DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 17-970/S-037/S-044/S-049

AstraZeneca Pharmaceuticals LP
1800 Concord Pike
P.O. Box 8355
Wilmington, DE 19803-8355

Attention: Laura Garcia-Davenport
Regulatory Affairs, Associate Director

Dear Ms. Garcia-Davenport:

Please refer to your supplemental new drug application dated April 18, 2002, received April 19, 2002, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for NOLVADEX (tamoxifen citrate) Tablets.

We also refer to your supplemental new drug applications dated September 18, 1997 (S-037), and June 24, 1999 (S-044), received September 22, 1997, and June 28, 1999, respectively.

We acknowledge receipt of amendments to S-044 dated February 25 and September 5, 2000, and July 2, 2001. We also acknowledge supplemental new correspondence submitted to S-046 dated December 6, 2001, January 4, January 7, and March 19, 2002.

Supplement 037 provides for an update to the **WARNINGS** and **ADVERSE REACTIONS** sections of the package insert. The changes proposed in S-037 were reviewed and approved with S-040 on October 29, 1998. S-037 has been superseded and will be Acknowledged and Retained.

Supplement 044 provides for Changes Being Effected revisions to the **ADVERSE REACTIONS, CONTRAINDICATIONS, WARNINGS,** and **PRECAUTIONS** sections of the package insert. The changes proposed in S-044 were incorporated into the proposed labeling submitted with S-049. S-044 has been superseded and will be Acknowledged and Retained.

Supplement 049 provides for the consolidation of all outstanding labeling changes, including the Dear Doctor letter, Black Box Warning, and wording regarding the adverse event of uterine sarcoma.

We have completed the review of supplement 049, 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 supplemental application is approved effective on the date of this letter.

However, we request that the following changes in the labeling be made so as to furnish adequate information for the safe and effective use of the drug:

- In the **WARNINGS** section, **Effects on the Uterus – Endometrial Cancer and Uterine Sarcoma** subsection, please provide updated FIGO substaging information for the three additional cases on tamoxifen and the one additional case on placebo identified during blinded follow-up of NSABP P-1.

The supplement should be submitted within 2 months.

The final printed labeling (FPL) for S-049 must be identical to the enclosed labeling (text for the package insert, text for the patient package insert).

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 supplement NDA 17-970/S-049." Approval of this submission by FDA is not required before the labeling is used.

If a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter) is issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 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 Christy Wilson, Consumer Safety Officer, at (301) 594-5761.

Sincerely,

{See appended electronic signature page}

Richard Pazdur, M.D.
Director
Division of Oncology Drug Products
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/

Richard Pazdur

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