



DEPARTMENT OF HEALTH & HUMAN SERVICES

ANDA 76-314

Food and Drug Administration  
Rockville MD 20857

SEP 11 2006

Mylan Pharmaceuticals Inc.  
Attention: S. Wayne Talton  
Vice President, Regulatory Affairs  
781 Chestnut Ridge Road  
P.O. Box 4310  
Morgantown, WV 26504-4310

Dear Sir:

This is in reference to your abbreviated new drug application (ANDA) dated December 26, 2001, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (the Act), for Topiramate Tablets 25 mg, 100 mg, & 200 mg.

Reference is made to our tentative approval letter dated April 23, 2003, for your Topiramate Tablets 25 mg, 100 mg, and 200 mg. We also acknowledge receipt of your amendments dated December 9, 2004, June 3, 2005, and January 18, and August 4, 2006. Your January 18, 2006, amendment provided for an additional strength, Topiramate Tablets 50 mg. We also acknowledge receipt of your correspondence dated September 30, 2003, March 2, March 22, April 26, July 21, September 10, and December 9, 2004, June 3, 2005, and February 28, and May 5, 2006, addressing recent patent and exclusivity issues associated with this application.

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. However, because of the patent issue noted below we are unable to approve your Topiramate Tablets 50 mg at this time. This application is approved, effective on the date of this letter, for your Topiramate Tablets 25 mg, 100 mg, and 200 mg. Your Topiramate Tablets 50 mg are considered to be tentatively approved, and they will not be eligible for final approval until the patent issue noted below has been satisfactorily resolved.

The reference listed drug (RLD) upon which you have based your ANDA, Topamax Tablets 25 mg, 50 mg, 100 mg, and 200 mg of Ortho-McNeil Pharmaceutical Inc. (Ortho-McNeil), is subject to periods of patent protection. The following patents and expiration dates are currently listed in the agency's publication titled Approved Drug Products with Therapeutic Equivalence Evaluations (the "Orange Book") for this drug product:

<u>U.S. Patent Number</u>	<u>Expiration Date</u>
4,513,006 (the '006 patent)	September 26, 2008
5,998,380 (the '380 patent)	October 13, 2015
6,503,884 (the '884 patent)	October 13, 2015
7,018,983 (the '983 patent)	October 13, 2015

With respect to the '380, '884, and '983 patents, your ANDA contains statements under section 505(j)(2)(A)(viii) of the Act declaring that that these are method of use patents, and that they do not claim any indication for which you are seeking approval under your ANDA.

With respect to the '006 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 Topiramate Tablets 25 mg, 50 mg, 100 mg, & 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 was brought against Mylan Pharmaceuticals Inc. (Mylan) for infringement of the '006 patent that was the subject of the paragraph IV certification. This action must have been brought against Mylan prior to the expiration of 45 days from the date the notice you provided under section 505(j)(2)(B)(i) was received by the NDA/patent holder(s). You have notified the agency that Mylan complied with the requirements of section 505(j)(2)(B) of the Act, and that litigation for infringement of the '006 patent was initiated against Mylan with respect to your Topiramate Tablets 25 mg, 100 mg and 200 mg in the United States District Court for the District of New Jersey [Ortho-McNeil Pharmaceutical Inc. v. Mylan Laboratories Inc. and Mylan Pharmaceuticals Inc., Civil Action No. 04-1689-MLC]. Although this litigation remains ongoing, the 30-month period identified in section 505(j)(5)(B)(iii) of the Act, during which time FDA was precluded from approving your ANDA for Topiramate Tablets 25 mg, 100 mg, and 200 mg has expired.

In addition, litigation was also brought against Mylan with respect to your Topiramate Tablets 50 mg and the '006 patent in the United States District Court for the District of New Jersey [Ortho-McNeil Pharmaceutical Inc. v. Mylan Laboratories Inc. and Mylan Pharmaceuticals Inc., Civil Action No. 3:06-00757-SRCTJB]. This litigation remains ongoing and the 30-month period identified in section 505(j)(5)(B)(iii) of the Act will not expire until 2008.

