DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-726/S-005

Novartis Pharmaceuticals Corporation
One Health Plaza, Building 105/2W200
Hanover, New Jersey 07936-1080

Attention: Arlene Wolny, Associate Director
Drug Regulatory Affairs

Dear Ms. Wolny:

Please refer to your supplemental new drug application dated June 30, 2000, received July 3, 2000, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Femara® (letrozole) tablets, 2.5 mg.

Your submission of August 29, 2002 constituted a complete response to our July 3, 2001 action letter.

This supplemental new drug application provides for changes to the package insert as a result of the completion of study 036, a study to compare the pharmacokinetics between healthy volunteers and hepatic impaired subjects; study P015, a drug interaction study between letrozole and Tamoxifen; and and study DMPK (CH) R0101153, an in vitro drug interaction study between letrozole and diazepam.

Studies 036 and DMPK (CH) R-0101153 were submitted to fulfill the following two postmarketing study commitments:

1. Study 036: As letrozole's primary route of elimination appears to be via hepatic metabolism, the potential for excessive concentrations in patients with impaired hepatic function is high. This is supported by the data that show that moderate hepatic impairment reduces letrozole clearance. A study describing letrozole pharmacokinetics in patients with severe hepatic impairment will be initiated in first quarter 1998. Since difficulties in recruitment of subjects with severe hepatic impairment are expected, completion of this study is projected no earlier than fourth quarter 1998.

2. Study DMPK (CH) R-203: A study investigating the drug interaction between letrozole and diazepam using in vitro techniques will be conducted. The results of the study will confirm the lack of pharmacokinetic drug interaction between letrozole and diazepam indicated in the analysis of the clinical data from the AR/BC2 trial. Study initiation is planned for first quarter 1998 and completion is expected in third quarter 1998.

We completed our review of this application. This application is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text.

We have concluded that the commitment to do a study investigating the drug interaction between letrozole and diazepam using in vitro techniques has been fulfilled. Please note that all phase 4 study commitments have now been fulfilled.

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert).

Please submit the FPL electronically according to the guidance for industry titled "Providing Regulatory Submissions in Electronic Format – NDA". Alternatively, you may 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 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 20-726/ S-005." Approval of this submission by FDA is not required before the labeling is used.

In addition, submit three copies of the introductory promotional materials that you propose to use for this product. Submit all proposed materials in draft or mock-up form, not final print. Send one copy to this division/ 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, MD 20857

If you issue a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter), 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 reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Ann Staten, Regulatory Project Manager, at (301) 594-0490.

Sincerely,

{See appended electronic signature page}

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