

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

21-610

21-611

APPROVAL LETTER

AP Letter
6/22/06



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-610

Endo Pharmaceuticals
100 Endo Blvd.
Chadds Ford, PA 19317

Attention: Robert A. Barto
Director, Regulatory Affairs

Dear Mr. Barto:

Please refer to your new drug application (NDA) dated December 19, 2002, received December 19, 2002, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for OPANA (Oxymorphone Hydrochloride) Extended-Release Tablets, 5 mg, 10 mg, 20 mg, and 40 mg.

We acknowledge receipt of your submissions dated January 17 and 24, February 4, 11, 13, and 20, April 15, July 8, 17, 22, and 31, August 6, 7, 13, 14, 19, 20, 21, 27, and 29, September 3, 4, 8, 11, 12, 15, 17, and 30, October 6, 8, 20, and 24, December 8, and 19, 2003, February 17 and March 24, 2004, December 22, 2005, and February 20, March 22, 24, and 28, April 3, May 8, 23, 26, and 31, and June 2, 9, 16, and 21, 2006.

The December 22, 2005, submission constituted a complete response to our October 15, 2003, action letter.

This new drug application provides for the use of OPANA (Oxymorphone Hydrochloride) Extended-Release Tablets for the relief of moderate-to-severe pain in patients requiring continuous, around-the-clock opioid treatment for an extended period of time.

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

We have completed our review of your Risk Minimization Action Plan and have found it adequate to support marketing of OPANA (Oxymorphone Hydrochloride) Extended-Release Tablets, 5 mg, 10 mg, 20 mg, and 40 mg. We recommend that you continue to collaborate with the Agency to further define and develop the relevant elements of the RMP.

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert, text for the patient package insert, immediate container and carton labels). Marketing the product(s) with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

Please submit an electronic version of the FPL according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA*. Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no more than 30 days after it is printed. Individually mount 15 of the copies on heavy-weight paper or similar material. For administrative purposes, designate this submission "**FPL for approved NDA 21-610.**" Approval of this submission by FDA is not required before the labeling is used.

All applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred. We are deferring pediatric studies for ages 0 to 17 years for this application.

Your deferred pediatric studies required under section 2 of the Pediatric Research Equity Act (PREA) are considered required postmarketing study commitments. The status of this postmarketing study shall be reported annually according to 21 CFR 314.81. This commitment is listed below.

1. Deferred pediatric study under PREA for the treatment moderate to severe pain in patients requiring continuous, around-the-clock opioid treatment for an extended period of time in pediatric patients ages 0 to 17.

Final Report Submission: June 30, 2011

Submit final study reports to this NDA. For administrative purposes, all submissions related to this/these pediatric postmarketing study commitment(s) must be clearly designated "**Required Pediatric Study Commitments**".

Submit clinical protocols to your IND for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all study final reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii), you should include a status summary of each commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies, number of patients entered into each study. All submissions, including supplements, relating to these postmarketing study commitments must be prominently labeled "**Postmarketing Study Commitment Protocol**", "**Postmarketing Study Commitment Final Report**", or "**Postmarketing Study Commitment Correspondence.**"

In addition, submit three copies of the introductory promotional materials that you propose to use for this product. Submit all proposed materials in draft or mock-up form, not final print. Send one copy to this division and two copies of both the promotional materials and the package insert directly to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications
5901-B Ammendale Road
Beltsville, MD 20705-1266

Please submit one market package of the drug product when it is available.

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We have not completed validation of the regulatory methods. However, we expect your continued cooperation to resolve any problems that may be identified.

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 Basham, Regulatory Project Manager, at (301) 796-1175.

Sincerely,

{See appended electronic signature page}

Bob Rappaport, MD
Director
Division of Anesthesia, Analgesia and
Rheumatology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

Enclosure

**Appears This Way
On Original**



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The December 22, 2005, submission constituted a complete response to our October 15, 2003, action letter.

This new drug application provides for the use of OPANA (Oxymorphone Hydrochloride) Tablets for relief of moderate to severe acute pain where the use of an opioid is appropriate.

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

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert, immediate container and carton labels). Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and unapproved new drug.

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Your deferred pediatric studies required under section 2 of the Pediatric Research Equity Act (PREA) are considered required postmarketing study commitments. The status of this postmarketing study shall be reported annually according to 21 CFR 314.81. This commitment is listed below.

1. Deferred pediatric study under PREA for the treatment of moderate to severe acute pain where the use of an opioid is appropriate in pediatric patients ages 0 to 17.

Final Report Submission: June 30, 2011

Submit final study reports to this NDA. For administrative purposes, all submissions related to this/these pediatric postmarketing study commitment(s) must be clearly designated "**Required Pediatric Study Commitments**".

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{See appended electronic signature page}

Bob Rappaport, MD
Director
Division of Anesthesia, Analgesia and
Rheumatology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

Enclosure