DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 020726/S-020 **SUPPLEMENT APPROVAL**

Novartis Pharmaceuticals Corporation
Attention: Lynne McGrath, MPH, Ph.D.
One Health Plaza
East Hanover, NJ 07936-1080

Dear Dr. McGrath:

Please refer to your July 1, 2009 Supplemental New Drug Application (sNDA), received July 1, 2009, submitted under section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Femara (letrozole) Tablets.

We acknowledge receipt of your submissions dated August 19, November 10, November 19, 2009, March 19, April 26, April 27, April 28, and April 30, 2010.

This "Prior Approval" supplemental new drug application provides reporting on the remaining mandatory Subpart H clinical trial to convert the approval from accelerated approval to full approval.

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

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, please submit the content of labeling [21 CFR 314.50(l)(1)(i)] in structured product labeling (SPL) format as described at http://www.fda.gov/oc/datacouncil/spl.html that is identical to the enclosed labeling (text for the package insert). For administrative purposes, please designate this submission, "SPL for approved NDA 020726/S-020.

SUBPART H FULFILLED

We approved S-011 and S-012 under the regulations at 21 CFR 314 Subpart H for accelerated approval of new drugs for serious or life-threatening illnesses. Approval of this supplement fulfills your commitments made under 21 CFR 314.

POSTMARKETING REQUIREMENTS AND COMMITMENT—FULFILLED

We have received the following submissions:

S-020, dated June 30, 2009, which contains the final reports for postmarketing requirement 1179-3, listed in the October 29, 2004 approval letter (required under Subpart H), for postmarketing commitment 1155-1, listed in the December 28, 2005 approval letter (required under Subpart H), and for postmarketing commitment 1155-4, listed in the December 28, 2005 approval letter (agreed-upon postmarketing commitment)

These commitments are listed below:

1179-3 To submit a final study report from the now closed BIG 1-98 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.

1155-1 To follow all patients in the BIG 1-98 trial for safety and efficacy until death or at least 5 years from randomization.

a. Submit annual reports of unblinded safety and efficacy data for BIG 1-98 in October 2006, and 2008.
b. Submit an annual report of unblinded safety data in October 2007.
c. Last patient last visit of BIG 1-98 is May 2008.
d. Submit the final BIG 1-98 study report relating to the Primary Core Analysis and the Second Primary Analysis (5 years treatment) in Q1 2009.

1155-4 Complete the BIG 1-98 post-baseline sub study (with post-baseline BMD & bone marker data), following patients up until 1 year after completion of the 5 years of adjuvant treatment.

a. Annual updates are not possible as the protocol pre-specified analysis is scheduled to be conducted in Q4 2009.
b. Last patient last visit for BIG 1-98 post-baseline sub study is May 2009
c. Submission of the final BIG 1-98 study report in Q4 2010

We have reviewed your submissions and conclude that the above requirements and commitment were fulfilled.

POSTMARKETING REQUIREMENT—RELEASED

We have received your submission dated June 30, 2009, referring to your postmarketing commitment required under Subpart H, listed in the December 28, 2005 approval letter for this application:

1155-3 Complete study CFEM345D2407: An open-label, randomized, multi-center study to evaluate the skeletal and lipid profile effects of letrozole and tamoxifen in postmenopausal women with resected, hormone receptor positive breast cancer.

a. Two-year data will be provided in the 2008 BIG 1-98 annual report

b. Last patient last visit for CFEM345D2407 is March 2011.
c. Submit the final CFEM345D2407 study report in Q4 2011.

We have reviewed your submission, in which you requested that this postmarketing commitment be changed from a mandatory Subpart H commitment to an agreed-upon postmarketing commitment. We agree that the postmarketing requirement under Subpart H may be released and replaced with an agreed-upon postmarketing commitment. Useful clinical data for skeletal and cardiovascular adverse reactions has been provided from the entire population of this trial. Laboratory data expected from trial CFEM345D2407 will be relatively less relevant when compared to the adverse reactions already submitted.

You are released from the above commitment because it has been converted to an agreed-upon postmarketing commitment, described below.

POSTMARKETING COMMITMENTS SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitments in your correspondence dated April 27, 2010. This commitment is listed below.

1155-5. Complete study CFEM345D2407: A study of an open-label, randomized, multi-center study to evaluate the skeletal and lipid profile effects of letrozole and tamoxifen in postmenopausal women with resected, hormone receptor positive breast cancer.
a. Two-year data will be provided in the 2008 BIG 1-98 annual report
b. Last patient last visit for CFEM345D2407 is March 2011.
c. Submit the final CFEM345D2407 study report in Q4 2011.

The milestones remain the same as those negotiated in 2004.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the package insert(s) to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications
5901-B Ammendale Road
Beltsville, MD 20705-1266

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the package insert(s), at the time of initial dissemination or publication, accompanied by a Form FDA 2253. For instruction on completing the Form FDA 2253, see page 2 of the Form. For more information about submission of promotional materials to the Division of Drug Marketing,

Advertising, and Communications (DDMAC), see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

LETTERS TO HEALTH CARE PROFESSIONALS

If you issue a letter communicating important safety related information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit an electronic copy of the letter to both this NDA and to the following address:

MedWatch
Food and Drug Administration
5600 Fishers Lane, Room 12B05
Rockville, MD 20857

REPORTING REQUIREMENTS

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 Alice Kacuba, Chief, Project Management Staff, at (301) 796-1381.

Sincerely,

{See appended electronic signature page}

Robert L. Justice, M.D., M.S.
Director
Division of Drug Oncology Products
Office of Oncology Drug Products
Center for Drug Evaluation and Research

Enclosure
Content of Labeling

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-20726	SUPPL-20	NOVARTIS PHARMACEUTICALS CORP	FEMARA
NDA-20726	PMR/PMC-1	NOVARTIS PHARMACEUTICALS CORP	FEMARA

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

AMNA IBRAHIM
04/30/2010
For Dr. Robert Justice