DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-541/S-010

AstraZeneca Pharmaceuticals LP
Attention: Mark Scott, Ph.D.
Executive Director, Regulatory Affairs
P.O. Box 8355
Wilmington, DE 19803-8355

Dear Dr. Scott:

Please refer to your supplemental new drug application dated March 4, 2002, received March 5, 2002, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for ARIMIDEX® (anastrozole) Tablets.

We acknowledge receipt of your submissions dated December 21, 2001; January 18 and 31; February 14; March 13; April 2, 3, 4, 12 and 18; May 8 and 29 (2), June 5, 7, 17, 19 (2), 20 (2) and 26; July 3 (3), 9, 10, 18, 19, 22, 23, 24, 25, 30 (2) and 31; August 16 and 23, 2002.

This supplemental new drug application provides for the use of ARIMIDEX® (anastrozole) Tablets for adjuvant treatment of postmenopausal women with hormone receptor positive early breast cancer.

We have completed the review of this supplemental application, as amended, according to the regulations for accelerated approval, and have concluded that adequate information has been presented to approve ARIMIDEX® (anastrozole) Tablets for use as recommended in the enclosed labeling text. Accordingly, the supplemental application is approved under 21 CFR 314 subpart H. Approval is effective on the date of this letter. Marketing of this drug product and related activities are to be in accordance with the substance and procedures of the referenced accelerated approval regulations.

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the 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 20-541/S-010." Approval of this submission by FDA is not required before the labeling is used.

Products approved under the accelerated approval regulations, 21 CFR 314.510, require further adequate and well-controlled studies to verify and describe clinical benefit. We remind you of your post marketing study (Subpart H post marketing commitments) specified in your submission dated September 5, 2002. These commitments, along with any completion dates agreed upon, are listed

below.

1. To submit a complete report of the updated ATAC data during 2004 to verify the safety and efficacy of Arimidex in the adjuvant treatment of postmenopausal women with hormone receptor-positive early breast cancer. The report will include an analysis of efficacy in the subgroup of patients who have received chemotherapy.

2. To conduct a double-blind, randomized, comparison trial using Arimidex with and without bisphosphonate therapy in early breast cancer patients. The design of this trial will be finalized in consultation with the Agency by November 1, 2002.

3. To submit a subprotocol and conduct a study to evaluate the development of hyperlipidemia and control of hyperlipidemia in patients on the ATAC trial.

Final study reports should be submitted to this NDA as a supplemental application. For administrative purposes, all submissions relating to this post marketing commitment must be clearly designated "Subpart H Post Marketing Commitments."

In addition, we note your following postmarketing commitments, specified in your submission dated September 5, 2002, that are not a condition of the accelerated approval. These commitments, along with any completion dates agreed upon, include:

1. In the NDA Annual Progress Reports provide information regarding the incidence of the pre-specified safety events and hypercholesterolemia for the treatment arms of the ATAC trial.

2. Continue to collect data in the ATAC trial on SAEs including fractures and those associated with hypercholesterolemia (i.e., cardiovascular and cerebrovascular adverse events) for an additional five years following discontinuation of treatment or breast cancer recurrence. Submit the safety report summarizing these data by January 1, 2011.

3. To submit a complete report of the updated ATAC data to verify the safety and efficacy of Arimidex in the adjuvant treatment of postmenopausal women with hormone receptor-positive early breast cancer when all patients on the ATAC trial have completed five years of treatment and two years of follow-up (approximately June 2007). The report will include an analysis of efficacy in the subgroup of patients who have received chemotherapy.

Submit clinical protocols 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."**

We also remind you that, under 21 CFR 314.550, after the initial 120 day period following this approval, you must submit all promotional materials, including promotional labeling as well as advertisements, at least 30 days prior to the intended time of initial dissemination of the labeling or initial publication of the advertisement.

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.

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}

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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