DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-726/S-011

Novartis Pharmaceuticals Corporation
Attention: Arlene Wolny
Associate Director, Drug Regulatory Affairs
One Health Plaza
East Hanover, New Jersey 07936-1080

Dear Ms. Wolny:

Please refer to your supplemental new drug application dated April 29, 2004, received April 29, 2004, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Femara® (letrozole tablets).

We acknowledge receipt of your submissions dated June 4 and 9; July 27; August 4, 10, 13 and 25; September 2; October 5, 25 and 29, 2004.

This new drug application provides for the use of Femara® for the extended adjuvant treatment of early breast cancer in postmenopausal women who have received five years of adjuvant tamoxifen therapy. The effectiveness of Femara in extended adjuvant treatment of early breast cancer is based on an analysis of disease-free survival in patients treated for a median of 24 months (see **CLINICAL PHARMACOLOGY Clinical Studies** subsection of the package insert). Further data will be required to determine long-term outcome.

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 Femara® (letrozole tablets) for use as recommended in the enclosed labeling text. Accordingly, the 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 20 paper copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please mount individually ten of the copies on heavy-weight paper or similar material. Alternatively, you may submit the FPL electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format – NDAs* (January 1999). For administrative purposes, this submission should be designated "**FPL for approved NDA 20-726/S-011**." 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 study of the drug to verify and describe clinical benefit. We remind you of your post marketing study (Subpart H Phase 4) commitments specified in your submission dated October 29, 2004. This commitment, along with any completion dates agreed upon, is listed below.

Due to the short follow-up period in trial MA-17, the data allow only preliminary conclusions regarding safety and efficacy. The following commitments under Subpart H (CFR 314.500) are designed to describe the ultimate outcome of patients treated with letrozole.

1. To continue collection of safety and efficacy data from the patients who were enrolled in the pivotal trial MA-17 and to summarize the findings in annual reports to the agency. Each patient should be followed until death or for at least five years and a final study report should be submitted. This commitment includes completion of the per protocol sub-studies on bone and lipid/cardiovascular effects from study MA-17 and to provide yearly updates of these studies in annual reports.

2. To submit the final study report, for trial MA-17, 6 months after all patients have received 5 years of letrozole therapy.

3. To submit a final study report from the now closed BIG 18-98 trial in order to further evaluate the long term safety of 5 years treatment with letrozole. The final study report should be submitted no more than 6 months after the protocol specified final analysis.

Final study reports should be submitted to this NDA as a supplemental application. For administrative purposes, all submissions relating to these Phase 4 commitments must be clearly designated "**Subpart H Phase 4 Commitments**."

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.

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) 594-5779**.**

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/

Grant Williams
10/29/04 04:30:11 PM
Signed for Dr. Pazdur