



ANDA 75-923

Endo Pharmaceuticals
Attention: Carol Patterson, Ph.D.
100 Endo Blvd.
Chadds Ford, PA 19317

Dear Dr. Patterson:

This is in reference to your abbreviated new drug application (ANDA) for Oxycodone Hydrochloride Extended-release Tablets, 10 mg, 20 mg, and 40 mg, which was approved on March 23, 2004, pursuant to section 505(j) of the Federal Food, Drug and Cosmetic Act (Act). The 80 mg strength was tentatively approved on the same day. Subsequently, the 80 mg strength was approved on September 29, 2004, after another applicant's 180-day generic drug exclusivity expired for that strength.

The listed drug product referenced in your application is Oxycontin (Oxycodone Hydrochloride) Extended-release Tablets of Purdue Pharma, L.P (Purdue). As you know, there are patents listed for this drug in FDA's *Approved Drug Products with Therapeutic Equivalence Evaluations* (the Orange Book). At the time your ANDA was submitted, the following patents were listed in the Orange Book.

| <u>Patent Number</u> | <u>Expiration Date</u> |
|-----------------------------|------------------------|
| 4,861,598 (the '598 patent) | August 29, 2006 |
| 4,970,075 (the '075 patent) | August 29, 2006 |
| 5,266,331 (the '331 patent) | October 26, 2007 |
| 5,549,912 (the '912 patent) | October 26, 2007 |
| 5,656,295 (the '295 patent) | October 26, 2007 |
| 5,508,042 (the '042 patent) | April 16, 2013 |

Endo submitted the first paragraph IV certification challenging the patents and thus was determined to be eligible for 180-day exclusivity for Oxycodone Hydrochloride Extended-release tablets 10 mg, 20 mg, and 40 mg, pursuant to section 505(j)(5)(B)(vi) of the Act. See the March 23, 2004 and September 29, 2004, approval letters to Endo.

Purdue sued Endo for infringement of the '912, '042, and '295 patents. You notified the Agency that on January 5, 2004, Judge Sidney H. Stein of the United States District Court for the Southern District of New York dismissed all patent claims against Endo, and declared that the '912, '042, and '295 patents are invalid, and enjoined the plaintiffs from enforcing those patents. FDA approved Endo's ANDA for Oxycodone Extended-release Tablets, 10 mg, 20 mg, and 40 mg on March 23, 2004 and the 80 mg tablets on September 29, 2004.

However, in a submission dated January 17, 2007, in which Endo changed its certifications to the '912, '042, and '295 from paragraph IV to paragraph III and requested conversion of its approval to tentative approval, Endo informed the Agency that a consent judgment was entered with respect to the '912, '042, and '295 patents on October 5, 2006, in the United States District Court for the Southern District of New York (Civil Action No. 00 Civ 8029, 01 CIV 2109, and 01 Civ. 8177). The order stated that

...the effective date of any approval of the Endo ANDA shall be no earlier than the date of the expiration of the last to expire of the Purdue Patents plus any period of exclusivity under the [F]ederal Food, Drug[,] and Cosmetic Act, 21 U.S.C. sections 301...

The court also permanently enjoined Endo “from (a) infringing the Purdue Patents, including but not limited to, making, having made, using, offering to sell, selling or importing Existing Endo Oxycodone Products pursuant to the Endo ANDA, or (b) submitting or maintaining, within the Endo ANDA, a certification regarding the Purdue Patents under 21 U.S.C. § 355(j)(2)(A)(vii)(IV) and 21 C.F.R. § 314.94(a)(12)(i)(A)(4); and (c) pursuant to 35 USC § 271(e)(4)(A)...”

Your ANDA was approved after the district court found that the patents were invalid. The statute anticipates that in some cases an ANDA may be approved before litigation concerning the listed patents is completed. Section 505(j)(5)(b)(iii). This leaves open the possibility that, as happened with these products, the approved drug products will later be found to infringe a listed patent.

Section 505(j) does not expressly provide for a change in approval status when the patent litigation results in a finding that one or more listed patents is infringed; however, provisions of the 1984 Drug Price Competition and Patent Term Restoration Act (Hatch-Waxman) codified in the Patent Code give the court hearing the patent litigation the authority to order the date of approval of an ANDA to be no earlier than the date of expiration of the infringed patent. 35 U.S.C. 271(e)(4).

When a court orders that the approval of an ANDA is not effective before a certain date, FDA may convert an approved ANDA to tentative approval status to reflect the court's order. This interpretation was upheld in November 2004, in *Teva Laboratories, Inc., v. Thompson*, 389 F.3d 1272, 1281-82 (D.C. Cir. 2004). Therefore, after consideration of the district court's October 5, 2006, consent judgment that the effective date of approval for the Endo ANDA be delayed until at least April 16, 2013, FDA is converting the final approval of Endo's Oxycodone Hydrochloride Extended-release Tablets, 10 mg, 20 mg, 40 mg, and 80 mg, including all amendments and supplements thereto, to a tentative approval. This change conforms the status of the application to the court's order.

A drug application that has an approval with a delayed effective date is not approved. Under FDA's regulations at 21 CFR 314.105 and longstanding practice, an approval with a delayed effective date is tentative. A tentative approval will not become final until FDA issues an approval letter. *Barr Labs., Inc. v. Thompson*, 238 F. Supp. 2d 236, 245-50 (D.D.C. 2002) (affirming FDA's decision that an approval with a delayed effective date is tentative).

The agency has found that, based upon the information you have presented, the drug described in your ANDA is safe and effective for use as recommended in the submitted labeling. Therefore, as noted, the application including all amendments and supplements thereto is **tentatively approved**. This determination is based upon information available to the agency at this time, i.e., information in your application and the status of current good manufacturing practices (CGMPs) of the facilities used in the manufacture and testing of the drug products, and is subject to change on the basis of new information that may come to our attention.

Because the agency is granting a **tentative approval** for this application, when you believe that your application may be considered for final approval, you must amend your application to notify the agency whether circumstances have or have not arisen that may affect the effective date of final approval. To reactivate your application, please submit an amendment prior to the date you believe your application will be eligible for final approval. This amendment should identify changes, if any, in the conditions under which the product was tentatively approved, and should include updated information such as final printed labeling, chemistry, manufacturing, and controls data as appropriate. Please note that this amendment should be submitted even if none of these changes were made. The amendment should be designated clearly in your cover letter as a **MINOR AMENDMENT**. In addition to this amendment, the agency may request at any time prior to the final date of approval that you submit an additional amendment containing the information described above. Any 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 procedures are subject to agency review before final approval of the application will be made.

The drug products that are the subject of this ANDA may not be marketed without final agency approval under section 505 of the Act. The introduction or delivery or introduction into interstate commerce of this drug before the effective final approval date is prohibited under section 301(d) of the Act. Also, until the agency issues the final approval letter, these drug products will not be listed in the Orange Book.

Please contact Cecelia Parise, R.Ph., Regulatory Policy Advisor to the Director, Office of Generic Drugs, at (301) 827-5845, for further information regarding this issue.

Sincerely,

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

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/s/

Gary Buehler
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