, Monte-Boquet E, Romá-Sánchez E, Casanova-Sorní C,Poveda-Andrés JL. Fetal exposure to 3,4-diaminopyridine in a pregnant woman with congenital myasthenia syndrome. Ann Pharmacother. 2006;40(4):762-766. [PubMed 16537815]
4. Wirtz PW, Titulaer MJ, Gerven JM, Verschuuren JJ. 3,4-diaminopyridine for the treatment of Lambert-Eaton myasthenic syndrome. Expert Rev Clin Immunol. 2010;6(6):867-874. doi: 10.1586/eci.10.57. [PubMed 20979551
5. Abenroth DC, Smith AG, Greenlee JE, et al. Lambert-Eaton myasthenic syndrome: Epidemiology and therapeutic response in the national veterans affairs population. Muscle Nerve. 2017 Sep;56(3):421-26
6. Ruzurgi (amifampridine) [prescribing information]. Princeton, NJ: Jacobus Pharmaceutical Company, Inc; May 2019