HELPING PATIENTS WITH LEMS

MOVE FORWARD

WITH FIRDAPSE® (AMIFAMPRIDINE)

FIRDAPSE is the only FDA-approved, evidence-based therapy for adults with Lambert-Eaton myasthenic syndrome (LEMS)

FIRDAPSE® (amifampridine) Tablets 10 mg

First-line therapy for adults with LEMS

SELECTED IMPORTANT SAFETY INFORMATION

FIRDAPSE can cause seizures. Do not use FIRDAPSE in patients with a history of seizures, or with a hypersensitivity to amifampridine or another aminopyridine.

Please see additional Important Safety Information on page 29 and full Prescribing Information on page 31.

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DISEASE BURDEN

LEMS FACTS

A brief overview of the impact of Lambert-Eaton myasthenic syndrome (LEMS)

DISEASE BURDEN

LEMS is a rare autoimmune neuromuscular disorder that **results in progressive, debilitating muscle weakness and fatigue**[1-3]

PREVALENCE

LEMS is estimated to affect 3,000 individuals in the US—**up to 50% of whom are currently undiagnosed or misdiagnosed**[4,5]

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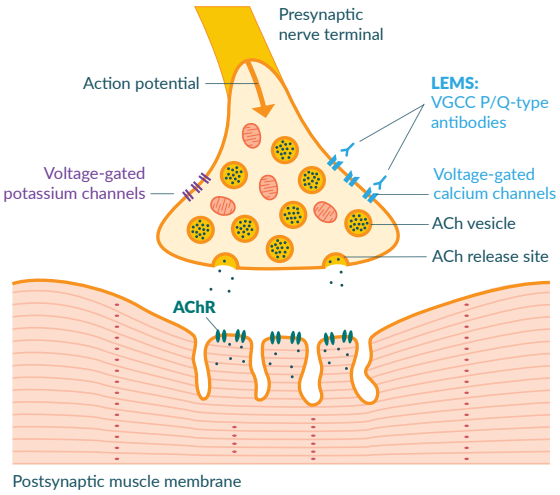
LEMS PATHOPHYSIOLOGY

The mechanism of disease occurs in the presynaptic nerve terminal



- IgG autoantibodies bind to P/Q-type voltage-gated calcium channels (VGCCs) on the presynaptic membrane and inhibit Ca^{2+} entry[1,5]
- Reduced intracellular Ca^{2+} limits exocytosis of acetylcholine (ACh) vesicles into the neuromuscular junction[1,5]
- Decreased ACh results in reduced muscle fiber contraction and onset of LEMS symptomatology[1,6]

P/Q-type VGCC autoantibodies are specific to LEMS, being found in >90% of patients with LEMS[7]

Learn about free anti-VGCC antibody testing from Catalyst at **FreeLEMStest.com**

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LEMS IS DEBILITATING AND PROGRESSIVE

LEMS symptoms contribute to a high level of disease burden, which can worsen over time[3,6,8]

IN A 2012 SURVEY OF PATIENTS LIVING WITH LEMS[3]:

75% reported partial or total restriction in activities of daily living, such as rising from a chair or climbing stairs

More than 50% reported severe leg weakness, dry mouth, and difficulty focusing their sight

58% were hospitalized prior to diagnosis, while **>90% were hospitalized after diagnosis**

Based on EQ-5D scores, the health-related quality of life for LEMS patients is **comparable to the most severe forms of multiple sclerosis**

In a 2001 study, 25% of LEMS patients required a wheelchair all the time or for mobilization outside of the home[8]

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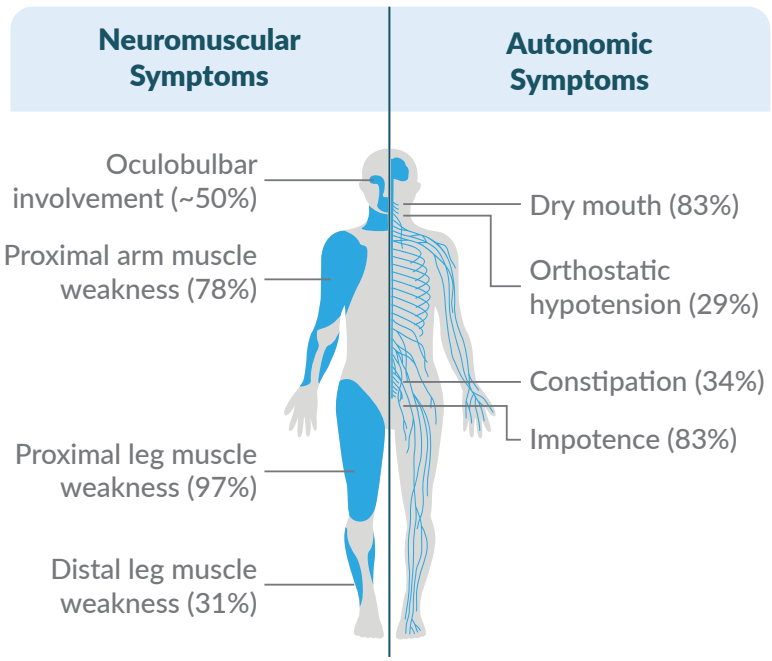
LEMS CLINICAL PRESENTATION

Early recognition of LEMS symptoms can lead to a quicker diagnosis and initiation of effective treatment[5]

LEMS IN ADULTS TYPICALLY PRESENTS AS[5]:

Proximal muscle weakness	Autonomic dysfunction	Hyporeflexia or areflexia



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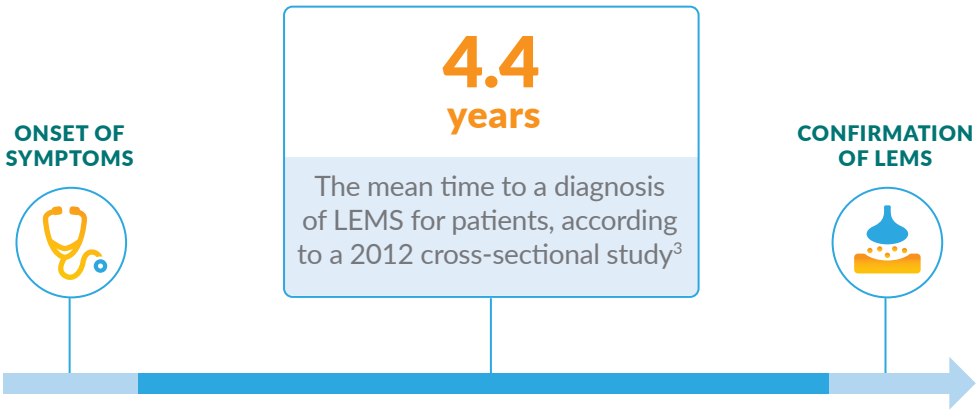
A CHALLENGING DIAGNOSIS

LEMS patients often experience a long diagnostic journey[3]



REASONS FOR THE DELAY:

- Nonspecific and fluctuating symptoms[5]
- Slow progression of disease[5]
- Misdiagnosis due to similar clinical presentation as other conditions[5,9]

The patient burden of LEMS is significant yet often underrecognized[3]

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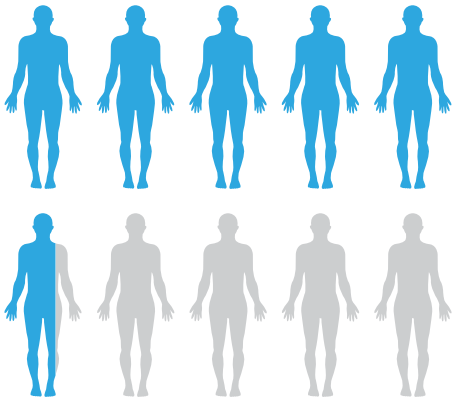
MISDIAGNOSIS IS COMMON

More than half of the patients in a 2011 patient cohort received an incorrect diagnosis[3]



58% of patients were misdiagnosed at least once in a cohort of 241 adult patients with LEMS.[3]

