

May 31, 2000

Teva Pharmaceuticals USA
Attention: Deborah A. Jaskot
U.S. Agent for: Pharmachemie B.V.
1510 Delp Drive
Kulpsville, PA 19443

Dear Madam:

This is in reference to your abbreviated new drug application dated August 26, 1994, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act (Act), for Tamoxifen Citrate Tablets USP, 10 mg (base).

Reference is also made to our tentative approval letters dated April 3, 1997, and March 9, 1999, and to your amendments dated April 18, and April 27, 2000.

The listed drug product referenced in your application is subject to a period of patent protection which expires August 20, 2002, (U.S. Patent No. 4,536,516, the "516" patent). Your application contains a patent certification under Section 505(j)(2)(A)(vii)(IV) of the Act stating that your manufacture, use, or sale of Tamoxifen Citrate Tablets, USP will not infringe on the patent or that the patent is otherwise invalid. You have informed the Agency that Zeneca Pharmaceuticals initiated a patent infringement suit against you in United States District Court for the District of Maryland (Zeneca Limited v. Pharmachemie B.V., Civil Action No. S96-884). You notified the Agency that the litigation was subsequently moved from the District of Maryland to the District of Massachusetts (Civil Action No. 96-12413-RCL), and that the 30-month period provided for under 21 CFR 314.107(b)(3) has expired.

As noted in our tentative approval letter dated March 9, 1999, the agency was precluded from granting final approval to your application because of its response to a Citizens Petition dated March 2, 1999 (Docket No. 98P-0493/PSA1&RC1). In the response, the agency agreed with the petitioner to stay the effective date of approval of any ANDA for this drug product

other than the ANDA submitted by Barr Laboratories, Inc., until 180 days after the date of the first commercial marketing of the drug product under Barr's ANDA, or the date of a decision of a court holding the tamoxifen patent to be invalid or not infringed. However, in a subsequent decision, Mylan Pharmaceuticals, Inc. v. Henney, No. 99-cv-862, slip op. at 33 (D.D.C. March 31, 2000), the court rejected FDA's interpretation of 314.94(a)(12)(viii) as described in its March 2, 1999 response. The court remanded the issue to the Agency to reinterpret the effect of the regulation on Barr's change from a paragraph IV to a paragraph III certification to U.S. Patent No. 4,536,516. The Agency has determined that Barr's change in certification makes it ineligible for 180-day exclusivity under Section 505(j)(5)(B)(iv) of the Federal Food Drug and Cosmetic Act. Barr's was the first substantially complete ANDA for Tamoxifen Citrate Tablets containing a paragraph IV certification. Please note that because Barr is no longer eligible for 180-day exclusivity, FDA will give final approval to any ANDA for Tamoxifen Citrate Tablets that is otherwise eligible for final approval.

We have completed the review of this abbreviated application and have concluded that the drug is safe and effective for use as recommended in the submitted labeling. Accordingly, the application is approved. The Division of Bioequivalence has determined your Tamoxifen Citrate Tablets USP, 10 mg (base) to be bioequivalent and, therefore, therapeutically equivalent to the listed drug (Nolvadex Tablets[®], 10 mg (base) of Astrazeneca Pharmaceuticals, L.P.). Your dissolution testing should be incorporated into the stability and quality control program using the same method proposed in your application.

Under Section 506A of the Act, certain changes in the conditions described in this abbreviated application require an approved supplemental application before the change may be made.

Post-marketing reporting requirements for this abbreviated 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.

We request that you submit, in duplicate, any proposed advertising or promotional copy which you intend to use in your initial advertising or promotional campaigns. Please submit all proposed materials in draft or mock-up form, not final print. Submit both copies together with a copy of the

proposed or final printed labeling to the Division of Drug Marketing, Advertising, and Communications (HFD-40). Please do not use Form FD-2253 (Transmittal of Advertisements and Promotional Labeling for Drugs for Human Use) for this initial submission.

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 our Division of Drug Marketing, Advertising, and Communications (HFD-40) with a completed Form FD-2253 at the time of their initial use.

Sincerely yours,

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