#### **I. Approval of Topiramate Tablets 25 mg, 100 mg, & 200 mg**

The Division of Bioequivalence has determined your Topiramate Tablets 25 mg, 100 mg, & 200 mg to be bioequivalent and therefore, therapeutically equivalent to the listed drug, Topamax Tablets 25 mg, 100 mg, and 200 mg, respectively, of Ortho McNeil Pharmaceutical, Inc. Your dissolution testing should be incorporated into the stability and quality control program using the same method proposed in your ANDA.

With respect to 180-day generic drug exclusivity, the agency has determined that Mylan was the first ANDA applicant to submit a substantially complete ANDA with a paragraph IV certification to the '006 patent for Topiramate Tablets 25 mg, 100 mg, and 200 mg. Therefore, with this approval, Mylan is eligible for 180-days of generic drug exclusivity for Topiramate Tablets 25 mg, 100 mg & 200 mg. This marketing exclusivity, which is provided for under section 505(j)(5)(B)(iv) of the Act, will begin to run from the earlier of the commercial marketing or court decision dates identified in section 505(j)(5)(B)(iv).<sup>1</sup> Please submit correspondence to this ANDA informing the agency of the date the exclusivity begins to run.

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.

Postmarketing reporting requirements for this ANDA application 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.

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<sup>1</sup> Because your ANDA was filed before the date of enactment of the Medicare Prescription Drug, Improvement and Modernization Act (MMA) (Public Law 108-173) on December 8, 2003, this reference to the 180-day exclusivity provision is to the section of the Act as in effect prior to December 8, 2003. See MMA § 1102(b)(1).

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 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.

## **II. Tentative Approval of Topiramate Tablets 50 mg**

As noted above, under section 505(j)(5)(B)(iii) of the Act we are unable at this time to grant final approval to your Topiramate Tablets 50 mg. Final approval cannot be granted until:

1. a. the expiration of the 30-month period provided for in section 505(j)(5)(B)(iii), or
- b. the date the court decides<sup>2</sup> that the '006 patent is invalid or not infringed. See sections 505(j)(5)(B)(iii)(I), (II), and (III) of the Act, or,
- c. the '006 patent has expired, and
2. The agency is assured there is no new information that would affect whether final approval should be granted.

To reactivate your ANDA prior to final approval, supplemental application 90 days prior to the date you believe that your Topiramate Tablets 50 mg will be eligible for final approval. This supplemental application should provide the

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<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.

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 your Topiramate Tablets 50 mg were 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 "SUPPLEMENTAL APPLICATION - EXPEDITED REVIEW REQUESTED".

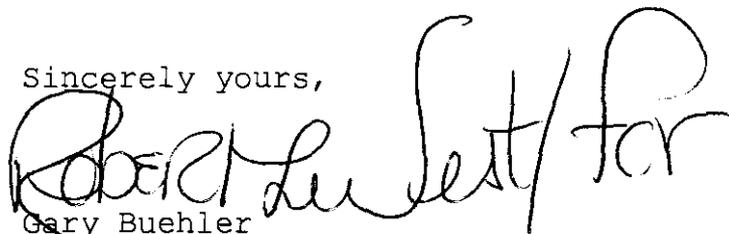
In addition to the Supplemental application requested above, the agency may request at any time prior to the date of final approval that you submit an additional amendment containing the requested information. Failure to submit either or, if requested, both amendments may result in rescission of the tentative approval status of your Topiramate Tablets 50 mg, 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 your Topiramate Tablets 50 mg 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 supplemental applications prior to final approval may also result in a delay in the issuance of the approval letter for your Topiramate Tablets 50 mg.

Your Topiramate Tablets 50 mg 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 501 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 a supplemental application providing for the final approval of your Topiramate Tablets, 50 mg, Please contact Thomas Hinchliffe, Pharm.D., Project Manager, at (301) 827-5771.

Sincerely yours,

A handwritten signature in black ink, appearing to read "Robert Lee West/for". The signature is written in a cursive, somewhat stylized script.

Gary Buehler

Director

Office of Generic Drugs

Center for Drug Evaluation and Research