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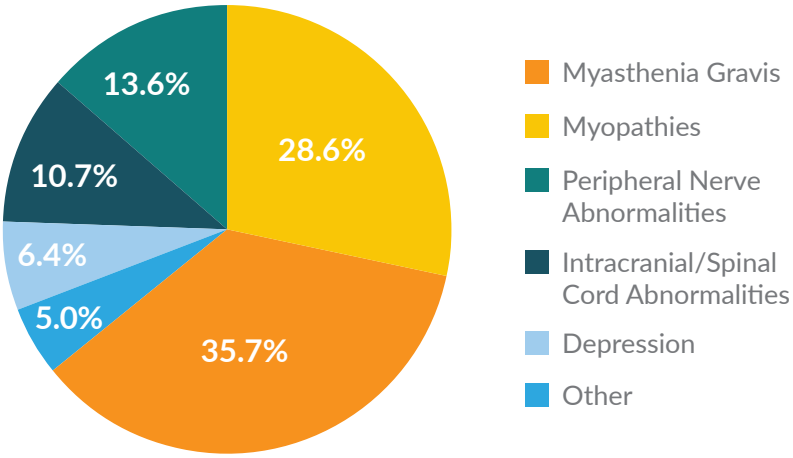
Myasthenia gravis (MG) is the most common misdiagnosis of LEMS[3]

COMMON LEMS MISDIAGNOSES[3]



More than 1/3 of misdiagnosed LEMS patients were initially diagnosed as having MG[3]

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DIFFERENTIATING LEMS FROM MG

Keys to a differential diagnosis of LEMS vs MG[3]

LEMS		MG
Ages of onset: 35 and 60		Ages of onset: 35 and 50
Symmetrical muscle weakness		Asymmetrical muscle weakness
Caudal-to-cranial pattern of spread		Craniocaudal pattern of spread
Mild, late-onset oculobulbar involvement		**Early and prominent oculobulbar involvement**
Absent or diminished tendon reflexes		Tendon reflexes typically preserved
Autonomic dysfunction		No autonomic dysfunction
Transient improvement with exercise		Weakness worsens with exercise

90% **of MG cases include early oculobulbar involvement (vs 5% in LEMS)[9]**

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DIAGNOSING LEMS

If you suspect that your adult patient may have LEMS, there are several clinical diagnostic methods that you can utilize to get them on the right treatment path[3]

SIGNS AND SYMPTOMS

A diagnosis of LEMS can be made based on clinical symptomatology and physical signs, including proximal muscle weakness, autonomic dysfunction, and areflexia[3]

ANTIBODY AND ELECTRODIAGNOSTIC TESTING MAY CONFIRM A LEMS DIAGNOSIS

Anti-VGCC antibody testing

Up to 90% of patients with LEMS will have elevated levels of P/Q-type VGCC antibodies[3,10,11]

Electrodiagnostic testing

Increment on high-frequency repetitive nerve stimulation or post-exercise potentiation can also confirm diagnosis[3]

Learn about free anti-VGCC antibody testing from Catalyst at FreeLEMStest.com

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CATALYST NO-COST ANTIBODY DIAGNOSTIC TESTING

A free program to help your patients find answers

Catalyst Pharmaceuticals, in collaboration with a national diagnostic lab provider, offers free anti-VGCC antibody testing for adult patients with symptoms suggestive of LEMS. The test is available to adult patients who already have a negative AChR antibody test or an equivocal EMG test for LEMS.

Testing for the presence of anti-VGCC antibodies can confirm a diagnosis of LEMS[3,10,11]

The presence of anti-VGCC antibodies can be detected in up to 90% of patients with LEMS[3,10,11]

To request a free anti-VGCC antibody test, visit FreeLEMStest.com

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LEMS TREATMENT CATEGORIES

Treatment of LEMS

ANTITUMOR THERAPY

- Essential for all patients with paraneoplastic LEMS[12]
- Can improve symptoms via reduction of antigenic stimulus for autoantibody production[12]

IMMUNOSUPPRESSIVE THERAPY

- Recommended for flares or when symptomatic treatment is not sufficient[12]
- No prospective, randomized controlled studies
- Only mild-to-moderate improvement in symptoms

NEUROMUSCULAR JUNCTION MODULATION

- Increase neuromuscular transmission of ACh (amifampridine) or inhibit degradation of ACh (pyridostigmine)[12]
- Minimal-to-moderate response with pyridostigmine monotherapy[12]

OFF-LABEL TREATMENTS FOR LEMS

Pyridostigmine (mestinon) offers limited treatment benefits

- Limited randomized trials and robust observation studies and clinical experience support the utility of pyridostigmine in myasthenia gravis[12,13]
- However, clinical data suggest that cholinesterase inhibitors, such as pyridostigmine, are generally not effective as monotherapies for LEMS[12-14]
- In a double-blind, randomized controlled trial comparing the clinical efficacy of amifampridine and pyridostigmine in LEMS, only amifampridine produced significant improvements in muscle strength and compound muscle action potential (CMAP) amplitudes[12,14]

IVIG used for short-term relief of symptoms

- IVIG (intravenous immunoglobulin) can be used as short-term maintenance treatment in patients with refractory weakness or an unsatisfactory response to symptomatic treatment[12]
  - Only one randomized study with IVIG shows significant improvements in limb, respiratory, and bulbar muscle function[12]
  - In a randomized crossover study, IVIG provided no statistical improvement in resting CMAP amplitudes vs placebo infusions[15]
- The role of long-term maintenance treatment in LEMS remains unclear[15]

FIRDAPSE

FIRDAPSE IS A FIRST-LINE TREATMENT FOR ADULTS WITH LEMS[16]

Choose the only FDA-approved therapy indicated for adults with LEMS[17,18]

FIRDAPSE has been tested in more than 70 clinical and nonclinical studies, including two positive Phase 3 studies, over a 9-year period[19]

In clinical trials, FIRDAPSE demonstrated[17,20]:

- A rapid onset of action
- Clinically meaningful improvements in muscle weakness and patient satisfaction

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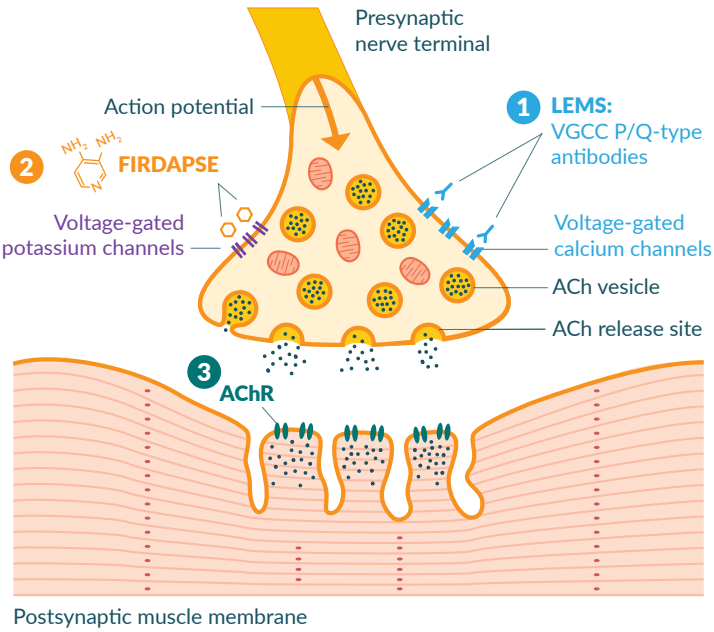
FIRDAPSE MECHANISM OF ACTION

FIRDAPSE acts at the presynaptic nerve terminal to restore neuromuscular transmission[17,21]



1. In LEMS, autoantibodies block the calcium channels in the nerve cells, reducing ACh release into the neuromuscular junction[1,3]
2. FIRDAPSE, a voltage-gated potassium channel blocker, specifically targets the presynaptic nerve terminal of the neuromuscular junction[17,21]
3. FIRDAPSE blocks potassium channels in the nerve cells, which allows more ACh to be released into the neuromuscular junction[17,21]*

*The mechanism by which FIRDAPSE exerts its therapeutic effect in LEMS patients has not been fully elucidated. FIRDAPSE is a broad-spectrum potassium channel blocker.

