Amifampridine Prior Authorization with Quantity Limit Program Summary

POLICY REVIEW CYCLE

Effective Date 05-01-2025

Date of Origin

FDA LABELED INDICATIONS AND DOSAGE

Agent(s)	FDA Indication(s)	Notes	Ref#
FIRDAPSE® (amifampridine) Tablet	Treatment of Lambert-Eaton myasthenic syndrome (LEMS) in adults and pediatric patients 6 years of age and older		1

See package insert for FDA prescribing information: https://dailymed.nlm.nih.gov/dailymed/index.cfm

CLINICAL RATIONALE

Lambert-Eaton myasthenic syndrome	Lambert-Eaton myasthenic syndrome (LEMS) is a rare autoimmune disorder characterized by the gradual onset of muscle weakness, especially of the pelvic and thigh muscles. Approximately 60 percent of LEMS cases are associated with a small cell lung cancer (SCLC), and the onset of LEMS symptoms often precedes the detection of the cancer. The LEMS patients with cancer tend to be older and nearly always have a long history of smoking. In cases in which there is no associated cancer, disease onset can be at any age.(3) LEMS may affect the patient's ability to engage in strenuous exercise and may make such activities as climbing stairs or walking up a steep walkway difficult. Onset is gradual, typically taking several weeks to many months. There is often a progression of symptoms whereby the shoulder muscles, muscles of the feet and hands, speech and swallowing muscles and eye muscles are affected in a stepwise fashion. The symptoms progress more quickly when LEMS is associated with cancer. Most LEMS patients also exhibit the following autonomic symptoms: dry mouth, constipation, impotence, and decreased sweating. LEMS patients with or without cancer may also undergo significant weight loss. The tendon reflexes are diminished or absent on examination. LEMS is often described as a clinical "triad" of proximal muscle weakness, autonomic symptoms and reduced tendon reflexes.(3) LEMS occurs because autoantibodies damage the "voltage-gated calcium channels (VGCC)" on the motor nerve membrane at the neuromuscular junction. These channels normally conduct calcium into the nerve resulting in release of acetylcholine. Acetylcholine helps in the communication between nerve cells and muscles and is one of a group of chemicals known as neurotransmitters, which help to transmit nerve impulses. The autoantibodies attack the VGCC resulting in less acetylcholine release. In LEMS cases associated with cancer, it is believed that autoantibodies created against the VGCC on the small-cell lung tumor damage the VGCC on the nerve. It is unknown what causes autoantibody production in cases not associated with cancer.(3) A differential diagnosis of LEMS must be determined due to its similarities in presentation to myasthenia gravis (MG) and Guillain-Barre syndrome.(3) Diagnosis of

	LEMS is based on clinical signs and symptoms, electrophysiological studies, repetitive nerve stimulation, and antibody testing. LEMS can be diagnosed when the patient is positive for antibodies against voltage-gated calcium channels (VGCC) unlike myasthenia gravis which has anti-acetylcholine receptor (AChR) and anti-muscle-specific tyrosine kinase (MuSK) antibodies. The P/Q-type voltage-gated calcium channel IgG antibody is present in over 90% of LEMS patients, making this excellent serological evidence to support the diagnosis. Clinical neurophysiology (nerve conductions studies, repetitive stimulation, and electromyography [EMG]) can confirm presynaptic disorder of neuromuscular transmission. On nerve conduction studies the compound muscle action potentials (CMAPs) are uniformly low in amplitude. CMAP shows a decrement to slow rates of repetitive stimulation as immediately following 10 seconds of brief muscle contraction a marked facilitation of the CMAP amplitude (greater than 100%) in over 90% of LEMS patients. Single fiber EMG is significantly abnormal in all patients with LEMS with a clear increase in jitter and blocking compared with MG continued activation of the LEMS muscle which results in a reduction in severity of jitter and blocking.(2) The first line and most effective symptomatic treatment in LEMS is 3,4-diaminopyridine (3,4-DAP), also known as amifampridine. Through blocking voltage-gated potassium channels, 3,4-DAP prolongs nerve terminal depolarization and increases acetylcholine release. Pyridostigmine can be an adjunctive drug for patients with LEMS although the benefits are limited but has a quick onset of benefit, favorable safety profile, widely available, and lower cost. Immune therapy has been utilized with some success, especially in severe or refractory disease or patients with limited benefit from amifampridine.(2)
Efficacy	FIRDAPSE (amifampridine) is a broad-spectrum potassium channel blocker and its mechanism of action is not fully understood. The efficacy of FIRDAPSE for the treatment of LEMS was demonstrated in two randomized, double-blind, placebo-controlled discontinuation studies. A total of 64 adults with LEMS enrolled in Study 1 (NCT01377922) and Study 2 (NCT02970162). The diagnosis was confirmed by either neurophysiology studies or a positive anti-P/Q type voltage-gated calcium channel antibody test. Patients were required to be on an adequate and stable dosage (30 to 80 mg daily) of amifampridine prior to entering the randomized discontinuation phases of both studies.(1) The two co-primary measures of efficacy in both studies were the change from baseline to the end of the discontinuation period in the Quantitative Myasthenia Gravis (QMG) score and in the Subject Global Impression (SGI) score. The QMG is a 13-item physician-rated categorical scale assessing muscle weakness. Higher scores represent greater impairment. The SGI is a 7-point scale on which patients rated their global impression of the effects of the study treatment on their physical well-being. Lower scores on the SGI represent lower perceived benefit with the study treatment. A key secondary efficacy endpoint was the clinical global impression improvement (CGI-I) score, a 7-point scale on which the treating physician rated the global impression of change in clinical symptoms. A higher CGI-I score indicates a perceived worsening of clinical symptoms.(1) Overall, QMG and SGI scores showed statistically significant differences with FIRDAPSE treated patients maintaining their muscle strength and reported a better sense of well-being compared to the placebo group. FIRDAPSE treated patients also had a statistically significant improvement in symptoms, behavior, and functional ability compared to placebo treated patients.(1)
Safety	FIRDAPSE is contraindicated in patients with:(1) • History of seizures • Hypersensitivity to amifampridine or another aminopyridine

