



ANDA 78-783

Par Pharmaceutical, Inc.  
Attention: Julie Szozda, Submissions Manager  
Regulatory Affairs  
One Ram Ridge Road  
Spring Valley, NY 10977

Dear Madam:

This is in reference to your abbreviated new drug application (ANDA) dated January 6, 2007, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (the Act), for Tramadol Hydrochloride Extended Release Tablets, 100 mg, and 200 mg.

Reference is also made to your amendments dated August 14, 2007; April 30, and June 5, 2009.

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 ANDA at this time because of the patent issue noted below. Therefore, the ANDA is **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. This letter does not address issues related to the 180-day exclusivity provisions under section 505(j)(5)(B)(iv) of the Act.

The reference listed drug (RLD) upon which you have based your ANDA, Ultram ER Tablets, 100 mg, and 200 mg, of Biovail Laboratories International, SRL, is subject to periods of patent protection. As noted in the agency's publication titled Approved Drug Products with Therapeutic Equivalence Evaluations (the "Orange Book"), U.S. Patent Nos. 6,254,887 (the '887 patent) and 7,074,430 (the '430 patent) are both scheduled to expire on May 10, 2014.

With respect to the '430 patent, the agency recognizes that this patent was late listed with respect to your ANDA and no certification is required. See 21 CFR 314.94(a)(12)(vi).

With respect to the '887 patent, your ANDA contains a paragraph IV certification under section 505(j)(2)(A)(vii)(IV) of the Act stating that the patent is invalid, unenforceable, or will not be infringed by your manufacture, use, or sale of Tramadol Hydrochloride Extended Release Tablets, 100 mg, and 200 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 is brought against Par Pharmaceutical, Inc. (Par) for infringement of the listed '887 patent. You notified the agency that Par complied with the requirements of section 505(j)(2)(B) of the Act, and litigation for infringement of the '887 patent was brought against Par in the United States District Court for the District of Delaware [Purdue Pharma Products L.P., Napp Pharmaceutical Group Ltd., Biovail Laboratories International, SRL, and Ortho-McNeil, Inc., Civil Action Nos. 07-414 and 07-666].

Therefore, final approval cannot be granted until:

1. a. the expiration of the 30-month period provided for in section 505(j)(5)(B)(iii),<sup>1</sup>
- b. the date the court decides<sup>2</sup> that the '887 patent is invalid or not infringed (see sections 505(j)(5)(B)(iii)(I), (II), and (III) of the Act), or
- c. the '887 patent has expired, and
2. The agency is assured there is no new information that would affect whether final approval should be granted.

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<sup>1</sup> Because information on the '887 patent was submitted to FDA before August 18, 2003, this reference to section 505(j)(5)(B)(iii) is to that section of the Act as in effect prior to December 8, 2003, when the Medicare Prescription Drug, Improvement and Modernization Act (MMA) (Public Law 108-173) was enacted. See MMA § 1101(c)(3).

<sup>2</sup> This decision may be either a decision of the district court or the court of appeals, whichever court is the first to decide that the patent is invalid or not infringed.

To reactivate your ANDA prior to final approval, please submit a "MINOR AMENDMENT - 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 - 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, 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 Laura Longstaff, Project Manager, at (240) 276-8566.

Sincerely yours,

*{See appended electronic signature page}*

Gary Buehler  
Director  
Office of Generic Drugs  
Center for Drug Evaluation and Research

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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.**  
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/s/

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Robert L. West  
7/8/2009 02:54:53 PM  
Deputy Director, for Gary Buehler