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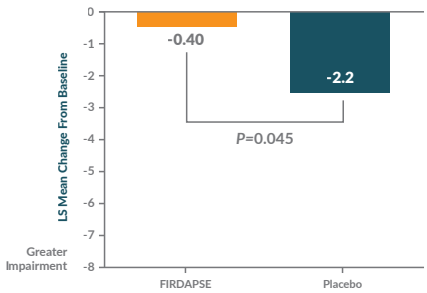
FIRDAPSE MAINTAINED MUSCLE STRENGTH

QMG* scores in two Phase 3 studies showed statistically significant differences between placebo-treated subjects and those treated with FIRDAPSE[17]

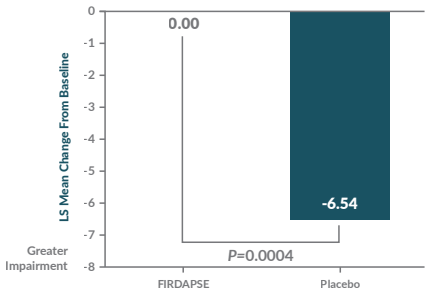
FIRDAPSE-treated subjects maintained their muscle strength, while those in the placebo group demonstrated a statistically significant decline.

COPRIMARY ENDPOINT

Study 1: Total QMG Changes From Baseline to Day 14 Coprimary Endpoint



Study 2: Total QMG Changes From Baseline to Day 4 Coprimary Endpoint



*The Quantitative Myasthenia Gravis (QMG) assessment is a 13-item, physician-rated categorical scale assessing muscle weakness. Each item is assessed on a 4-point scale, where a score of 0 represents no weakness, and a score of 3 represents severe weakness (total score ranges from 0 to 39). Higher scores represent greater impairment.

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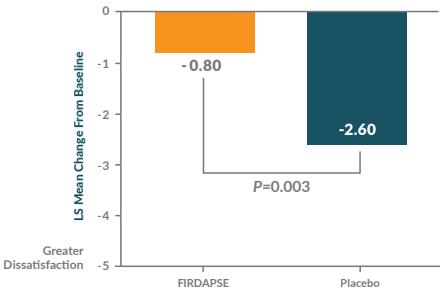
FIRDAPSE IMPROVED PATIENTS' PERCEPTION OF WELL-BEING

SGI* scores in two Phase 3 studies showed statistically significant differences between placebo-treated subjects and those treated with FIRDAPSE[17]

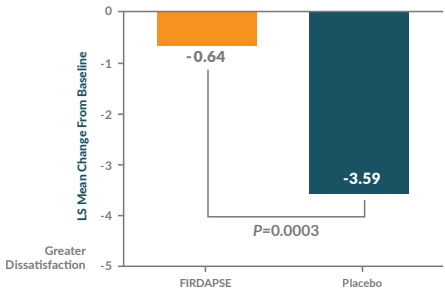
FIRDAPSE-treated subjects reported a better sense of well-being compared to those in the placebo group.

COPRIMARY ENDPOINT

Study 1: SGI Changes From Baseline to Day 14 Coprimary Endpoint



Study 2: SGI Changes From Baseline to Day 4 Coprimary Endpoint



*The Subject Global Impression (SGI) assessment is a 7-point scale on which patients rate 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. The 7-point SGI scale: 1=terrible; 2=mostly dissatisfied; 3=mixed; 4=partially satisfied; 5=mostly satisfied; 6=pleased; 7=delighted.

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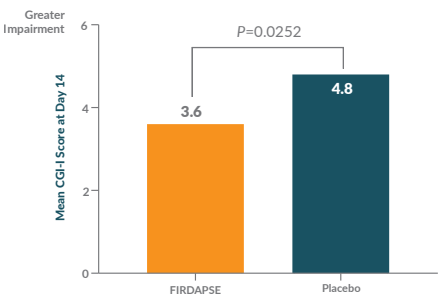
FIRDAPSE IMPROVED CLINICIANS' IMPRESSION OF PATIENT WELL-BEING

CGI-I* scores in two Phase 3 studies showed statistically significant differences between placebo-treated subjects and those treated with FIRDAPSE[20]

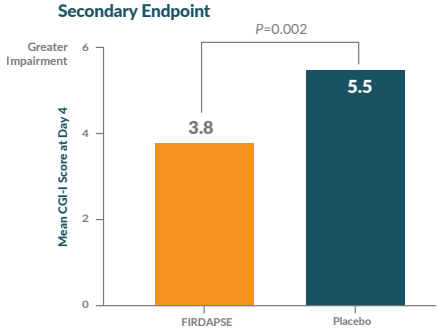
FIRDAPSE-treated subjects demonstrated a statistically significant improvement in symptoms, behavior, and functional ability compared to those in the placebo group.

SECONDARY ENDPOINT

Study 1: CGI-I Scores at Day 14
Secondary Endpoint



Study 2: CGI-I Scores at Day 4
Secondary Endpoint



*The Clinical Global Impression of Improvement (CGI-I) is a subjective, investigator-assessed overall impression of improvement or worsening in symptoms. The 7-point scale is scored from 1, "very much improved," to 7, "very much worse," based on symptoms, behavior, and functional ability. CGI-I scores were collected as a secondary endpoint during this study.

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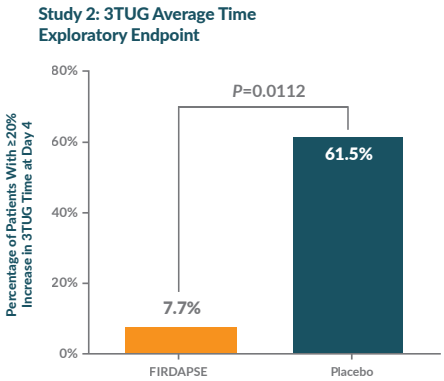
FIRDAPSE MAINTAINED FUNCTIONAL MOBILITY

3TUG* scores in a Phase 3 study showed statistically significant differences between placebo-treated subjects and those treated with FIRDAPSE[20]

The proportion of patients with a ≥20% increase in the Triple-Timed Up-and-Go Test (3TUG) average time was statistically significantly higher in the placebo group compared to the FIRDAPSE group.

EXPLORATORY ENDPOINT



*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. Individuals perform the test 3 consecutive times without pause, and the final measurement is the average time required to complete each of the 3 repetitions. Based on 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 endpoint.

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SAFETY AND TOLERABILITY

Clinical studies have shown that FIRDAPSE is well tolerated. Most of the reported adverse events during these studies were mild to moderate[17,20]

ADVERSE REACTIONS IN ≥5% OF PATIENTS WITH LEMS NEWLY TREATED WITH FIRDAPSE[17]

ADVERSE REACTION	FIRDAPSE % (N=42)
Paresthesia*	62
Upper Respiratory Tract Infection	33
Abdominal Pain	14
Nausea	14
Diarrhea	14
Headache	14
Elevated Liver Enzymes†	14
Back Pain	14
Hypertension	12
Muscle Spasms	12
Dizziness	10
Asthenia	10
Muscular Weakness	10
Pain in Extremity	10
Cataract	10
Constipation	7
Bronchitis	7
Fall	7
Lymphadenopathy	7

During the study, the majority of patients (62%) with no prior exposure to amifampridine experienced transient paresthesia while taking FIRDAPSE.

Most instances diminished during the course of the study.[17]

*Includes paresthesia, oral paresthesia, oral hypesthesia
†Includes elevated alanine aminotransferase (ALT), aspartate aminotransferase (AST), lactate dehydrogenase (LDH), and gamma-glutamyl transferase (GGT)

SELECTED IMPORTANT SAFETY INFORMATION

In patients with renal impairment or hepatic impairment, FIRDAPSE should be initiated at the lowest recommended starting dosage (15 mg/day), and patients should be closely monitored for adverse reactions. The effects of FIRDAPSE have not been studied in patients with hepatic impairment.

