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## REMS DOCUMENT

**Initial REMS Approval: 1/2010**

**Most Recent Modification: 11/2011**

### **NDA 22-250 AMPYRA<sup>®</sup> (dalfampridine) EXTENDED RELEASE TABLETS**

Acorda Therapeutics, Inc.  
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## **RISK EVALUATION AND MITIGATION STRATEGY (REMS)**

### **I. GOALS**

The goals of the AMPYRA REMS are:

- To inform healthcare providers about the risk of drug-associated seizures in patients treated with AMPYRA.
- To inform healthcare providers about the change of the established name from fampridine to dalfampridine.
- To inform patients about the serious risks associated with AMPYRA therapy.

### **II. REMS ELEMENTS**

#### **A. Medication Guide**

- A Medication Guide will be attached to each unit of AMPYRA and dispensed with each AMPYRA prescription in compliance with 21 CFR 208.24.

A copy of the Medication Guide is included in Appendix A.

#### **B. Communication Plan**

Acorda will implement a communication plan to support implementation of this REMS. This communication plan will comprise:

- Dear Healthcare Professional Letters to prescribers and pharmacists. The initial letters will be distributed within 60 days of approval of AMPYRA.

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Annual letters to both groups will be sent within 60 days of the anniversary date of approval for AMPYRA and every year for the next three years.

The letters are described in greater detail below.

#### Dear Prescriber Letter

The Dear Prescriber Letter will be sent by targeted mailing to educate prescribers about the proper distribution and safe use of AMPYRA. The mailing list will consist of the following professionals:

- Prescribers who wrote at least one prescription for an immunomodulator drug approved for MS within the past 2 years
- Prescribers who have written a prescription for AMPYRA
- Specialists in Pain Management and Rehabilitation (PM&R) who have treated symptoms of Multiple Sclerosis based upon ICD9 codes.

The letter will describe the following key risk messages of the REMS:

- The potential risk of seizure associated with AMPYRA. Clinical studies indicate doses greater than 10 mg twice daily may increase the risk of seizure.
- Selection of the appropriate patient population, specifically patients without a history of seizures and without moderate or severe renal impairment.
- AMPYRA (dalfampridine) has also been known as fampridine, 4-aminopyridine, or 4-AP.
- Appropriate prescribing, including the importance of discontinuing pharmacy-compounded formulations of the drug prior to initiating therapy with AMPYRA.
- Informing prescribers that a pharmacy-compounded formulation of the drug should not be substituted for AMPYRA due to the unknown pharmacokinetics of compounded formulations and the potential for overdose and increased risk of seizures.
- Informing prescribers not to take AMPYRA in addition to a compounded formulation of the drug (4-aminopyridine, 4-AP, fampridine).

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- The importance of discontinuing AMPYRA and reporting the event promptly to Acorda should a patient experience a seizure.

The mailing will also include the Prescribing Information (PI) and the Medication Guide. The letter will urge HCPs to counsel patients about the risks and benefits of AMPYRA, the importance of taking AMPYRA as prescribed, and the need to notify their HCP of all medications they are taking.

Additional PIs and Medication Guides will be available upon request through Acorda's toll free support line, the product website, or via Acorda's representatives and field-based Medical Affairs staff.

In order to ensure that HCPs remain informed of the AMPYRA REMS, the Dear Prescriber Letter will be sent annually for three years, and revised appropriately to convey pertinent updated safety information included in the label. Any known new prescribers will also be targeted. The letter may be sent earlier if new safety information becomes available for AMPYRA. The annual mailing will include the current versions of the PI and the Medication Guide.

#### Dear Pharmacist Letter

A Dear Pharmacist Letter will be provided to all pharmacies and key pharmacy organizations. The letter will serve to educate these pharmacists about the potential risks associated with substituting AMPYRA with a compounded formulation of the drug and about the change in the established name from fampridine to dalfampridine. The letter will also inform pharmacists that AMPYRA is contraindicated in patients with moderate or severe renal impairment. The mailing will also include a copy of the PI and the Medication Guide.

Prescribing Information and additional Medication Guides will be made available via Acorda's toll free support line or the product website. In order to ensure that pharmacists remain informed of the AMPYRA REMS, the Dear Pharmacist Letter will be sent annually for three years from the approval of AMPYRA, and revised appropriately to convey pertinent updated safety information included in the label. The letter may be sent earlier if new safety information becomes available. All mailings will include the current versions of the PI and the Medication Guide.

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### **C. Timetable for Submission of Assessments**

Acorda will submit REMS Assessments to FDA 18 months, 3 years and 7 years from the date of the initial approval of the AMPYRA REMS on January 22, 2010. To facilitate inclusion of as much information as possible while allowing reasonable time to prepare the submission, the reporting interval covered by each assessment should conclude no earlier than 60 days before the submission date for that assessment. Acorda will submit each assessment—so that it will be received by the FDA on or before the due date.

