DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug
Administration
Rockville MD 20857

NDA 21-109
NDA 17-970/S-050

AstraZeneca Pharmaceuticals, LP
Attention: Laura Garcia-Davenport
Associate Director, Regulatory Affairs
1800 Concord Pike
PO Box 8355
Wilmington, DE 19803-8355

Dear Ms. Davenport:

Please refer to your new drug application (NDA 21-109) dated February 28, 2002, received March 1, 2002, and your supplemental new drug application (NDA 17-970/S-050) dated August 6, 2002, received August 26, 2002, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Nolvadex (tamoxifen citrate) 20 mg tablets.

We acknowledge receipt of your submissions to NDA 2-109 dated April 9, 12, and 18, May 14, 16, 23, and 28, June 18 and 27, July 17(2), 29, and 31, and August 6 and 10, 2002. We also refer to the August 28 and 29, 2002, teleconferences between you and Dr. Monika Johnson of this Division.

This new drug application (NDA 21-109) was submitted to provide the pediatric clinical study report that responded to a Written Request dated April 5, 2000, for tamoxifen citrate 20 mg tablets to obtain safety, efficacy, and pharmacokinetic information in girls with McCune-Albright Syndrome. The results of this study are added to the **CLINICAL PHARMACOLOGY** section, **CLINCIAL STUDY** section, **PRECAUTIONS** section, and the **ADVERSE REACTIONS** section of the package insert and the **"Who should not take Nolvadex?"** section of the patient package insert. The supplemental new drug application provides for the addition of this information to the approved labeling for NDA 17-970.

We have completed our review of these applications, as amended. They are approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text and with the minor editorial revisions listed below, which have been incorporated in the enclosed labeling.

1. The phrase "endometrial adenocarcinoma and uterine sarcoma" has been replaced with the phrase "uterine malignancies, stroke and pulmonary embolism" in the last sentence of the second paragraph in the "**Pediatric Patients**" subsection of the **CLINICAL PHARMACOLOGY**, **Special Populations** section.

2. The phrase "endometrial adenocarcinoma and uterine sarcoma" has been replaced with the phrase "uterine malignancies, stroke and pulmonary embolism" in the last sentence of the "**Pediatric Use**" paragraph in the **PRECAUTIONS** section.

3. In the **ADVERSE REACTIONS** section, the "**Pediatric Patients – McCune-Albright Syndrome**" subsection has been moved to immediately precede the "Postmarketing experience" subsection.

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert, text for the patient package insert), which incorporates these revisions into your labeling submitted on August 6, 2002. The revisions listed above were agreed to in the August 28 and 29, 2002, telephone conversations.

These revisions are terms of the NDA approval. Marketing the product before making the revisions, exactly as stated, in the product's labeling 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 21-109 and NDA 17-970/S-050." Approval of this submission by FDA is not required before the labeling is used.

In addition, please submit three copies of the introductory promotional materials that you propose to use for this product. All proposed materials should be submitted in draft or mock-up form, not final print. Please submit one copy to this Division 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 note your intention (described in your August 10, 2002, letter) to follow pediatric patients for five years after completion of treatment in the McCune-Albright study and to submit safety information in your annual reports.

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81). All 15-day alert reports, periodic (including quarterly) adverse drug experience reports, field alerts, annual reports, supplements, and other submissions should be

addressed to the original NDA 17-970 for this drug product, **not to this NDA**. In the future, do not make submissions to this NDA except for the final printed labeling requested above.

If you have any questions, call Monika Johnson, PharmD, Regulatory Project Manager, at (301) 827-6370.

Sincerely,

{See appended electronic signature page}

David G. Orloff, M.D.
Director
Division of Metabolic and Endocrine Drug Products
Office of Drug Evaluation II
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/

David Orloff

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