DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 022321/S-010

SUPPLEMENT APPROVAL

AlPharma Pharmaceuticals LLC
c/o: Pfizer Inc.
235 East 42nd Street
New York, NY 10017

Attention: Lisa Malandro, M.B.A.
Director, Worldwide Regulatory Affairs

Dear Ms. Malandro:

Please refer to your Supplemental New Drug Application (sNDA) dated and received October 23, 2012, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for EMBEDA (morphine sulfate and naltrexone hydrochloride extended-release) Capsules.

We acknowledge receipt of your amendment dated March 28, 2013.

This supplemental new drug application proposes modifications to the approved risk evaluation and mitigation strategy (REMS) for EMBEDA.

We have completed our review of this supplemental application, as amended. It is approved, effective on the date of this letter.

RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS

The REMS for EMBEDA was originally approved on August 13, 2009, and modified on July 9, 2012. The REMS consists of a Medication Guide, elements to assure safe use, and a timetable for submission of assessments of the REMS. Your proposed modifications to the REMS consist of:

- Revisions to *Section VI. Specific Drug information for ER/LA Opioid Analgesic Products* of the FDA Blueprint
- Revisions to the REMS Website, including the landing page and the webpage listing covered products under the REMS program
- Revisions to individual product Medication Guides for relevant drugs
- Revision to the REMS document to remove ANDA holders from the Timetable for Submission of Assessments

Your proposed modified REMS, submitted on March 28, 2013, and appended to this letter, is approved.

The timetable for submission of assessments of the REMS will remain the same as that approved on July 9, 2012. There are no changes to the REMS assessment plan described in our July 9, 2012 letter.

This REMS uses a single, shared system for the elements to assure safe use and the REMS assessments. This single, shared system, known as the ER/LA Opioid Analgesic REMS Program, currently includes the products listed in Appendix 1. Other products may be added in the future if additional NDAs or ANDAs are approved.

We remind you that section 505-1(f)(8) of FDCA prohibits holders of an approved covered application with elements to assure safe use from using any element to block or delay approval of an application under section 505(b)(2) or (j). A violation of this provision in 505-1(f) could result in enforcement action.

The requirements for assessments of an approved REMS under section 505-1(g)(3) include with respect to each goal included in the strategy, an assessment of the extent to which the approved strategy, including each element of the strategy, is meeting the goal or whether one or more such goals or such elements should be modified.

In addition to the assessments submitted according to the timetable included in the approved REMS, you 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 the 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 022321 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 022321 REMS ASSESSMENT

NEW SUPPLEMENT FOR NDA 022321
PROPOSED REMS MODIFICATION

NEW SUPPLEMENT (NEW INDICATION FOR USE)
FOR NDA 022321
REMS ASSESSMENT
PROPOSED REMS MODIFICATION (if included)

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

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 Lisa E. Basham, Senior Regulatory Health Project Manager, at (301) 796-1175.

Sincerely,

{See appended electronic signature page}

Judith A. Racoosin, M.D., M.P.H.
Deputy Director for Safety
Division of Anesthesia, Analgesia,
and Addiction Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

ENCLOSURE:
REMS

Appendix 1 List of applications

NDA 021260	AVINZA (morphine sulfate) extended-release capsules and its generic equivalent
NDA 021306	BUTRANS (buprenorphine) Transdermal System for transdermal administration
NDA 006134	DOLOPHINE (methadone hydrochloride) tablets and its generic equivalents
ANDA 087997	Methadone Oral Solution and its generic equivalents ANDA 087393 Methadone Oral Solution and its generic equivalents ANDA 089897 Methadone Oral Concentrate
NDA 019813	DURAGESIC (Fentanyl Transdermal System) for transdermal administration and its generic equivalents
NDA 022321	EMBEDA (morphine sulfate and naltrexone hydrochloride) extended- release capsules
NDA 021217	EXALGO (hydromorphone HCl) Extended-Release Tablets
NDA 020616	KADIAN (morphine sulfate) extended-release capsules and its generic equivalent
NDA 019516	MS CONTIN (morphine sulfate) controlled-release tablets and its generic equivalents
NDA 200533	NUCYNTA ER (tapentadol) extended-release oral tablets
NDA 201655	OPANA ER (oxymorphone hydrochloride) Extended-Release tablets
NDA 021610	OPANA ER (oxymorphone hydrochloride) Extended-Release tablets and its generic equivalents
NDA 022272	OXYCONTIN (oxycodone hydrochloride controlled-release) Tablets

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

/s/

JUDITH A RACOOSIN
04/15/2013