## FDA-Approved Patient Labeling

### MEDICATION GUIDE FOR AMPYRA<sup>®</sup> (am-PEER-ah) (dalfampridine) Extended Release Tablets

Read this Medication Guide before you start taking AMPYRA.

Read this Medication Guide before you start taking AMPYRA 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 AMPYRA?**

AMPYRA can cause seizures.

- Your chance of having a seizure is higher if you take too much AMPYRA or if you have kidney problems.
- Do not take AMPYRA if you have ever had a seizure.
- Before taking AMPYRA tell your doctor if you have kidney problems.
- Take AMPYRA exactly as prescribed by your doctor. See “How do I take AMPYRA?”

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

#### **What is AMPYRA?**

AMPYRA is a prescription medicine used to help improve walking in people with multiple sclerosis (MS). This was shown by an increase in walking speed.

It is not known if AMPYRA is safe or effective in children less than 18 years of age.

#### **Who should not take AMPYRA?**

**Do not take AMPYRA if you:**

- have ever had a seizure

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- have certain types of kidney problems

### **What should I tell my doctor before taking AMPYRA?**

#### **Before you take AMPYRA, tell your doctor if you:**

- have any other medical conditions
- are taking compounded 4-aminopyridine (fampridine, 4-AP)
- are pregnant or plan to become pregnant. It is not known if AMPYRA will harm your unborn baby. You and your doctor will decide if you should take AMPYRA while you are pregnant
- are breast-feeding or plan to breast-feed. It is not known if AMPYRA passes into your breast milk. You and your doctor should decide if you will take AMPYRA or breast-feed. You should not do both.

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

Know the medicines you take. Keep a list of them and show it to your doctor and pharmacist when you get a new medicine.

### **How should I take AMPYRA?**

- Take AMPYRA exactly as your doctor tells you to take it. Do not change your dose of AMPYRA.
- Take one tablet of AMPYRA 2 times each day about 12 hours apart. Do not take more than 2 tablets of AMPYRA in a 24-hour period.
- Take AMPYRA tablets whole. Do not break, crush, chew or dissolve AMPYRA tablets before swallowing. If you cannot swallow AMPYRA tablets whole, tell your doctor.
- AMPYRA is released slowly over time. If the tablet is broken, the medicine may be released too fast. This can raise your chance of having a seizure.
- AMPYRA can be taken with or without food.
- If you miss a dose of AMPYRA, do not make up the missed dose. Do not take 2 doses at the same time. Take your next dose at your regular scheduled time.
- If you take too much AMPYRA, call your doctor or go to the nearest hospital emergency room right away.
- Do not take AMPYRA together with other aminopyridine medications, including compounded 4-AP (sometimes called 4-aminopyridine, fampridine).

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## **What are the possible side effects of AMPYRA?**

### **AMPYRA may cause serious side effects, including:**

- Kidney or bladder infections

See “What is the most important information I should know about AMPYRA?”

The most common side effects of AMPYRA include:

- urinary tract infection
- trouble sleeping (insomnia)
- dizziness
- headache
- nausea
- weakness
- back pain
- problems with balance
- multiple sclerosis relapse
- burning, tingling or itching of your skin
- irritation in your nose and throat
- constipation
- indigestion
- pain in your throat

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 AMPYRA. For more information, ask your doctor or pharmacist.

Call your doctor for medical advice about side effects. You may report side effects to the FDA at 1-800-FDA-1088.

### **How should I store AMPYRA?**

- Store AMPYRA at 59°F to 86°F (15°C to 30°C).
- Safely throw away AMPYRA that is out of date or no longer needed.

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

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## **General Information about the safe and effective use of AMPYRA**

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use AMPYRA for a condition for which it was not prescribed. Do not give AMPYRA to other people, even if they have the same symptoms that you have. It may harm them.

This Medication Guide summarizes the most important information about AMPYRA. If you would like more information, talk with your doctor. You can ask your pharmacist or doctor for information about AMPYRA that is written for health professionals.

For more information, go to [www.AMPYRA.com](http://www.AMPYRA.com) or call 1-800-367-5109.

## **What are the ingredients in AMPYRA?**

**Active ingredient:** dalfampridine (previously called fampridine)

**Inactive ingredients:** colloidal silicon dioxide, hydroxypropyl methylcellulose, magnesium stearate, microcrystalline cellulose, polyethylene glycol, and titanium dioxide.

Distributed by: Acorda Therapeutics, Inc.

Hawthorne, NY 10532

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*This Medication Guide has been approved by the U.S. Food and Drug Administration.*

AMPYRA<sup>®</sup> is a registered trademark of Acorda Therapeutics, Inc.

Manufactured for Acorda under license from Elan Pharma International Ltd. (EPIL), Ireland, utilizing EPIL's MatriX Drug Absorption System (MXDAS<sup>®</sup> technology).

MXDAS<sup>®</sup> is a registered trademark of Elan Pharma International Ltd. (EPIL).

U.S. Patent Nos.: US 5,540,938 and US 5,370,879

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