DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Silver Spring, MD 20993

NDA 022068/S001

SUPPLEMENT APPROVAL
RELEASE FROM POSTMARKETING
COMMITMENT

Novartis Pharmaceuticals
Attention: Dr. Darshan Wariabharaj, Associate Director
Drug Regulatory Affairs
One Health Plaza
East Hanover, NJ 07936-1080

Dear Dr. Wariabharaj:

Please refer to your supplemental new drug application dated December 7, 2007, received December 7, 2007, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Tasigna (nilotinib) 200 milligram tablets.

We also refer to our letters dated February 5 and May 29, 2009, and your submissions dated April 4, July 28, October 28, 2008, April 2, June 26, September 28, 2009, February 10, and March 2, 2010.

Your submission of July 29, 2008, constituted a complete response to our March 27, 2008, action letter.

This supplemental new drug application proposes a revised safety risk management plan (RMP) in response to your post-marketing study commitment reiterated below:

6. Submit a supplement containing a revised version of the complete RiskMAP (goals and objectives, tools, implementation plan, evaluation plan and reports to the agency) including all supporting materials. This should incorporate the amendments agreed to in correspondence of October 22 and October 26, 2007.

RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS

Section 505-1 of the FDCA authorizes FDA to require the submission of a Risk Evaluation and Mitigation Strategy (REMS) if FDA becomes aware of new safety information and makes a determination that such a strategy is necessary to ensure that the benefits of the drug outweigh the risks (section 505-1(a)).

Since Tasigna (nilotinib) was approved on October 29, 2007, we have become aware of new cases of QT prolongation from the Periodic Safety Update Report for the period February 1, 2008 to July 31, 2008. QT prolongation is a serious safety risk which may cause ventricular arrhythmias and death. We consider this information to be "new safety information" as defined in section 505-1(b) of FDCA.

Your proposed REMS, submitted on July 29, 2008, amended on April 2, 2009, June 26, 2009, September 28, 2009, February 10, 2010, and March 2, 2010, and appended to this letter, is approved. The REMS consists of a Medication Guide, a communication plan, and a timetable for submission of assessments of the REMS.

The REMS assessment plan should include but is not limited to the following:

1. An evaluation of patients' and prescribers' understanding of the risks of Tasigna (nilotinib).
2. A report on periodic assessments of the distribution and dispensing of the Medication Guide in accordance with 21 CFR 208.24.
3. A report on failures to adhere to distribution and dispensing requirements of the Medication Guide, and corrective actions taken to address noncompliance.
4. A narrative summary and analysis of the following cases reported with use of Tasigna (nilotinib): QT-prolongation, ventricular arrhythmias, sudden deaths, medication errors involving dosing outside the labeled dosing intervals, and interactions with other drugs and food.
5. A report on the status of prescriber education, including the type and number of prescribers educated, the number and percentage of likely prescribers who received educational kits by hand delivery, and the number and percentage of likely prescribers who received the kits by shipment.
6. A review of administrative claims data: an analysis of co-prescribing Tasigna (nilotinib) with CYP3A4 inhibitors and QT-prolonging drugs and dose-reduction as well as a report of the use of ECG testing in relation to dispensed prescriptions.
7. Based on the information provided, an assessment and conclusion of whether the REMS is meeting its goals, and whether modifications to the REMS are needed.

Assessments of an approved REMS must include, under section 505-1(g)(3)(B) and (C), information on the status of any postapproval study or clinical trial required under section 505(o) or otherwise undertaken to investigate a safety issue. You can satisfy these requirements in your REMS assessments by referring to relevant information included in the most recent annual report required under section 506B and 314.81(b)(2)(vii) and including any updates to the status information since the annual report was prepared. Failure to comply with the REMS assessments provisions in section 505-1(g) could result in enforcement action.

We remind you that in addition to the assessments submitted according to the timetable included in the approved REMS, you must submit a REMS assessment and may propose a modification to the approved REMS when you submit a supplemental application for a new indication for use as described in section 505-l(g)(2)(A) of FDCA.

Prominently identify subsequent submissions containing REMS assessments or proposed modifications of the REMS with the following wording in bold capital letters at the top of the first page of the submission:

NDA 022068 REMS ASSESSMENT

NEW SUPPLEMENT FOR NDA 022068
PROPOSED REMS MODIFICATION
REMS ASSESSMENT

NEW SUPPLEMENT (NEW INDICATION FOR USE) FOR NDA 022068
REMS ASSESSMENT
PROPOSED REMS MODIFICATION

If you do not submit electronically, please send 5 copies of REMS-related submissions.

We request that the revised labeling, including the Medication Guide, approved today be available on your website within 10 days of receipt of this letter.

You previously committed to conduct the following postmarketing commitment. The postmarketing commitment number below corresponds to the number used in the approval letter of October 29, 2007.

6. Submit a supplement containing a revised version of the complete RiskMAP (goals and objectives, tools, implementation plan, evaluation plan and reports to the agency) including all supporting materials. This should incorporate the amendments agreed to in correspondence of October 22 and October 26, 2007.

   Submission: by November 30, 2007.

As noted in our letter dated February 5, 2009, we are releasing this commitment because it has been incorporated into the approved REMS.

LETTERS TO HEALTH CARE PROFESSIONALS

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
Food and Drug Administration
5515 Security Lane
HFD-001, Suite 5100
Rockville, MD 20852

The final agreed-upon product labeling is attached. We will transmit the SPL version of the labeling submitted on March 2, 2010, to the National Library of Medicine for public dissemination. Marketing the product with labeling that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

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, please call Susan Jenney, Regulatory Project Manager, at (301)796-0062.

Sincerely,

{See appended electronic signature page}

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

Enclosure: Package Insert and Appendix A (REMS and all REMS materials)

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22068	SUPPL-1	NOVARTIS PHARMACEUTICALS CORP	TASIGNA

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

/s/

ROBERT L JUSTICE
03/15/2010