ANDA 079046

Actavis South Atlantic LLC
Attention: Monique Weitz
Senior Director, Regulatory Affairs
12800 N.W. 2nd Street
Suite 190
Sunrise, FL 33325

Dear Madam:

This is in reference to your abbreviated new drug application (ANDA) dated June 8, 2007,[1] submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (the Act), for Oxymorphone Hydrochloride Extended-release Tablets, 5 mg, 7.5 mg, 10 mg, 15 mg, 20 mg, 30 mg, and 40 mg.

Reference is made to your amendments dated February 8, March 19, May 2, May 29, June 24, June 30, August 14, August 15, 2008; April 2, August 11, September 3, 2009; January 29, June 14, September 3, September 14, November 2, November 12, and November 15, 2010. Reference is also made to your patent amendments dated March 5, April 11, July 25, 2008; and November 19, 2010.

We have completed the review of this ANDA, and based upon the information you have presented to date we have concluded that the drug is safe and effective for use as recommended in the submitted labeling. However, we are unable to grant final approval to your Oxymorphone Hydrochloride Extended-release Tablets, 5 mg, 10 mg, 20 mg, 30 mg, and 40 mg, at this time because of the patent issue noted below. Therefore, only your Oxymorphone Hydrochloride Extended-release Tablets, 7.5 mg and 15 mg, are **approved**. The 5 mg, 10 mg, 20 mg, 30 mg, and 40 mg strengths are **tentatively approved**.

The RLD upon which you have based your ANDA, Opana ER Tablets of Endo Pharmaceuticals, Inc. (Endo), is subject to periods of patent protection. The following patents and their expiration dates are currently listed in the agency's publication titled

[1] This ANDA was not officially received until December 5, 2007, at which time it provided for the 5 mg, 10 mg, 20 mg, and 40 mg strengths only. The 7.5 mg and 15 mg strengths were submitted in an amendment dated May 29, 2008. The 30 mg strength was submitted in an amendment dated June 30, 2008.

Approved Drug Products with Therapeutic Equivalence Evaluations (the “Orange Book”):

U.S. Patent Number	Expiration Date
5,662,933 (the '933 patent)	September 9, 2013
5,958,456 (the '456 patent)	September 9, 2013
7,276,250 (the '250 patent)	February 4, 2023

With respect to each of these patents, your ANDA contains paragraph IV certifications under section 505(j)(2)(A)(vii)(IV) of the Act stating that each patent is invalid, unenforceable, or will not be infringed by your manufacture, use, or sale of Oxymorphone Hydrochloride Extended-release Tablets, 5 mg, 7.5 mg, 10 mg, 15 mg, 20 mg, 30 mg, and 40 mg, under this ANDA. Section 505(j)(5)(B)(iii) of the Act provides that approval of an ANDA shall be made effective immediately, unless an action was brought against Actavis South Atlantic LLC (Actavis South) for infringement of one or more of these patents that were the subject of the paragraph IV certifications. You notified the agency that Actavis South complied with the requirements of section 505(j)(2)(B) of the Act, and that litigation for infringement of the '456 patent was brought against Actavis South in the United States District Court for the District of Delaware [Endo Pharmaceuticals, Inc. and Penwest Pharmaceutical Co. v. Actavis South Atlantic LLC, Civil Action No. 08-3482]. You have notified the agency that on February 26, 2009, Actavis South Atlantic LLC entered into a settlement agreement with Endo Pharmaceuticals, Inc. and Penwest Pharmaceutical Co. and the case was dismissed.