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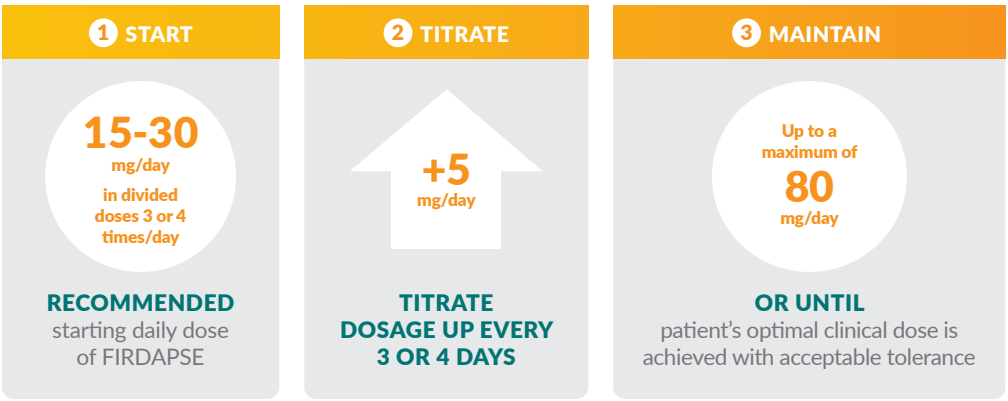
DOSING AND TITRATION WITH 10-MG FIRDAPSE TABLETS

Help patients reach their optimal therapeutic dose



Titration is a critical step for new adult patients who are just getting started on FIRDAPSE and have not taken amifampridine before. By guiding your patients through the titration process, you can help:

- Determine their optimal therapeutic dose of FIRDAPSE
- Maximize neuromuscular benefit
- Minimize issues with tolerability

In Phase 3 clinical studies, the mean total daily FIRDAPSE dose was 60 mg/day[19]

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PATIENT SUPPORT

Catalyst PATHWAYS™

ENROLL YOUR PATIENTS TODAY FOR ACCESS TO A WORLD OF COMPREHENSIVE SUPPORT

Catalyst Pathways™ Enrollment Form

Catalyst PATHWAYS

ENROLLMENT FORM INSTRUCTIONS

The path to Catalyst Pathways™ support starts with a completed Enrollment Form

Catalyst Pathways is a comprehensive program that assists patients and their families throughout their treatment journey. It can help your patients receive delivery of FIRDAPSE® (amifampridine), determine insurance coverage, understand out-of-pocket costs, and access a variety of educational resources.

Sign-up can be completed in three easy steps:

STEP 1

Complete the Enrollment Form in its entirety.

- Sections 1 and 2 can be filled out by the patient or the prescriber.
- Sections 3, 4, and 5 should be filled out by the prescriber.
  - Section 4 is the prescription (Rx) and should be filled out according to the label on the FIRDAPSE package insert.
  - Adult patients with Lambert-Eaton myasthenic syndrome (LEMS) who have never been treated with amifampridine (or 3,4-DAP) may be eligible for the My FIRDAPSE Therapeutic Dose Program. Through this program, they may receive up to 60 days of medication at no charge for initial titration. If a physician would like for their patient to participate in this program, the physician should check the box indicating so in Section 4. For full eligibility requirements or to learn more about this program, contact a Catalyst Pathways team member at 1-833-422-8259.
  - Section 5 includes Medical Criteria that should be filled out by the prescriber. This section validates the patient's diagnosis of LEMS.
- Prescriber must sign and date where indicated on page 1.
- Patient must sign and date where indicated on page 1.
- Please include a copy of the patient's insurance card (front and back).

STEP 2

The patient must sign and date the Patient Authorization of the Enrollment Form (Section 6 on page 2) to be enrolled in Catalyst Pathways.

This step is necessary in order for Catalyst Pathways personnel to communicate with the patient's healthcare provider, insurance company, and financial assistance organizations (as necessary).

STEP 3

Fax the signed Enrollment Form to Catalyst Pathways at 1-833-422-8260.

If you have any questions, please call us at
1-833-4-CATALYST (1-833-422-8259)
7:00 AM – 7:00 PM Central Time

Fax#: 1-833-422-8260
Phone#: 1-833-4-CATALYST (1-833-422-8259)
*Please submit both pages.

Phone # 1-833-4-CATALYST (1-833-422-8259) Fax # 1-833-422-8260 Website: www.YourCatalystPathways.com Page 1 of 2

2 easy ways to get started

1. Complete the Enrollment Form at **YourCatalystPathways.com**
2. Contact a FIRDAPSE representative at **1-833-4-CATALYST (1-833-422-8259)**

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Romy, living with LEMS

Personalized support programs and a dedicated team optimize your patients' treatment experience

The My FIRDAPSE Therapeutic Dose Program is designed to help new patients achieve prompt and proper treatment of their LEMS symptoms

Financial Assistance options include a copay support program to reduce out-of-pocket costs

Care Coordinators provide a warm welcome into the program and introduce patients to their dedicated team

Patient Access Liaisons provide a go-to, local resource for one-on-one disease education, as well as treatment and insurance support

Insurance Navigators facilitate the handling of complicated insurance and reimbursement issues that may arise

SELECTED IMPORTANT SAFETY INFORMATION

FIRDAPSE can cause seizures. Do not use FIRDAPSE in patients with a history of seizures, or with a hypersensitivity to amifampridine or another aminopyridine.

Please see additional Important Safety Information on page 29 and full Prescribing Information on page 31.

FIRDAPSE® (amifampridine) Tablets 10 mg

ACCESS AND AFFORDABILITY

Catalyst Pathways programs have helped patients gain first access to treatment and minimized their out-of-pocket (OOP) costs for FIRDAPSE[19]

THROUGH CATALYST PATHWAYS:

275 amifampridine-naïve patients gained their **first access to therapy**[19]

of patients pay nothing for their FIRDAPSE prescription[19]

Patients with commercial or government insurance now average

$1.66 per month in OOP costs[19]

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SELECTED IMPORTANT SAFETY INFORMATION

FIRDAPSE can cause seizures. Do not use FIRDAPSE in patients with a history of seizures, or with a hypersensitivity to amifampridine or another aminopyridine.

Please see additional Important Safety Information on page 29 and full Prescribing Information on page 31.

FIRDAPSE® (amifampridine) Tablets 10 mg

INDICATION AND IMPORTANT SAFETY INFORMATION

INDICATIONS AND USAGE:
FIRDAPSE is a potassium channel blocker indicated for the treatment of Lambert-Eaton myasthenic syndrome (LEMS) in adults.

CONTRAINDICATIONS
FIRDAPSE is contraindicated in patients with:

- A history of seizures
- Hypersensitivity to amifampridine phosphate or another aminopyridine

WARNINGS AND PRECAUTIONS
Seizures: FIRDAPSE can cause seizures. Consider discontinuation or dose-reduction of FIRDAPSE in patients who have a seizure while on treatment. FIRDAPSE is contraindicated in patients with a history of seizures.

Hypersensitivity: If a hypersensitivity reaction such as anaphylaxis occurs, FIRDAPSE should be discontinued and appropriate therapy initiated.

ADVERSE REACTIONS
The most common (> 10%) adverse reactions are: paresthesia, upper respiratory tract infection, abdominal pain, nausea, diarrhea, headache, elevated liver enzymes, back pain, hypertension, and muscle spasms.

To report SUSPECTED ADVERSE REACTIONS, contact Catalyst Pharmaceuticals at 1-844-347-3277 (1-844-FIRDAPSE) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please see full Prescribing Information on page 31.

FIRDAPSE® (amifampridine) Tablets 10 mg

THE FACTS ON LAMBERT-EATON MYASTHENIC SYNDROME (LEMS)

An autoimmune neuromuscular disorder that leads to progressive, debilitating muscle weakness and fatigue[1-3]

Defining symptoms include proximal muscle weakness, autonomic dysfunction, and hyporeflexia or areflexia[5]

Affects ~3,000 people in the US—more than half of whom are misdiagnosed, usually with myasthenia gravis[4,5]

Can be diagnosed by clinical signs and confirmed by anti-VGCC antibody testing and/or electrodiagnostic testing[5]

FIRDAPSE is the only FDA-approved, evidence-based treatment for adults with LEMS[17,18]

SELECTED IMPORTANT SAFETY INFORMATION

FIRDAPSE can cause seizures. Do not use FIRDAPSE in patients with a history of seizures, or with a hypersensitivity to amifampridine or another aminopyridine.