REFERENCES

Number	Reference
1	FIRDAPSE Prescribing Information. Catalyst Pharmaceuticals. May 2024.
2	Pascuzzi RM, Bodkin CL. Myasthenia gravis and Lambert-Eaton Myasthenic Syndrome: New developments in Diagnosis and treatment. *Neuropsychiatric Disease and Treatment*. 2022;Volume 18:3001-3022. doi:10.2147/ndt.s296714
3	Lambert-Eaton Myasthenic Syndrome - Symptoms, causes, treatment | NORD. National Organization for Rare Disorders. https://rarediseases.org/rare-diseases/lambert-eaton-myasthenic-syndrome/
4	Reference no longer used

POLICY AGENT SUMMARY PRIOR AUTHORIZATION

Target Brand Agent(s)	Target Generic Agent(s)	Strength	Targeted MSC	Available MSC	Final Age Limit	Preferred Status
Firdapse	amifampridine phosphate tab	10 MG	M ; N ; O ; Y	N		

POLICY AGENT SUMMARY QUANTITY LIMIT

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	QL Amount	Dose Form	Day Supply	Duration	Addtl QL Info	Allowed Exceptions	Targeted NDCs When Exclusions Exist
Firdapse	Amifampridine Phosphate Tab 10 MG (Base Equivalent)	10 MG	300	Tablets	30	DAYS			

CLIENT SUMMARY – PRIOR AUTHORIZATION

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
			Commercial ; HIM ; ResultsRx
Firdapse	amifampridine phosphate tab	10 MG	Commercial ; HIM ; ResultsRx

CLIENT SUMMARY – QUANTITY LIMITS

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Firdapse	Amifampridine Phosphate Tab 10 MG (Base Equivalent)	10 MG	Commercial ; HIM ; ResultsRx

PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
	Initial Evaluation

Module	Clinical Criteria for Approval
	Target Agent(s) will be approved when ALL of the following are met: 1. The patient has a diagnosis of Lambert Eaton myasthenic syndrome (LEMS) confirmed by at least ONE of the following: (medical records required) A. Neurophysiology study (e.g., nerve conduction studies [CMAP], EMG, repetitive stimulation) **OR** B. Anti-P/Q-type voltage-gated calcium channels (VGCC) antibody testing **AND** 2. If the patient has an FDA labeled indication, then ONE of the following: A. The patient's age is within FDA labeling for the requested indication for the requested agent **OR** B. There is support for using the requested agent for the patient's age for the requested indication **AND** 3. The prescriber is a specialist in the area of the patient's diagnosis (e.g., neurologist, oncologist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND** 4. The patient does NOT have any FDA labeled contraindications to the requested agent **Length of Approval:** 6 months Note: Quantity Limit applies, please see Quantity Limit Criteria **Renewal Evaluation** **Target Agent(s)** will be approved when ALL of the following are met: 1. The patient has been previously approved for the requested agent through the plan's Prior Authorization process [Note: patients not previously approved for the requested agent will require initial evaluation review] **AND** 2. The patient has had clinical benefit with the requested agent **AND** 3. The prescriber is a specialist in the area of the patient's diagnosis (e.g., neurologist, oncologist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND** 4. The patient does NOT have any FDA labeled contraindications to the requested agent **Length of Approval:** 12 months Note: Quantity Limit applies, please see Quantity Limit Criteria

QUANTITY LIMIT CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
QL with PA	**Quantity limit for the Target Agent(s)** will be approved when the following is met: 1. The requested quantity (dose) does NOT exceed the program quantity limit **Length of Approval:** up to 12 months