I. Approval of Oxymorphone Hydrochloride Extended-release Tablets, 7.5 mg and 15 mg

With respect to your Oxymorphone Hydrochloride Extended-release Tablets, 7.5 mg and 15 mg, we have concluded that adequate information has been presented to demonstrate that the drug is safe and effective for use as recommended in the submitted labeling. Accordingly, your Oxymorphone Hydrochloride Extended-release Tablets, 7.5 mg, and 15 mg, are approved, effective on the date of this letter. The Division of Bioequivalence has determined your Oxymorphone Hydrochloride Extended-release Tablets 7.5 mg, and 15 mg, to be bioequivalent and, therefore, therapeutically equivalent to the RLD), Endo’s Opana ER Tablets, 7.5 mg, and 15 mg. Your dissolution testing should be incorporated into the stability and quality control program using the same method proposed in your ANDA. The “interim” dissolution specifications are as follows:

Method: 500 mL of phosphate buffer, pH 4.5 at 37°C±0.5°C
Using apparatus 2 (paddle) [redacted] (b) (4) at 50 rpm.

Specifications: 1 hr: [redacted] (b) (4)
4 hr:
6 hr:

These "interim" dissolution test(s) and tolerances should be finalized by submitting dissolution data from the first three production size batches. These data should be submitted as a "Special Supplement – Changes Being Effected" if there are no revisions to be made to the "interim" specifications, or if the final specifications are tighter than the "interim" specifications. In all other instances, the information should be submitted in the form of a Prior Approval Supplement.

With respect to 180-day generic drug exclusivity for Oxymorphone Hydrochloride Extended-release Tablets, 7.5 mg and 15 mg, Actavis South was the first ANDA applicant to submit a substantially complete ANDA for Oxymorphone Hydrochloride Extended-release Tablets, 7.5 mg and 15 mg, with a paragraph IV certification to the patents listed above. However, your eligibility for 180-day exclusivity was forfeited under section 505(j)(5)(D)(i)(IV). Your amendment for the 7.5 mg and 15 mg strengths was filed on May 29, 2008, and your ANDA was never granted tentative approval. 30 months from the date of filing that amendment was November 29, 2010; therefore, this ANDA was not granted tentative approval within the 30-month period described in section 505(j)(5)(D)(i)(IV). We also have determined that this delay was not caused by a change in or review of the requirements for approval of this ANDA after your ANDA, or the May 29, 2008 amendment, was filed, nor was the delay caused by a related citizen petition[2] that would extend the 30-month period as described in section 505(q)(1)(G) of the Act. We therefore conclude that the 180-day exclusivity period described in section 505(j)(5)(B)(iv) of the Act for Oxymorphone Hydrochloride Extended-release Tablets, 7.5 mg and 15 mg, was forfeited by Actavis South.

Under section 506A of the Act, certain changes in the conditions described in this ANDA require an approved supplemental application before the change may be made.

Please note that if FDA requires a Risk Evaluation & Mitigation Strategy (REMS) for a listed drug, an ANDA citing that listed

[2] Although a related citizen petition (Docket No. FDA-2010-P-0243) was received May 13, 2010, and answered on Nov 8, 2010, FDA has reviewed the record of your ANDA and has determined that issues unrelated to those raised in the petition were the cause of the delay.

drug also will be required to have a REMS. See section 505-1(i) of the Act.

Postmarketing reporting requirements for this ANDA are set forth in 21 CFR 314.80-81 and 314.98. The Office of Generic Drugs should be advised of any change in the marketing status of this drug.

Promotional materials may be submitted to FDA for comment prior to publication or dissemination. Please note that these submissions are voluntary. If you desire comments on proposed launch promotional materials with respect to compliance with applicable regulatory requirements, we recommend you submit, in draft or mock-up form, two copies of both the promotional materials and package insert(s) 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

We call your attention to 21 CFR 314.81(b)(3) which requires that all promotional materials be submitted to the Division of Drug Marketing, Advertising, and Communications with a completed Form FDA 2253 at the time of their initial use.

You have been requested to provide information after the ANDA has been approved. Any information submitted to meet the conditions requested in this letter is considered a "Post Approval Commitment Response." To alert the Office of Generic Drug staff to the fact that you are providing post approval commitment information, please designate your submission in your cover letter as "POST APPROVAL COMMITMENT RESPONSE."

