DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 21-344

AstraZeneca Pharmaceuticals
Attention: Anthony Rogers
Vice President, Regulatory Affairs
1800 Concord Pike
P.O. Box 8355
Wilmington, DE 19803-8355

Dear Mr. Rogers:

Please refer to your new drug application (NDA) dated March 28, 2001, received March 28, 2001, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for FASLODEX® (fulvestrant) Injection.

We acknowledge receipt of your submissions dated January 18; April 9; May 25; June 5; July 19 and 20; August 9, 28 and 31; September 13 and 28; October 11, 12, 18 (2), 24 and 29; November 9 and 13 (2); December 10, 11, 14 and 31, 2001; January 22, 30 and 31; February 1 and 11; and April 16 and 22, 2002.

This new drug application provides for the use of FASLODEX® (fulvestrant) Injection for the treatment of hormone receptor positive metastatic breast cancer in postmenopausal women with disease progression following antiestrogen therapy.

We have completed the review of this application, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the agreed upon enclosed labeling text. Accordingly, the application is approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert, immediate container and carton labels). Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

Please submit the copies of final printed labeling (FPL) electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA* (January 1999). Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FPL for approved NDA 21-344." Approval of this submission by FDA is not required before the labeling is used.

We remind you of your postmarketing study commitments in your facsimile dated April 25, 2002. These commitments are listed below.

1. To perform a study of the effect of ketoconazole treatment on the pharmacokinetics of fulvestrant following intravenous dosing of fulvestrant.

   In order to be interpretable, the commitment is to perform a study with a sufficient number of subjects and measurements. A sufficient number is one that results in a confidence interval of the ratio (ketoconazole + fulvestrant: fulvestrant alone) of the log-transformed AUC_{0-t} for the treatments of 0.40 or less.

Protocol Submission:	Within 2 months of the date of this letter.
Study Start:	Within 4 months of the date of this letter.
Final Report Submission:	Within 10 months of the date of this letter.

2. To update survival data on the randomized studies #20 and #21 and to submit a study report when 75% of the patients have died.

3. To submit reports of all medication errors, both potential and actual, that occur within the United States with Faslodex for two years following the date of approval. Potential errors should be reported and summarized quarterly. All actual errors should be submitted within 15 days regardless of patient outcome. Yearly reports of potential and actual errors occurring with FASLODEX should be submitted for two years following the date of approval. Within one month of approval, AstraZeneca Pharmaceuticals will meet with FDA to clarify the meaning of the terms potential medication error and actual medication error.

Submit the clinical protocol for the ketoconazole interaction study to your IND for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all study final reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii), you should include a status summary of each commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies, number of patients entered into each study. All submissions, including supplements, relating to these postmarketing study commitments must be prominently labeled **"Postmarketing Study Protocol", "Postmarketing Study Final Report", or "Postmarketing Study Correspondence."**

Validation of the regulatory methods has not been completed. At the present time, it is the policy of the Center not to withhold approval because the methods are being validated. Nevertheless, we expect your continued cooperation to resolve any problems that may be identified.

Be advised that, as of April 1, 1999, all applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred (63 *FR* 66632). We are waiving the pediatric study requirement for this action on this application.

use for this product. All proposed materials should be submitted in draft or mock-up form, not final print. Please send one copy to the Division of Oncology Drug Products and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising, and Communications, HFD-42
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, call Amy Baird, Consumer Safety Officer, at (301) 594-5771.

Sincerely,

{See appended electronic signature page}

Robert Temple, M.D.
Director
Office of Drug Evaluation I
Center for Drug Evaluation and Research

Enclosure

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Robert Temple
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