DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 022250/S-004

SUPPLEMENT APPROVAL
ACKNOWLEDGE REMS ASSESSMENT
REMOVE REMS ELEMENT

Acorda Therapeutics
Attention: Brian A. Walter, PhD
Vice President, Regulatory Affairs
420 Saw Mill River Road
Ardsley, NY 10502

Dear Dr. Walter:

Please refer to your Supplemental New Drug Application (sNDA) dated January 20, 2012, received January 20, 2012, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Ampyra (dalfampridine) Extended Release Tablets.

We acknowledge receipt of your amendments dated February 15, 2012, April 18, 2012, and July 17, 2012, and of your risk evaluation and mitigation strategy (REMS) assessment dated July 21, 2011. After consultation between the Office of Surveillance and Epidemiology and the Office of New Drugs, we found the REMS assessment to be complete.

This "Prior Approval" supplemental new drug application proposes to modify the approved REMS and to eliminate the requirement for the Medication Guide as an element of the approved Ampyra (dalfampridine) REMS. It also proposes to revise the Ampyra (dalfampridine) labeling to inform prescribers about the importance of estimating creatinine clearance before initiating treatment with Ampyra and to add information about the postmarketing experience with Ampyra.

We have completed our review of this supplemental application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed, agreed-upon labeling text.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Content of labeling must be identical to the enclosed labeling (text for the package insert, Medication

Guide) with the addition of any labeling changes in pending "Changes Being Effected" (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

Information on submitting SPL files using eLIST may be found in the guidance for industry titled "SPL Standard for Content of Labeling Technical Qs and As" at http://www.fda.gov/downloads/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible via publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications for this NDA, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in MS Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes and annotate each change. To facilitate review of your submission, provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

We request that the labeling approved today be available on your website within 10 days of receipt of this letter.

CARTON AND IMMEDIATE CONTAINER LABELS

Submit final printed carton and container labels that are identical to the carton and immediate container labels submitted on July 17, 2012, as soon as they are available, but no more than 30 days after they are printed.

Please submit these labels electronically according to the guidance for industry titled "Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (June 2008)." Alternatively, you may submit 12 paper copies, with 6 of the copies individually mounted on heavy-weight paper or similar material. For administrative purposes, designate this submission "**Product Correspondence – Final Printed Carton and Container Labels for approved NDA 022250/S-004**." Approval of this submission by FDA is not required before the labeling is used.

RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS

The REMS for Ampyra (dalfampridine) was originally approved on January 22, 2010, and the most recent REMS modification was approved on November 17, 2011. The REMS consists of a Medication Guide, communication plan, and a timetable for submission of assessments of the REMS.

Your proposed modifications to the REMS consist of the following:

- a revised Medication Guide to change the name of the manufacturer from Elan Pharma International Ltd. (EPIL) to Alkermes Pharma Ireland Limited (APIL)
- a revised REMS document that:
    - provides for sending the Dear Prescriber Letter to specialists in Physical Medicine and Rehabilitation rather than Pain Management and Rehabilitation
    - indicates that the Dear Prescriber Letter will communicate (1) the importance to counsel patients on the necessity to adhere to the prescribing guidelines and approved dosing schedule for Ampyra, and (2) a description of the post-marketing seizure experience.
- an updated Dear Prescriber Letter and Dear Pharmacist Letter that (1) include post-marketing seizure experience, including case counts and characteristics of patients in whom seizures occurred, (2) revise the term "specialty pharmacies" to "closed pharmacy distribution network", and (3) clarify chemical names for the compounded formulation (i.e., 4-aminopyridine, 4-AP, fampridine).

Your proposed modification to the REMS also consists of eliminating the requirement for the Medication Guide as an element of the REMS.

We have determined that maintaining the Medication Guide as part of the approved labeling is adequate to address the serious and significant public health concern and meets the standard in 21 CFR 208.1. Therefore, it is no longer necessary to include the Medication Guide as an element of the approved REMS to ensure that the benefits of Ampyra (dalfampridine) outweigh the risks.

Your proposed modified REMS, submitted on July 17, 2012, and appended to this letter, is approved.

The modified REMS consists of a communication plan and a timetable for submission of assessments of the REMS.

We remind you that the Medication Guide will continue to be part of the approved labeling for Ampyra (dalfampridine) in accordance with 21 CFR 208.

The timetable for submission of assessments of the REMS will remain the same as that approved on January 22, 2010.

