



NDA 022068/S-006

**SUPPLEMENT APPROVAL  
FULFILLMENT OF POSTMARKETING  
COMMITMENT**

Novartis Pharmaceuticals Corporation  
One Health Plaza  
East Hanover, NJ 07936-1080

Attention: Darshan Wariabharaj  
Senior Associate Director, DRA

Dear Mr. Wariabharaj:

Please refer to your Supplemental New Drug Application (sNDA) dated March 12, 2010, received March 15, 2010, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Tassigna<sup>®</sup> (nilotinib) 200 mg Capsules.

We acknowledge receipt of your amendments dated June 29, November 2, December 9 and 10, 2010, and also your risk evaluation and mitigation strategy (REMS) assessment dated January 10, 2011.

This "Prior Approval" supplemental new drug application provides for revisions to the package insert and the Medication Guide based on 24-month follow-up data on all patients with imatinib-resistant or -intolerant chronic myeloid leukemia in chronic and accelerated phases as well as proposed modifications to the approved REMS.

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

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

**CONTENT OF LABELING**

As soon as possible, but no later than 14 days from the date of this letter, submit, using the FDA automated drug registration and listing system (eLIST), the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format, as described at <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>, that is identical to the enclosed labeling (text for the package insert, text for Medication Guide) and include the labeling changes proposed in any pending "Changes Being Effectuated" (CBE)

supplements and any annual reportable changes not included in the enclosed labeling. Information on submitting SPL files using eLIST may be found in the guidance for industry titled "SPL Standard for Content of Labeling Technical Qs and As" at <http://www.fda.gov/downloads/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf>.

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications for this NDA, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in MS Word format that includes the changes approved in this supplemental application.

### **SUBPART H FULFILLED**

We approved this NDA 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 commitment made under 21 CFR 314.510 for the original NDA approval dated October 29, 2007.

### **RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS**

The REMS for Tassigna<sup>®</sup> was originally approved on March 15, 2010, and a REMS modification was approved on June 17, 2010. The REMS consists of a Medication Guide, communication plan, and a timetable for submission of assessments of the REMS. Your proposed modifications to the REMS consist of a revised Medication Guide and revised communication plan to reflect new information provided in S-006, including updated dosing information concerning mixing the contents of the capsules with applesauce.

Your proposed modified REMS, submitted on January 10, 2011, and appended to this letter, is approved.

The timetable for submission of assessments of the REMS will remain the same as that approved on March 15, 2010. There are also no changes to the REMS assessment plan described in our March 15, 2010, letter.

We remind you that 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. With respect to any such postapproval study, you must include the status of such study, including whether any difficulties completing the study have been encountered. With respect to any such postapproval clinical trial, you must include the status of such clinical trial, including whether enrollment has begun, the number of participants enrolled, the expected completion date, whether any difficulties completing the clinical trial have been encountered, and registration information with respect to requirements under subsections (i) and (j) of section 402 of the Public Health Service Act. 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

21 CFR 314.81(b)(2)(vii) and including any material or significant 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 also 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 505-1(g)(2)(A) of the FDCA.

If you currently distribute or plan to distribute an authorized generic product under this NDA, you will also need to submit a REMS, REMS supporting document, and any required appended documents for that authorized generic, to this NDA. In other words, you must submit a complete proposed REMS that relates only to the authorized generic product. Review and approval of the REMS is required before you may market your product.

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

**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 included)**

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

**POSTMARKETING COMMITMENTS – FULFILLED**

We have received your submission dated March 12, 2010, containing the final report for the following postmarketing commitment listed in the October 29, 2007, approval letter.

**1225-1:**

To submit the complete study report (with at least 24 months follow-up of all patients) and data from study 2101, a Phase 2 multicenter study of nilotinib in patients with imatinib resistant or intolerant chronic myeloid leukemia in chronic and accelerated phases respectively (arms 4 & 3, respectively).

Protocol Submission: Study 2101 filed to IND 69,764 in April 2004 (SN 000)  
Study Start: May 2004  
Final Report Submission: by August 2010

We have reviewed your submission and conclude that the above commitment was fulfilled.

We remind you that there are other postmarketing commitments listed in the October 29, 2007, approval letter and a Subpart H postmarketing requirement listed in the June 17, 2010, approval letter for Supplement 005, that are still open.

### **PROMOTIONAL MATERIALS**

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit the following, in triplicate, (1) a cover letter requesting advisory comments, (2) the proposed materials in draft or mock-up form with annotated references, and (3) 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

You must submit final promotional materials and package insert(s), accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 314.81(b)(3)(i)]. Form FDA 2253 is available at <http://www.fda.gov/opacom/morechoices/fdaforms/cder.html>; instructions are provided on 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 decide to 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, at least 24 hours prior to issuing the letter, an electronic copy of the letter to this NDA to the following address:

MedWatch Program  
Office of Special Health Issues  
Food and Drug Administration  
10903 New Hampshire Ave  
Building 32, Mail Stop 5353  
Silver Spring, MD 20993

### **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 Christy Cottrell, Regulatory Project Manager, at (301) 796-4256.

Sincerely,

*{See appended electronic signature page}*

Ann T. Farrell, M.D.  
Acting Director  
Division of Hematology Products  
Office of Oncology Drug Products  
Center for Drug Evaluation and Research

ENCLOSURES:

Content of Labeling  
REMS

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

/s/  
-----

ANN T FARRELL  
01/14/2011