As soon as possible, but no later than 14 days from the date of this letter, submit, using the FDA automated drug registration and listing system (eLIST), the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format, as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm, that is identical in content to the approved labeling (including the package insert, and any patient package insert and/or Medication Guide that may be required). 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/U_CM072392.pdf The SPL will be accessible via publicly available labeling repositories.

II. Tentative Approval of Oxymorphone Hydrochloride Extended-release Tablets, 5 mg, 10 mg, 20 mg, 30 mg, and 40 mg

Your Oxymorphone Hydrochloride Extended-release Tablets, 5 mg, 10 mg, 20 mg, 30 mg, and 40 mg, are **tentatively approved**. This determination is based upon information available to the agency at this time (i.e., information in your ANDA and the status of current good manufacturing practices (cGMPs) of the facilities used in the manufacturing and testing of the drug product) and is therefore subject to change on the basis of new information that may come to our attention.

We are unable to grant final approval to your Oxymorphone Hydrochloride Extended-release Tablets, 5 mg, 10 mg, 20 mg, 30 mg, and 40 mg, at this time because prior to the submission of your ANDA, another applicant submitted an ANDA providing for Oxymorphone Hydrochloride Extended-release Tablets, 5 mg, 10 mg, 20 mg, 30 mg, and 40 mg, and containing a paragraph IV certification to the '933, '456, and '250 patents. Your ANDA insofar as these strengths will be eligible for final approval on the date that is 180 days after the date the agency receives notice, with respect to the other ANDA, of the commercial marketing date identified in section 505(j)(5)(B)(iv) of the Act.

To reactivate your ANDA prior to final approval of the 5 mg, 10 mg, 20 mg, 30 mg, and 40 mg strengths, please submit a "***MINOR AMENDMENT TO ORIGINAL #2 – FINAL APPROVAL REQUESTED***" 90 days prior to the date you believe that your ANDA will be eligible for final approval. This amendment should provide the legal/regulatory basis for your request for final approval and should include a copy of a court decision, or a settlement or licensing agreement, as appropriate. It should also identify changes, if any, in the conditions under which the ANDA was tentatively approved, i.e., updated information such as final-printed labeling, chemistry, manufacturing, and controls data as appropriate. This amendment should be submitted even if none of these changes were made, and it should be designated clearly in your cover letter as a ***MINOR AMENDMENT TO ORIGINAL #2 – FINAL APPROVAL REQUESTED***.

In addition to the amendment requested above, the agency may request at any time prior to the date of final approval that you

submit an additional amendment containing the requested information. Failure to submit either or, if requested, both amendments may result in rescission of the tentative approval status of your ANDA, or may result in a delay in the issuance of the final approval letter.

Any significant changes in the conditions outlined in this ANDA as well as changes in the status of the manufacturing and testing facilities' compliance with current good manufacturing practices (cGMPs) are subject to agency review before final approval of the application will be made. Such changes should be categorized as representing either “major” or “minor” changes to Original #2, and they will be reviewed according to OGD policy in effect at the time of receipt. The submission of multiple amendments prior to final approval may also result in a delay in the issuance of the final approval letter.

This drug product may not be marketed without final agency approval under section 505 of the Act. The introduction or delivery for introduction into interstate commerce of this drug product before the final approval date is prohibited under section 301 of the Act. Also, until the agency issues the final approval letter, this drug product will not be deemed to be approved for marketing under section 505 of the Act, and will not be listed in the “Orange Book.”

For further information on the status of this application, or prior to submitting additional amendments, please contact Thomas Hinchliffe, Pharm.D., Project Manager, at (240) 276-8433.

Sincerely yours,

{See appended electronic signature page}

Keith Webber, Ph.D.
Deputy Director
Office of Pharmaceutical Science
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/

KEITH O WEBBER
12/13/2010