Please see additional Important Safety Information on page 29 and full Prescribing Information on page 31.

Catalyst pharmaceuticals

FIRDAPSE® (amifampridine) Tablets 10 mg

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use FIRDAPSE® safely and effectively. See full prescribing information for FIRDAPSE®.

FIRDAPSE® (amifampridine) tablets, for oral use
Initial U.S. Approval: 2018

----------INDICATIONS AND USAGE----------

FIRDAPSE is a potassium channel blocker indicated for the treatment of Lambert-Eaton myasthenic syndrome (LEMS) in adults. (1)

----------DOSAGE AND ADMINISTRATION----------

- The recommended starting dosage is 15 mg to 30 mg daily taken orally in divided doses (3 to 4 times daily). (2.1)
  - Starting dosage is 15 mg daily for patients with renal impairment, hepatic impairment, and in known N-acetyltransferase 2 (NAT2) poor metabolizers (2.2, 2.3, 2.4)
- Dosage can be increased by 5 mg daily every 3 to 4 days. (2.1)
- Dosage is not to exceed a maximum of 80 mg daily. (2.1)
- The maximum single dose is 20 mg. (2.1)

----------DOSAGE FORMS AND STRENGTHS----------

- Tablets: 10 mg, functionally scored. (3)

----------CONTRAINDICATIONS----------

FIRDAPSE is contraindicated in patients with:

- A history of seizures (4)
- Hypersensitivity to amifampridine or another aminopyridine (4)

----------WARNINGS AND PRECAUTIONS----------

- Seizures: FIRDAPSE can cause seizures. Consider discontinuation or dose-reduction of FIRDAPSE in patients who have a seizure while on treatment. (5.1)
- Hypersensitivity reactions: If a hypersensitivity reaction such as anaphylaxis occurs, FIRDAPSE should be discontinued and appropriate therapy initiated. (5.2)

----------ADVERSE REACTIONS----------

The most common (> 10%) adverse reactions are: paresthesia, upper respiratory tract infection, abdominal pain, nausea, diarrhea, headache, elevated liver enzymes, back pain, hypertension, and muscle spasms. (6)

To report SUSPECTED ADVERSE REACTIONS, contact Catalyst Pharmaceuticals at 1-844-347-3277 (1-844-FIRDAPSE) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

----------DRUG INTERACTIONS----------

- Drugs that lower seizure threshold: The concomitant use of FIRDAPSE and drugs that lower seizure threshold may lead to an increased risk of seizures. (7.1)
- Drugs with cholinergic effects: The concomitant use of FIRDAPSE and drugs with cholinergic effects (e.g., direct or indirect cholinesterase inhibitors) may increase the cholinergic effects of FIRDAPSE and of those drugs, and increase the risk of adverse reactions. (7.2)

----------USE IN SPECIFIC POPULATIONS----------

- Pregnancy: Based on animal data, may cause fetal harm (8.1)

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide

Revised: 11/2018

FULL PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

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

2 DOSAGE AND ADMINISTRATION

2.1 Dosage Information

- The recommended starting dosage of FIRDAPSE is 15 mg to 30 mg daily, taken orally in divided doses (3 to 4 times daily).
- The dosage can be increased by 5 mg daily every 3 or 4 days.
- The maximum recommended total daily dosage is 80 mg.
- The maximum single dose is 20 mg.
- If a dose is missed, patients should not take double or extra doses.

2.2 Patients with Renal Impairment

The recommended starting dosage of FIRDAPSE in patients with renal impairment (creatinine clearance 15 to 90 mL/min) is 15 mg daily, taken orally in 3 divided doses. No dosage recommendation for FIRDAPSE can be made for patients with end-stage renal disease *[see Use in Specific Populations (8.6) and Clinical Pharmacology (12.3, 12.5)]*.

2.3 Patients with Hepatic Impairment

The recommended starting dosage of FIRDAPSE in patients with any degree of hepatic impairment is 15 mg daily, taken orally in 3 divided doses *[see Use in Specific Populations (8.7) and Clinical Pharmacology (12.3, 12.5)]*.

2.4 Known N-acetyltransferase 2 (NAT2) Poor Metabolizers

The recommended starting dosage of FIRDAPSE in known N-acetyltransferase 2 (NAT2) poor metabolizers is 15 mg daily, taken orally in 3 divided doses *[see Use in Specific Populations (8.8) and Clinical Pharmacology (12.3, 12.5)]*.

2.5 Administration Instructions

FIRDAPSE can be taken without regard to food.

3 DOSAGE FORMS AND STRENGTHS

FIRDAPSE tablets contain 10 mg amifampridine and are white to off-white, round, and functionally scored. Each tablet is debossed on the non-scored side with “CATALYST” and on the scored side with “211” above the score and “10” below the score.

4 CONTRAINDICATIONS

FIRDAPSE is contraindicated in patients with:

- A history of seizures *[see Warnings and Precautions (5.1)]*
- Hypersensitivity to amifampridine phosphate or another aminopyridine *[see Warnings and Precautions (5.2)]*

5 WARNINGS AND PRECAUTIONS

5.1 Seizures

FIRDAPSE can cause seizures. Seizures have been observed in patients without a history of seizures taking FIRDAPSE at the recommended doses, at various times after initiation of treatment, at an incidence of approximately 2%. Many of the patients were taking medications or had comorbid medical conditions that may have lowered the seizure threshold *[see Drug Interactions (7.1)]*. Seizures may be dose-dependent. Consider discontinuation or dose-reduction of FIRDAPSE in patients who have a seizure while on treatment. FIRDAPSE is contraindicated in patients with a history of seizures.

5.2 Hypersensitivity

In clinical trials, hypersensitivity reactions and anaphylaxis associated with FIRDAPSE administration have not been reported. Anaphylaxis has been reported in patients taking another aminopyridine; therefore, it may occur with FIRDAPSE. If anaphylaxis occurs, administration of FIRDAPSE should be discontinued and appropriate therapy initiated.

6 ADVERSE REACTIONS

The following serious adverse reactions are described elsewhere in the labeling:

- Seizures *[see Warnings and Precautions (5.1)]*
- Hypersensitivity *[see Warnings and Precautions (5.2)]*

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

In controlled and uncontrolled trials (Study 1 and 2) in patients with LEMS, 63 patients were treated with FIRDAPSE, including 40 patients treated for more than 6 months, and 39 patients treated for more than 12 months. In an expanded access program, 139 patients with LEMS were treated with FIRDAPSE, including 102 patients treated for more than 6 months, 77 patients treated for more than 12 months, and 53 patients treated for more than 18 months.

Study 1 was a double-blind, placebo-controlled, randomized discontinuation study in adults with LEMS. Following an initial open-label run-in phase (up to 90 days), patients were randomized to either continue FIRDAPSE treatment or transition to placebo, for a 14-day double-blind phase. Following final assessments, patients were allowed to resume FIRDAPSE treatment for up to 2 years (open-label long-term safety phase of the study).

During the open-label run-in phase of Study 1, 53 patients received FIRDAPSE for an average of 81 days at a mean daily dosage of 50.5 mg/day. The mean patient age was 52.1 years and 66% were female. There were 42 patients who had no prior exposure to FIRDAPSE at the initiation of this study. Table 1 shows adverse reactions with an incidence of 5% or greater occurring in the 42 LEMS patients newly initiated on treatment with FIRDAPSE during the run-in phase of the study.

