DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville, MD 20857

ANDA 76-184

Barr Laboratories, Inc.
Attention: Nicholas Tantillo
Senior Director, Regulatory Affairs
225 Summit Avenue
Montvale, NJ 07645

Dear Sir:

This is in reference to your abbreviated new drug application (ANDA) dated June 4, 2001, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (the Act), for Alendronate Sodium Tablets USP, 35 mg (base) and 70 mg (base) intended for once weekly dosing.

Reference is also made to the tentative approval letter issued by this office on April 23, 2002, and to your amendments dated October 31, 2005; April 2, June 1, August 15, and November 30, 2007; and January 4, 2008.

We have completed the review of this ANDA, and have concluded that adequate information has been presented to demonstrate that your Alendronate Sodium Tablets USP, 35 mg (base) and 70 mg (base) are safe and effective for once-weekly use as recommended in the submitted labeling. However, because of the 180-day generic drug exclusivity issue explained below, at this time we are unable to grant final approval to your Alendronate Sodium Tablets USP, 35 mg. Therefore, only your Alendronate Sodium Tablets USP, 70 mg is approved, effective on the date of this letter. Your Alendronate Sodium Tablets USP, 35 mg, remains tentatively approved and will not be eligible for final approval until the 180-day generic drug exclusivity period associated with the 35 mg strength has expired.

As discussed in our tentative approval letter, the reference listed drug (RLD) upon which you have based your ANDA, Fosamax Tablets, 35 mg (base) and 70 mg (base) of Merck and Co., Inc. (Merck), is subject to periods of patent protection. The following patents and expiration dates (with pediatric exclusivity attached) are currently listed in the agency's publication titled Approved Drug Products with Therapeutic Equivalence Evaluations (the "Orange Book") for this drug product:

U.S. Patent Number	Expiration Date
4,621,077 (the '077 patent)	February 6, 2008
5,358,941 (the '941 patent)	June 2, 2013
5,681,590 (the '590 patent)	June 2, 2013
5,849,726 (the '726 patent)	December 6, 2015
5,994,329 (the '329 patent)	January 17, 2019
6,008,207 (the '207 patent)	December 6, 2015
6,015,801 (the '801 patent)	January 17, 2019
6,090,410 (the '410 patent)	June 2, 2013
6,225,294 (the '294 patent)	January 17, 2019

With respect to all nine 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 Alendronate Sodium Tablets USP, 35 mg and 70 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 Barr Laboratories Inc. (Barr) for infringement of one or more of the patents that were the subjects of the paragraph IV certifications. This action must have been brought against Barr 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 notified the agency that Barr complied with the requirements of section 505(j) (2) (B) of the Act, and that litigation for infringement of the nine patents was brought against Barr in the United States District Court for the District of Delaware [Merck & Co. v. Barr Laboratories, Inc., Civil Action Nos. 01-597]. You notified the agency of the agreed order entered into between Merck & Co., Inc. and Barr on March 6, 2003, in the United States District Court for the Southern District of New York [Civil Action No. 01-CV-8223] which upholds the ruling for dismissal of the '941, '590, '726, '207, '801, '410, and the '294 patents by the United States District Court of Delaware [Merck & Co., Inc. v. TEVA Pharmaceuticals USA, Inc.]. Furthermore, you have notified the agency of the final judgment entered on March 14, 2007, in the United States District Court for the Southern District of New York [Civil Action No. 01-CV-8223] upholding the ruling on the '077 patent in Merck's favor [Civil Action No. 00-035-JJF, USDC D. Del] and on the '329 patent in Barr's favor [CV No. 01-0048-JJF, USDC D. Del].

1. Approval of Alendronate Sodium Tablets USP, 70 mg

The Division of Bioequivalence has determined your Alendronate Sodium Tablets USP, 70 mg, to be bioequivalent and, therefore, therapeutically equivalent to the RLD, Merck's Fosamax Tablets, 70 mg (base). 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, we note that Barr was the first ANDA applicant to submit a substantially complete ANDA for Alendronate Sodium Tablets USP, 70 mg, with a paragraph IV certification to the '294 patent. Therefore, with this approval, Barr Laboratories, Inc. is eligible for 180 days of generic drug exclusivity for Alendronate Sodium Tablets USP, 70 mg. Barr will share this exclusivity with TEVA Pharmaceuticals USA (TEVA) because TEVA was the first ANDA applicant to submit a substantially complete ANDA with a paragraph IV certification to the other patents. This 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).[2] 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.

Post-marketing 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 your Alendronate Sodium Tablets USP, 70 mg.

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 materials for any subsequent advertising or promotional campaign be submitted to the Division of Drug Marketing, Advertising, and Communications with a completed Form FDA 2253 at the time of their initial use.

[2] 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).

II. Tentative Approval of Alendronate Sodium Tablets USP, 35 mg

We are unable to grant final approval to your Alendronate Sodium Tablets USP, 35 mg, at this time because TEVA's ANDA providing for the 35 mg strength and containing paragraph IV certifications to the patents listed in the Orange Book was submitted to the agency prior to the submission of your ANDA. TEVA's ANDA, therefore, is entitled to 180-day generic drug exclusivity for Alendronate Sodium Tablets USP, 35 mg. Accordingly, your Alendronate Sodium Tablets USP, 35 mg will be eligible for final approval on the date that is 180 days after the agency receives notice, with respect to TEVA's ANDA, of the earlier of the commercial marketing or court decision dates identified in section 505(j)(5)(B)(iv) of the Act.

Our decision to continue the tentative approval to your Alendronate Sodium Tablets USP, 35 mg, is based upon information currently available to the agency, i.e., data in your ANDA and the status of current good manufacturing practices (cGMPs) of the facilities used in the manufacture and testing of the drug product. This decision is subject to change on the basis of new information that may come to our attention.

To reactivate this ANDA to provide for final approval of your Alendronate Sodium Tablets USP, 35 mg, please submit a "Supplemental Application – Expedited Review Requested" 90 days prior to the date you believe that these products will be eligible for final approval. Your supplement must provide a summary of the legal basis upon which you believe the ANDA should be approved, as well as:

1. updated information related to final-printed labeling or chemistry, manufacturing and controls data, or any other change in the conditions outlined in this ANDA, or
2. a statement that no such changes have been made to the ANDA since the date of tentative approval.

Any changes in the conditions outlined in this ANDA and 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 Alendronate Sodium Tablets USP, 35 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.

In addition to the supplement requested above, the agency may request at any time prior to the final date of approval that you submit an additional supplement containing the requested information. Failure to submit either supplement may result in rescission of this tentative approval determination, or delay in issuance of the final approval letter.

Your Alendronate Sodium Tablets USP, 35 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 a drug before the effective final approval date is prohibited under section 501 of the Act. Also, until the agency issues the final approval letter, your Alendronate Sodium Tablets USP, 35 mg will not be listed in the "Orange Book."

For further information on the status of this ANDA, or prior to submitting a supplement providing for the final approval of your Alendronate Sodium Tablets USP, 35 mg, please contact Rosalyn Adigun, Project Manager, at 240-276-8518.

Sincerely yours,

{See appended electronic signature page}

Gary Buehler
Director
Office of Generic Drugs
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/

Robert L. West
2/6/2008 07:23:34 AM
for Gary Buehler