



ANDA 203506

**ANDA APPROVAL**

Ranbaxy Inc.  
U.S. Agent For: Sun Pharmaceutical Industries Limited  
600 College Road East, Suite 2100  
Princeton, NJ 08540  
Attention: Sameer Manan  
Director, Regulatory Affairs

Dear Sir:

This is in reference to your abbreviated new drug application (ANDA) dated November 8, 2011, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (FDCA), for Oxymorphone Hydrochloride Extended-release Tablets, 5 mg, 7.5 mg, 10 mg, 15 mg, 20 mg, 30 mg and 40 mg.

Reference is also made to the Complete Response letter issued by this office on August 1, 2013, and to your amendments dated November 18, 2013; January 16, April 30, and August 21, 2014.

We have completed the review of this ANDA and 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 the ANDA is approved, effective on the date of this letter. The Division of Bioequivalence has determined your Oxymorphone Hydrochloride Extended-release Tablets, 5 mg, 7.5 mg, 10 mg, 15 mg, 20 mg, 30 mg and 40 mg, to be bioequivalent and, therefore, therapeutically equivalent to the reference listed drug (RLD), Opana ER Tablets, 5 mg, 7.5 mg, 10 mg, 15 mg, 20 mg, 30 mg and 40 mg of Endo Pharmaceuticals Inc. (Endo).

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:

Medium	pH 4.5 Phosphate Buffer	
Volume	900 mL	
Apparatus	II (Paddle)	
Speed	50 rpm	
Temperature	37°C ± 0.5°C	
Specification(s)	<u>Time (hour)</u>	<u>% Released</u>
	1 hour	(b) (4) %
	4 hours	(b) (4) %
	10 hours	NLT (b) (4) %

The “interim” dissolution test(s) and tolerances should be finalized by submitting dissolution data for the first three production size batches. Data should be submitted as a Special Supplement – Changes Being Effected when there are no revisions to the “interim” specifications or when 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.

The RLD upon which you have based your ANDA, Endo’s Opana ER Tablets, is subject to a period of patent protection. As noted in the agency's publication titled Approved Drug Products with Therapeutic Equivalence Evaluations (the “Orange Book”), U.S. Patent No. 7,276,250 (the '250 patent), is scheduled to expire on February 4, 2023.

Your ANDA contains a paragraph IV certification under section 505(j)(2)(A)(vii)(IV) of the Act stating that the '250 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. You have notified the agency that Sun Pharmaceutical Industries Limited (Sun) complied with the requirements of section 505(j)(2)(B) of the Act, and that no action for infringement was brought against Sun within the statutory 45-day period.

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

### **RISK EVALUATION AND MITIGATION STRATEGY (REMS) REQUIREMENT**

Section 505-1 of the FDCA authorizes FDA to require the submission of a risk evaluation and mitigation strategy (REMS) if FDA determines that such a strategy is necessary to ensure that the benefits of the drug outweigh the risks [section 505-1(a)]. In accordance with section 505-1(i) of FDCA, an ANDA is required to have a REMS if the applicable listed drug has an approved REMS.

The details of the REMS requirements were outlined in our REMS notification letter dated April 5, 2012. In that letter, you were also notified that in the interest of public health and to minimize the burden on the healthcare delivery system of having multiple unique REMS programs, a single, shared system should be used to implement the REMS for applicants of Extended-Release and Long-Acting (ER/LA) opioid analgesics.

Your proposed REMS, submitted August 21, 2014, and appended to this letter, is approved. The REMS consists of a Medication Guide and elements to assure safe use. The details for what should be included in joint assessments completed under the ER/LA Opioid Analgesics REMS are listed in Appendix 1.

This REMS uses a single, shared system for the elements to assure safe use and the REMS assessments. This single, shared system is known as the ER/LA Opioid Analgesics REMS. This single, shared system, known as the ER/LA Opioid Analgesics REMS Program, currently includes the products listed on the FDA REMS website available at

<http://www.fda.gov/downloads/Drugs/DrugSafety/InformationbyDrugClass/UCM348818.pdf>

Other products may be added in the future if additional NDAs or ANDAs are approved.

Under section 505-1(g)(2)(C), FDA can require the submission of a REMS assessment if FDA determines that an assessment is needed to evaluate whether the approved strategy should be modified to ensure the benefits outweigh the risks of the drug or to minimize burden on the healthcare system of complying with the REMS.

We remind you that section 505-1(f)(8) of the 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.

Prominently identify the submission containing a proposed modification of the REMS or any REMS assessments with the following wording in bold capital letters at the top of the first page of the submission:

**ANDA 203506  
REMS ASSESSMENT**

**NEW SUPPLEMENT FOR ANDA 203506  
PROPOSED REMS MODIFICATION**

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  
Office of Prescription Drug Promotion  
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 Office of Prescription Drug Promotion with a completed Form FDA 2253 at the time of their initial use.

The Generic Drug User Fee Amendments of 2012 (GDUFA) (Public Law 112-144, Title III) established certain provisions with respect to self-identification of facilities and payment of annual facility fees. Your ANDA identifies at least one facility that is subject to the self-identification requirement and payment of an annual facility fee. Self-identification must occur

by June 1 of each year for the next fiscal year. Facility fees must be paid each year by the date specified in the Federal Register notice announcing facility fee amounts. All finished dosage forms (FDFs) or active pharmaceutical ingredients (APIs) manufactured in a facility that has not met its obligations to self-identify or to pay fees when they are due will be deemed misbranded. This means that it will be a violation of federal law to ship these products in interstate commerce or to import them into the United States. Such violations can result in prosecution of those responsible, injunctions, or seizures of misbranded products. Products misbranded because of failure to self-identify or pay facility fees are subject to being denied entry into the United States.

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/UCM072392.pdf>. The SPL will be accessible via publicly available labeling repositories.

Sincerely yours,

**William P.  
Rickman -S**

For Carol A. Holquist, RPh  
Acting Deputy Director  
Office of Regulatory Operations  
Office of Generic Drugs  
Center for Drug Evaluation and Research

Digitally signed by William P. Rickman -S  
DN: c=US, o=U.S. Government, ou=HHS,  
ou=FDA, ou=People,  
0.9.2342.19200300.100.1.1=1300043242,  
cn=William P. Rickman -S  
Date: 2015.04.24 13:26:01 -04'00'

ENCLOSURE:

Appendix 1  
REMS