Table 1. Adverse Reactions in ≥5% of LEMS Patients Newly Treated with FIRDAPSE in Study 1

Adverse Reaction	FIRDAPSE N=42 %
Paresthesia*	62
Upper respiratory tract infection	33
Abdominal pain	14
Nausea	14
Diarrhea	14
Headache	14
Elevated liver enzymes**	14
Back pain	14
Hypertension	12
Muscle spasms	12
Dizziness	10
Asthenia	10
Muscular weakness	10
Pain in extremity	10
Cataract	10
Constipation	7
Bronchitis	7
Fall	7
Lymphadenopathy	7

*Includes paresthesia, oral paresthesia, oral hypoesthesia

**Includes elevated alanine aminotransferase (ALT), aspartate aminotransferase (AST), lactate dehydrogenase (LDH), and gamma-glutamyl transferase (GGT)

Other Adverse Reactions
In the overall population treated in Study 1 (n=53), including the double-blind phase and the 2-year open-label long-term safety phase, additional adverse reactions occurring in at least 5% of the patients included: dyspnea, urinary tract infection, gastroesophageal reflex, insomnia, peripheral edema, pyrexia, viral infection, blood creatine phosphokinase increase, depression, erythema, hypercholesterolemia, and influenza. These patients received a mean daily dosage of 66 mg of FIRDAPSE.

7 DRUG INTERACTIONS

7.1 Drugs that Lower Seizure Threshold
The concomitant use of FIRDAPSE and drugs that lower seizure threshold may lead to an increased risk of seizures *[see Warnings and Precautions (5.1)]*. The decision to administer FIRDAPSE concomitantly with drugs that lower the seizure threshold should be carefully considered in light of the severity of the associated risks.

7.2 Drugs with Cholinergic Effects
The concomitant use of FIRDAPSE and drugs with cholinergic effects (e.g., direct or indirect cholinesterase inhibitors) may increase the cholinergic effects of FIRDAPSE and of those drugs and increase the risk of adverse reactions.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy
Risk Summary
There are no data on the developmental risk associated with the use of FIRDAPSE in pregnant women. In animals studies, administration of amifampridine phosphate to rats during pregnancy and lactation resulted in developmental toxicity (increase in stillbirths and pup deaths, reduced pup weight, and delayed sexual development) at doses associated with maternal plasma drug levels lower than therapeutic drug levels (see Animal Data). In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively. The background risk of major birth defects and miscarriage for the indicated population is unknown.

Data
Animal Data
Oral administration of amifampridine phosphate (0, 7.5, 22.5, or 75 mg/kg/day) to female rats prior to and during mating and continuing throughout organogenesis produced no adverse effects on embryofetal development. Plasma amifampridine exposure (AUC) at the highest dose tested is approximately 7 times that in humans at the maximum recommended human dose (MRHD) of 80 mg amifampridine/day. Oral administration of amifampridine phosphate (0, 9, 30, or 57 mg/kg/day) to pregnant rabbits throughout organogenesis produced no adverse effects on embryofetal development. The highest dose tested is approximately 7 times the MRHD (80 mg/day amifampridine) on a body surface area (mg/m^2) basis.

Oral administration of amifampridine phosphate (0, 7.5, 22.5, or 75 mg/kg/day) to female rats throughout pregnancy and lactation resulted in an increase in stillbirths and pup deaths, reduced pup weight, and delayed sexual development in female pups at the mid and high doses tested. The no-effect dose (7.5 mg/kg/day amifampridine phosphate) for adverse developmental effects is associated with a plasma amifampridine exposure (AUC) less than that in humans at the MRHD.

8.2 Lactation
Risk Summary
There are no data on the presence of FIRDAPSE in human milk, the effects on the breastfed infant, or the effects on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for FIRDAPSE and any potential adverse effects on the breastfed infant from FIRDAPSE or from the underlying maternal condition.

In lactating rat, amifampridine was excreted in milk and reached levels similar to those in maternal plasma.

8.4 Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

8.5 Geriatric Use

Clinical studies of FIRDAPSE did not include sufficient numbers of subjects aged 65 and over (19 of 63 patients in Studies 1 and 2) to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy *[see Dosage and Administration (2.2, 2.3) and Drug Interactions (7.2, 7.3)]*.

8.6 Renal Impairment

Renal clearance is an elimination pathway for amifampridine and the inactive metabolite, 3-N-acetyl amifampridine, and exposure of amifampridine is higher in subjects with renal impairment *[see Clinical Pharmacology (12.3)]*. Therefore, in patients with renal impairment, FIRDAPSE should be initiated at the lowest recommended starting dosage (15 mg/day), and patients should be closely monitored for adverse reactions *[see Dosage and Administration (2.2)]*. Consider dosage modification or discontinuation of FIRDAPSE for patients with renal impairment as needed based on clinical effect and tolerability. The safety, efficacy, and pharmacokinetics of amifampridine have not been studied in patients with end-stage renal disease (CLcr <15 mL/min or patients requiring dialysis). No dosage recommendation for FIRDAPSE can be made for patients with end-stage renal disease.

8.7 Hepatic Impairment

The effects of FIRDAPSE have not been studied in patients with hepatic impairment. FIRDAPSE is extensively metabolized by N-acetyltransferase 2 (NAT2) and hepatic impairment may cause an increase in exposure. Therefore, initiate FIRDAPSE in patients with any degree of hepatic impairment at the lowest recommended starting dosage (15 mg/day) and monitor for adverse reactions *[see Dosage and Administration (2.3)]*. Consider dosage modification or discontinuation of FIRDAPSE for patients with hepatic impairment as needed based on clinical effect and tolerability.

8.8 NAT2 Poor Metabolizers

Exposure of FIRDAPSE is increased in patients who are N-acetyltransferase 2 (NAT2) poor metabolizers *[see Clinical Pharmacology (12.5)]*. Therefore, initiate FIRDAPSE in patients who are known NAT2 poor metabolizers at the lowest recommended starting dosage (15 mg/day) and monitor for adverse reactions *[see Dosage and Administration (2.4)]*. Consider dosage modification of FIRDAPSE for patients who are known NAT2 poor metabolizers as needed based on clinical effect and tolerability.

10 OVERDOSAGE

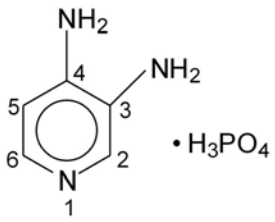
Overdose with FIRDAPSE was not reported during clinical studies.

In a case report, a 65-year-old patient with LEMS inadvertently received a total daily amifampridine dose of 360 mg/day (more than 4 times the maximum recommended total daily dose) and was hospitalized for general weakness, paresthesia, nausea, vomiting, and palpitations. The patient developed convulsions and paroxysmal supraventricular tachycardia, and four days after admission, experienced cardiac arrest. The patient was resuscitated and ultimately recovered following withdrawal of amifampridine.

Patients with suspected overdose with FIRDAPSE should be monitored for signs or symptoms of exaggerated FIRDAPSE adverse reactions or effects, and appropriate symptomatic treatment instituted immediately.

11 DESCRIPTION

The active ingredient of FIRDAPSE is amifampridine phosphate, which is a voltage-gated potassium channel blocker. Amifampridine phosphate is described chemically as 3,4-diaminopyridine phosphate with a molecular weight of 207.1 and a molecular formula of $C_5H_7N_3 \cdot H_3PO_4$. The structural formula is:



Amifampridine phosphate is a white, crystalline powder that is freely soluble in water, and slightly soluble in solvents ethanol, methanol and acetic acid. A 1% aqueous solution of amifampridine phosphate has a pH of 4.4 at ambient conditions.

Each FIRDAPSE tablet contains 10 mg amifampridine (equivalent to 18.98 mg amifampridine phosphate). The tablet formulation includes the following inactive ingredients: calcium stearate, colloidal silicon dioxide, and microcrystalline cellulose.

FIRDAPSE tablets are intended for oral administration only.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The mechanism by which amifampridine exerts its therapeutic effect in LEMS patients has not been fully elucidated. Amifampridine is a broad spectrum potassium channel blocker.

12.2 Pharmacodynamics

The effect of FIRDAPSE on QTc interval prolongation was studied in a double blind, randomized, placebo and positive controlled study in 52 healthy individuals who are slow acetylators. At an exposure 2-fold the expected maximum therapeutic exposure of amifampridine, FIRDAPSE did not prolong QTc to any clinically relevant extent.

12.3 Pharmacokinetics

The pharmacokinetics of amifampridine are similar between healthy individuals and LEMS patients. Following single and multiple doses, AUC, C_{max} and C_{min} were highly variable between individuals. FIRDAPSE exposure increased proportionally with dose across the range of 20 mg to 80 mg single oral doses.

