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RESEARCH**

APPLICATION NUMBER:

22-250s000

OTHER ACTION LETTERS



NDA 22-250

FILING COMMUNICATION

Acorda Therapeutics, Inc.
Attention: Brian A. Walter, Ph.D.
Senior Director, Regulatory Affairs
15 Skyline Drive
Hawthorne, NY 10532

Dear Dr. Walter:

Please refer to your new drug application (NDA) dated April 22, 2009, received April 22, 2009, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act, for fampridine Sustained-Release (SR) tablets, 10 mg.

We also refer to your submissions dated May 8, 15, 20, and 28, and June 22 and 24, 2009.

We are reviewing your application according to the processes described in the Guidance for Review Staff and Industry: Good Review Management Principles and Practices for PDUFA Products. Therefore, we have established internal review timelines as described in the guidance, which includes the timeframes for FDA internal milestone meetings (e.g., filing, planning, mid-cycle, team and wrap-up meetings). Please be aware that the timelines described in the guidance are flexible and subject to change based on workload and other potential review issues (e.g., submission of amendments). We will inform you of any necessary information requests or status updates following the milestone meetings or at other times, as needed, during the process. If major deficiencies are not identified during the review, we plan to communicate proposed labeling and, if necessary, any postmarketing commitment requests by October 1, 2008. During our filing review of your application, we identified the following potential review issues:

NONCLINICAL

1. (b) (4) potentially genotoxic impurities in the drug substance and/or drug product have been identified: (b) (4)

We acknowledge that you have submitted *in vitro* genotoxicity assays (Ames, chromosomal aberration in CHO cells) for (b) (4) and that these assays adequately address the genotoxic potential of this impurity. We also acknowledge that you have provided in Amendment N0012 (June 22, 2009) Derek for Windows reports for (b) (4) of the impurities listed, including (b) (4). However, since we do not consider a negative result in a

Derek report definitive for regulatory purposes, these reports do not adequately address our concern regarding the genotoxic potential of the (b) (4) other impurities assessed.

Therefore, each of the remaining (b) (4) impurities identified as potentially genotoxic would need to be either reduced to a maximum daily intake of $\leq 1.5 \mu\text{g}/\text{day}$ or determined to be negative when tested directly in *in vitro* genotoxicity assays (i.e., an *in vitro* bacterial reverse mutation assay and either an *in vitro* cytogenetic assay in mammalian cells or an *in vitro* mouse lymphoma tk assay (with colony sizing)) (cf., Guidance for Industry—Q3A Impurities in New Drug Substances [February 2003, ICH, Revision 1], and Guidance for Industry—Q3B(R) Impurities in New Drug Products [November 2003, ICH, Revision 1]).

2. You have not provided sufficient data to support your proposed specification limit of (b) (4) for the (b) (4) impurity. The specification limit of (b) (4) exceeds the 0.5% qualification threshold (cf. Guidance for Industry—Q3B(R) Impurities in New Drug Products [November 2003, ICH, Revision 1]). As noted, the *in vitro* genotoxicity assays adequately address the genotoxic potential of this impurity; however, to qualify an impurity in a drug product intended for chronic use we generally also require a 3-month repeat-dose toxicity study and an embryofetal study, each in a single species.

SAFETY

1. Please explain how you defined abnormal renal function for your analysis of AEs that is summarized in ISS table 32.2.2.4.
1. A search of the AE data set identified one pregnancy during fampridine trials. Did you identify any other pregnancies in fampridine trials? If so, please provide details for these events.
2. In the Summary of Clinical Safety you state that no indications have been found of abuse potential of fampridine. How did you assess the abuse potential of fampridine?
3. Please provide additional details of the overdose for patient #10 from study SCI-F301. You should include how much fampridine the patient took, describe the circumstances surrounding the event (why the overdose occurred), report the duration of associated symptoms, and report any other pertinent information about the event.

We are providing the above comments to give you preliminary notice of potential review issues. Our filing review is only a preliminary evaluation of the application and is not indicative of deficiencies that may be identified during our review. Issues may be added, deleted, expanded upon, or modified as we review the application.

If you have not already done so, you must submit the content of labeling [21 CFR 314.50(l)(1)(i)] in structured product labeling (SPL) format as described at

<http://www.fda.gov/oc/datacouncil/spl.html>. The content of labeling must be in the Prescribing Information (physician labeling rule) format.

Please respond only to the above requests for additional information. While we anticipate that any response submitted in a timely manner will be reviewed during this review cycle, such review decisions will be made on a case-by-case basis at the time of receipt of the submission.

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication in pediatric patients unless this requirement is waived, deferred, or inapplicable.

Because fampridine for this indication has orphan drug designation, you are exempt from this requirement.

If you have any questions, call James H. Reese, Ph.D., RAC, Senior Regulatory Health Project Manager, at 301-796-1136.

Sincerely,

{See appended electronic signature page}

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

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

/s/

Russell Katz

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