



NDA 021588/S-030  
NDA 021588/S-031

**SUPPLEMENT APPROVAL**

Novartis Pharmaceuticals Corporation  
Attention: John A. Robinson, Ph.D.  
Senior Associate Director, Drug Regulatory Affairs  
Oncology Global Development  
One Health Plaza  
East Hanover, NJ 07936-1080

Dear Dr. Robinson:

Please refer to your Supplemental New Drug Applications (sNDAs) dated June 2, 2010, received June 2, 2010, and November 18, 2010, received November 18, 2010, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Gleevec<sup>®</sup> (imatinib mesylate) Tablets, 100 mg and 400 mg.

We acknowledge receipt of your amendments dated October 14, 2010; December 9, 2010; February 9, 2011; March 1, 2011; March 10, 2011; March 31 (3 electronic), 2011; and April 1 (electronic), 2011.

The "Prior Approval" supplemental new drug application (S-030) provides the final clinical study report of the newly diagnosed pediatric Ph+ CML trial, to supply FDA requested information and to provide proposed draft labeling (post-marketing commitment 1068-1).

The "Prior Approval" supplemental new drug application (S-031) provides labeling revisions involving hepatotoxicity, growth retardation, and tumor lysis syndrome in the Highlights of Prescribing Information, Full Prescribing Information-Warnings and Precautions (5.4, 5.12 and 5.13) and Adverse Reactions Sections (Postmarketing Experience 6.13).

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

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>. Content of labeling must be identical to the enclosed labeling (text for the package insert) with the

addition of any labeling changes in pending “Changes Being Effected” (CBE) supplements, as well as 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, as well as annual reportable changes and annotate each change. To facilitate review of your submission, provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

#### **SUBPART H FULFILLED**

We approved supplemental NDA, S-016 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, S-030, fulfills your commitment made under 21 CFR 314.510.

#### **POSTMARKETING COMMITMENT FULFILLED**

We have received your submission dated June 2, 2010, containing the final report for the following postmarketing commitment listed in the September 27, 2006, approval letter.

1068-1	To follow up safety and efficacy information for Study 2108. Updated status reports to be submitted in March 2007 and March 2008. Provision of further long term data will be reassessed following the submission of the March 2008 study status report and will depend on the number of patients still on study at that time.
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We have reviewed your submission and conclude that the above commitment was fulfilled.

We remind you that there are postmarketing commitments listed in the December 19, 2008, approval letter and the March 25, 2011, postmarketing commitments acknowledgment letter (a result of the fulfilled postmarketing commitments in our October 19, 2006, approval letter) that are still open.

## **REQUIRED PEDIATRIC ASSESSMENTS**

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

Because none of these criteria apply to your application, you are exempt from this requirement.

## **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>.

All promotional materials that include representations about your drug product must be promptly revised to be consistent with the labeling changes approved in this supplement, including any new safety information [21 CFR 314.70(a)(4)]. The revisions in your promotional materials should include prominent disclosure of the important new safety information that appears in the revised package labeling. Within 7 days of receipt of this letter, submit your statement of intent to comply with 21 CFR 314.70(a)(4) to the address above or by fax to 301-847-8444.

## **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 Yolanda Adkins, Regulatory Project Manager, at (301) 796-2850.

Sincerely,

*{See appended electronic signature page}*

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

ENCLOSURE:  
Package Insert

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**This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.**  
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/s/  
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ANN T FARRELL  
04/01/2011