Absorption

Amifampridine peak plasma concentration is reached 20 minutes to 1 hour after administration. Food does not have a clinically significant effect on the exposure of amifampridine.

Elimination

Amifampridine is eliminated primarily through metabolism to 3-N-acetyl-amifampridine and to a smaller extent through the kidneys. The terminal half-life ranges from 1.8 to 2.5 hours in healthy subjects.

Metabolism

Amifampridine is extensively metabolized by N-acetyltransferase 2 (NAT2) to 3-N-acetyl-amifampridine, which is considered an inactive metabolite.

Excretion

Following administration of FIRDAPSE to healthy subjects, 93% to 100% of the administered dose was eliminated in the urine as amifampridine or 3-N-acetyl amifampridine over 24 hours.

Specific Populations

Patients with Renal Impairment

Pharmacokinetic data are available from a study of 24 otherwise healthy subjects with impaired renal function who received a single 10-mg dose of FIRDAPSE. The exposure of amifampridine (measured as AUC) was 2- to 3-fold higher in subjects with moderate (CLcr 30-59 mL/min) or severe (CLcr 15-29 mL/min) renal impairment than in subjects with normal renal function (CLcr greater than or equal to 90 mL/min). Compared with subjects with normal renal function, subjects with mild renal impairment (CLcr 60-89 mL/min) had a 36% increase in exposure. Therefore, FIRDAPSE should be initiated at the lowest recommended starting dosage (15 mg/day) in patients with renal impairment, and such patients should be closely monitored for adverse reactions *[see Dosage and Administration (2.2) and Use in Specific Populations (8.6)]*. C_{max} was marginally affected by renal impairment.

12.5 Pharmacogenomics

Genetic variants in the N-acetyltransferase gene 2 (NAT2) affect the rate and extent of FIRDAPSE metabolism. Poor metabolizers, also referred to as "slow acetylators" (i.e., carriers of two reduced function alleles), have 3.5- to 4.5-fold higher C_{max}, and 5.6- to 9-fold higher AUC than normal metabolizers, also referred to as "fast/rapid acetylators" (i.e., carriers of two normal function alleles). Therefore, FIRDAPSE should be initiated at the lowest recommended starting dosage (15 mg/day) in known NAT2 poor metabolizers, and such patients should be closely monitored for adverse reactions *[see Dosage and Administration (2.4) and Use in Specific Populations (8.8)]*. In the general population, the NAT2 poor metabolizer phenotype prevalence is 40–60% in the White and African American populations, and in 10–30% in Asian ethnic populations (individuals of Japanese, Chinese, or Korean descent).

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenicity
In a 104-week carcinogenicity study, oral administration of amifampridine phosphate (0, 15, 48, or 105 mg/kg/day) resulted in an increase in uterine tumors (endometrial carcinoma and combined endometrial adenoma/endometrial carcinoma/squamous cell carcinoma) at the mid and high doses tested. The low dose, not associated with an increase in tumors, is similar to the maximum recommended human dose (80 mg/day amifampridine) on a body surface area (mg/m^2 basis).

Mutagenesis
Amifampridine phosphate was negative in the *in vitro* bacterial reverse mutation and *in vivo* rat micronucleus assays. Amifampridine phosphate was positive for clastogenicity in the *in vitro* mouse lymphoma *tk* assay in the absence of metabolic activation.

Impairment of Fertility
Oral administration of amifampridine phosphate (0, 7.5, 22.5, or 75 mg/kg/day) to male and female rats prior to and during mating, and continuing in females throughout organogenesis, produced no adverse effects on fertility. Plasma amifampridine exposure (AUC) at the highest dose tested is approximately 7 times that in humans at the maximum recommended human dose (MRHD) of 80 mg amifampridine/day.

14 CLINICAL STUDIES

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 (age 21 to 88 years) with LEMS were enrolled (Study 1 and Study 2). The studies enrolled patients with a confirmed diagnosis of LEMS based on 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 phosphate prior to entering the randomized discontinuation phases of both studies.

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. Each item is assessed on a 4-point scale, where a score of 0 represents no weakness, and a score of 3 represents severe weakness (total score 0-39). 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.

Study 1 (NCT01377922)

After an initial open-label run-in phase, 38 patients were randomized in a double-blind fashion to either continue treatment with FIRDAPSE (n=16) or to a downward titration to placebo (n=22) over 7 days. Following the downward titration period, patients remained on blinded FIRDAPSE or placebo for 7 more days. Efficacy was assessed at Day 14 of the double-blind period. Patients

were allowed to use stable dosages of peripherally acting cholinesterase inhibitors or oral immunosuppressants. Twenty-six percent of patients randomized to FIRDAPSE were receiving cholinesterase inhibitors, versus 36% in the placebo group, and 28% of patients randomized to FIRDAPSE were receiving oral immunosuppressant therapies, versus 34% in the placebo group.

Patients had a median age of 54 years (range: 21 to 88 years), 61% were female, and 90% were White. Eighty-four percent of patients had a diagnosis of autoimmune LEMS, and 16% of patients had a diagnosis of paraneoplastic LEMS.

During the double-blind period (from Baseline to Day 14), the QMG scores tended to worsen in both treatment groups, but there was significantly greater worsening in the placebo group than in the FIRDAPSE group (p=0.045). Similarly, the SGI score tended to worsen in both treatment groups during the double-blind period, but there was significantly greater worsening in the placebo group than in the FIRDAPSE group (p=0.003), as summarized in Table 2. These results indicate that in Study 1, patients randomized to placebo had a significantly greater worsening of muscle weakness and of global impression of the effects of the study treatment on their physical well-being, compared to patients who continued FIRDAPSE in the double-blind period.

Table 2. Change from Baseline to Day 14 in QMG Score and SGI Score in Study 1

Assessment	FIRDAPSE (n=16)	Placebo (n=21)
Primary Endpoints		
QMG Score[a]		
Baseline (mean)	6.4	5.6
Change from Baseline (Least Square Mean)	0.4	2.2
FIRDAPSE-placebo Treatment Difference (Least Square Mean (95% CI))	–1.7 (–3.4, –0.0)	
p-value[c]	0.045	
SGI Score[b]		
Baseline (mean)	5.6	5.9
Change from Baseline (Least Square Mean)	-0.8	-2.6
FIRDAPSE-placebo Treatment Difference, (Least Square Mean (95% CI))	1.8 (0.7, 3.0)	
p-value[c]	0.003	

a. QMG Score range 0 (no impairment) to 39 (worst impairment)
b. SGI Score range 0 (least perceived benefit) to 7 (most perceived benefit)
c. Pairwise contrast at Day 14 from mixed-effects model with repeated measures.

The CGI-I score was significantly greater for patients randomized to placebo than for patients who continued treatment with FIRDAPSE, with a mean difference between FIRDAPSE and placebo of -1.1 (p=0.02), indicating that clinicians perceived a greater worsening of clinical symptoms in patients who were randomized to placebo and discontinued from FIRDAPSE treatment, compared to patients who continued FIRDAPSE in the double-blind period.

Study 2 (NCT02970162)

Patients on stable treatment with FIRDAPSE were randomized 1:1 in a double-blind fashion to either continue treatment with FIRDAPSE (n=13) or change to placebo (n=13) for 4 days. Efficacy was assessed at the end of the 4-day double-blind discontinuation period. Patients were allowed to use stable doses of peripherally acting cholinesterase inhibitors or corticosteroids. Sixty-one percent of patients randomized to FIRDAPSE were receiving cholinesterase inhibitors, versus 54% of patients randomized to placebo. Corticosteroid use was similar between FIRDAPSE and placebo (8%). Patients with recent use of immunomodulatory therapies (e.g., azathioprine, mycophenolate, cyclosporine), rituximab, intravenous immunoglobulin G, and plasmapheresis were excluded from the study. Patients had a median age of 55.5 years (range: 31 to 75 years), 62% were female, and 88% were White.