The revised REMS assessment plan should include, but is not limited to, the following:

1. A summary of all reported seizures with analysis of adverse event reporting by prescriber type. We request that you submit all adverse reports of seizures as expedited reports.
2. An evaluation of healthcare providers' understanding of the serious risks of Ampyra (dalfampridine).
3. Specification of measures that would be taken to increase awareness if surveys of HCPs indicate that provider awareness is not adequate.
4. Date(s) and method(s) of distribution of the Dear Prescriber and Dear Pharmacist letters.

5. The number of recipients of the Dear Prescriber and Dear Pharmacist letters at each distribution.
6. The number of returned mailings for each distribution.
7. A list of all documents included in each distribution, including the modification date of each document.
8. Based on the information submitted, an assessment and conclusion of whether the REMS is meeting its goals, and whether modifications to the REMS are needed.
9. Information on the status of any postapproval study or clinical trial required under section 505(o)(3) or otherwise undertaken to investigate a safety issue. With respect to any such postapproval study, you must include the status of such study, including whether any difficulties completing the study have been encountered. With respect to any such postapproval clinical trial, you must include the status of such clinical trial, including whether enrollment has begun, the number of participants enrolled, the expected completion date, whether any difficulties completing the clinical trial have been encountered, and registration information with respect to requirements under subsections (i) and (j) of section 402 of the Public Health Service Act. You can satisfy these requirements in your REMS assessments by referring to relevant information included in the most recent annual report required under section 506B and 21 CFR 314.81(b)(2)(vii) and including any material or significant updates to the status information since the annual report was prepared. Failure to comply with the REMS assessments provisions in section 505-1(g) could result in enforcement action.

In addition to the assessments submitted according to the timetable included in the approved REMS, you must submit a REMS assessment and may propose a modification to the approved REMS when you submit a supplemental application for a new indication for use as described in section 505-1(g)(2)(A) of FDCA.

If the assessment instruments and methodology for your REMS assessments are not included in the REMS supporting document, or if you propose changes to the submitted assessment instruments or methodology, you should update the REMS supporting document to include specific assessment instrument and methodology information at least 90 days before the assessments will be conducted. Updates to the REMS supporting document may be included in a new document that references previous REMS supporting document submission(s) for unchanged portions. Alternatively, updates may be made by modifying the complete previous REMS supporting document, with all changes marked and highlighted. Prominently identify the submission containing the assessment instruments and methodology with the following wording in bold capital letters at the top of the first page of the submission:

NDA/BLA 022250 REMS CORRESPONDENCE
(insert concise description of content in bold capital letters, e.g.,
UPDATE TO REMS SUPPORTING DOCUMENT - ASSESSMENT METHODOLOGY)

An authorized generic drug under this NDA must have an approved REMS prior to marketing. Should you decide to market, sell, or distribute an authorized generic drug under this NDA, contact us to discuss what will be required in the authorized generic drug REMS submission.

Prominently identify the submission containing the REMS assessments or proposed modifications of the REMS with the following wording in bold capital letters at the top of the first page of the submission as appropriate:

NDA 022250 REMS ASSESSMENT

NEW SUPPLEMENT FOR NDA 022250
PROPOSED REMS MODIFICATION
REMS ASSESSMENT

NEW SUPPLEMENT (NEW INDICATION FOR USE)
FOR NDA 022250
REMS ASSESSMENT
PROPOSED REMS MODIFICATION (if included)

If you do not submit electronically, please send 5 copies of REMS-related submissions.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit the following, in triplicate, (1) a cover letter requesting advisory comments, (2) the proposed materials in draft or mock-up form with annotated references, and (3) the package insert(s) to:

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion (OPDP)
5901-B Ammendale Road
Beltsville, MD 20705-1266

You must submit final promotional materials and package insert(s), accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 314.81(b)(3)(i)]. Form FDA 2253 is available at http://www.fda.gov/opacom/morechoices/fdaforms/cder.html; instructions are provided on page 2 of the form. For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Nicole L. Bradley, PharmD, Regulatory Project Manager, at (301) 796-1930.

Sincerely,

{See appended electronic signature page}

Russell G. Katz, MD
Director
Division of Neurology Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

ENCLOSURES:
Content of Labeling
Carton and Container Labeling
REMS

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

ERIC P BASTINGS on behalf of RUSSELL G KATZ
07/20/2012