From Baseline to Day 4, there was significantly greater worsening in the QMG score in the placebo group than in the FIRDAPSE group (p=0.0004), and also significantly greater worsening in the SGI score in the placebo group than in the FIRDAPSE group

(p=0.0003), as summarized in Table 3. These results indicate that in Study 2, patients randomized to placebo had a significantly greater worsening of muscle weakness and of global impression of the effects of the study treatment on their physical well-being, compared to patients who continued FIRDAPSE in the double-blind period.

Table 3. Change from Baseline to Day 4 in QMG Scores and SGI Scores in Study 2

Assessment	FIRDAPSE (n=13)	Placebo (n=13)
QMG Scores[a]		
Baseline, Mean	7.8	8.5
Change from Baseline, Least Square Mean[c]	0.00	6.54
FIRDAPSE-placebo Treatment Difference, Least Square Mean (95% CI)	-6.54 (-9.78, -3.29)	
p-value[d]	0.0004	
SGI Scores[b]		
Baseline, Mean	6.1	5.8
Change from Baseline, Least Square Mean[c]	-0.64	-3.59
FIRDAPSE-placebo Treatment Difference, Least Square Mean (95% CI)	2.95 (1.53, 4.38)	
p-value[d]	0.0003	

a. QMG Score range 0 (no impairment) to 39 (worst impairment)
b. SGI Score range 0 (least perceived benefit) to 7 (most perceived benefit)
c Change from baseline for QMG total score was modeled as the response, with fixed effects terms for treatment and QMG at Baseline.
d p-value based on the Wilcoxon Rank Sum Test for treatment differences.

The clinical global impression improvement (CGI-I) score was significantly greater for patients randomized to placebo than for patients who continued treatment with FIRDAPSE, with a mean difference between FIRDAPSE and placebo of -2.7 (p=0.002), indicating that clinicians perceived a greater worsening of clinical symptoms in patients who were randomized to placebo and discontinued from FIRDAPSE treatment, compared to patients who continued FIRDAPSE in the double-blind period.

16 HOW SUPPLIED/ STORAGE AND HANDLING

16.1 How Supplied

FIRDAPSE 10 mg tablets are white to off white, round, and functionally scored. Each tablet is debossed on the non-scored side with "CATALYST" and on the scored side with "211" above the score and "10" below the score. Tablets can be divided in half at the score. FIRDAPSE is supplied as follows:

Child Resistant Blister Pack

- blister pack containing 10 tablets NDC 69616-211-04
- carton containing 12 blister packs (120 tablets total) NDC 69616-211-06

Bottles

- 60 tablets NDC 69616-211-08
- 240 tablets NDC 69616-211-03

16.2 Storage and Handling

Store FIRDAPSE tablets at 20°C to 25°C (68°F to 77°F) with excursions permitted from 15°C to 30°C (59°F to 86°F) [see USP controlled room temperature].

17 PATIENT COUNSELING INFORMATION

Advise the patient and/or caregiver to read the FDA-approved patient labeling (Medication Guide).

Risk of Seizures
Inform patients that FIRDAPSE can cause seizures, and to notify their healthcare provider if they experience a seizure *[see Warnings and Precautions (5.1)]*.

Hypersensitivity
Instruct patients to inform their healthcare provider if they have signs or symptoms of hypersensitivity, and to seek emergency help if symptoms of anaphylaxis occur *[see Warnings and Precautions (5.2)]*.

FIRDAPSE Dosing
Instruct patients to take FIRDAPSE exactly as prescribed. Patients should carefully follow the dose escalation schedule provided by their healthcare provider to safely achieve the therapeutic dosage *[see Dosage and Administration (2)]*. Inform patients that the tablets may be divided in half at the score, if needed. Instruct patients not to take a double dose to make up for a missed dose.

Drug Interactions
Instruct patients to notify their healthcare provider prior to starting any new medication, including over-the-counter drugs *[see Drug Interactions (7)]*.

Storage
Advise patients to store FIRDAPSE at 68ºF to 77ºF (20ºC to 25ºC).

Distributed by Catalyst Pharmaceuticals, Inc., Coral Gables, FL 33134.

MEDICATION GUIDE
FIRDAPSE® (FIR-dapse)
(amifampridine)
tablets, for oral use

Read this Medication Guide before you start taking FIRDAPSE and each time you get a refill. There may be new information. This information does not take the place of talking with your doctor about your medical condition or your treatment.

What is the most important information I should know about FIRDAPSE?
FIRDAPSE can cause seizures.

- You could have a seizure even if you never had a seizure before.
- **Do not** take FIRDAPSE if you have ever had a seizure.

Stop taking FIRDAPSE and call your doctor right away if you have a seizure while taking FIRDAPSE.

What is FIRDAPSE?
FIRDAPSE is a prescription medicine used to treat Lambert-Eaton myasthenic syndrome (LEMS) in adults.
It is not known if FIRDAPSE is safe or effective in children.

Do not take FIRDAPSE if you:

- have ever had a seizure.
- are allergic to amifampridine phosphate, or another aminopyridine.

Before you take FIRDAPSE, tell your doctor about all of your medical conditions. including if you:

- are taking another aminopyridine, such as compounded 3,4-diaminopyridine (3,4-DAP)
- have had a seizure
- have kidney problems
- liver problems
- are pregnant or plan to become pregnant. It is not known if FIRDAPSE will harm your unborn baby. You and your doctor will decide if you should take FIRDAPSE while you are pregnant.
- are breastfeeding or plan to breastfeed. It is not known if FIRDAPSE passes into your breast milk. Talk to your doctor about the best way to feed your baby while taking FIRDAPSE.

Tell your doctor about all the medicines you take, including prescription and over-the-counter medicines, vitamins and herbal supplements.

How should I take FIRDAPSE?

- Take FIRDAPSE exactly as your doctor tells you to take it. Do not change your dose of FIRDAPSE.
- Do not take more than 2 tablets of FIRDAPSE at one time or more than 8 tablets in a 24-hour period.
- FIRDAPSE can be taken with or without food.
- If you miss a dose of FIRDAPSE, skip that dose and take your next dose at your next scheduled dose time. Do not double your dose to make up the missed dose.
- Do not take FIRDAPSE together with other medicines known to increase the risk of seizures.
- If you take too much FIRDAPSE, call your doctor or go to the nearest hospital emergency room right away.

What are the possible side effects of FIRDAPSE?
FIRDAPSE may cause serious side effects, including:

- **Seizures. See "What is the most important information I should know about FIRDAPSE?"**
- **Serious allergic reactions, such as anaphylaxis.** FIRDAPSE can cause serious allergic reactions. Stop taking FIRDAPSE and call your doctor right away or get emergency medical help if you have:
  - shortness of breath or trouble breathing
  - swelling of your throat or tongue
  - hives

The most common side effects of FIRDAPSE include:

- tingling around the mouth, tongue, face, fingers, toes, and other body parts

- upper respiratory infection
- stomach pain
- nausea
- diarrhea
- headache
- increased liver enzymes
- back pain
- high blood pressure
- muscle spasms

Tell your doctor if you have any side effect that bothers you or that does not go away.
These are not all the possible side effects of FIRDAPSE.
Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store FIRDAPSE?

- Store FIRDAPSE at 68ºF to 77ºF (20ºC to 25ºC).
- Safely throw away FIRDAPSE that is out of date or no longer needed.

Keep FIRDAPSE and all medicines out of the reach of children.

General Information about the safe and effective use of FIRDAPSE

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use FIRDAPSE for a condition for which it was not prescribed. Do not give FIRDAPSE to other people, even if they have the same symptoms that you have. It may harm them.
If you would like more information, talk to your doctor or pharmacist. You can ask your pharmacist or doctor for information about FIRDAPSE that is written for health professionals.

What are the ingredients in FIRDAPSE?

Active ingredient: amifampridine
Inactive ingredients: calcium stearate, colloidal silicon dioxide, and microcrystalline cellulose.

Distributed by Catalyst Pharmaceuticals, Inc., Coral Gables, FL 33134
For more information, go to www.YourCatalystPathways.com or call 1-833-422-8259
This Medication Guide has been approved by the U.S. Food and Drug Administration. Revised: 11/2018