DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 021588/S-035 **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 Application (sNDA) dated August 2, 2011, received August 2, 2011, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Gleevec® (imatinib mesylate) Tablets, 100 mg and 400 mg.

We also refer to our approval letter dated January 31, 2012, which contained the following errors:

Part of the approved S-035 labeling supplement included the addition of a new section 2.9 Dosage and Administration Adjuvant GIST in the Full Prescribing Information. However, with this addition, subsequent sections following 2.9 were not renumbered correctly resulting in two sections titled with 2.9. Section 2.9, 2.10 and 2.11 of the Dosage and Administration in the Full Prescribing Information have now been renumbered in the S-035 labeling to 2.10, 2.11, and 2.12 respectively. References to these sections in the following locations required correcting Highlights of Prescribing Information (Dosage and Administration, Drug Interactions), Full Prescribing Information Table of Contents (Dosage and Administration), Full Prescribing information Dosage and Administration, Warnings and Precautions (5.2, 5.4), Adverse Reactions (6.1, 6.11), Drug Interactions (7.1), and Use in Specific Populations (8.6, 8.7).

This replacement approval letter incorporates the correction of the error. The effective approval date will remain January 31, 2012, the date of the original approval letter.

We acknowledge receipt of your amendments dated October 20, 2011; November 1, 2011; November 2, 2011; November 14, 2011; December 1, 2011; December 9, 2011; December 20, 2011, January 12, 2012; January 26, 2012; January 27 (3), 2012 and January 30 (2 e-mails), 2012.

This “Prior Approval” supplemental new drug application proposes conversion of accelerated approval to full approval of the indication for adjuvant treatment of adult patients following complete resection of Kit (CD117) positive gastrointestinal stromal tumors (GIST) and provides updated Gleevec prescribing information.

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.

CONTENT OF LABELING

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).

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 this drug product for this indication has an orphan drug designation, you are exempt from this requirement.

SUBPART H FULFILLED

We approved NDA 021588/S-025, 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 requirements made under 21 CFR 314.510.

We have received your submissions dated August 2, 2011 (111-4); November 2, 2011 (111-1), and December 1, 2011 (111-2 and 111-3), containing the final reports for the following postmarketing requirements listed in the December 19, 2008, approval letter.

111-1. To complete the ongoing clinical trial entitled "A single phase III randomized double-blind study of adjuvant imatinib versus placebo in patients who had complete gross resection of their primary gastrointestinal stromal tumor (GIST)" and provide a report and datasets at four years of follow-up for relapse-free survival.

Protocol Submission: NA
Trial Start Date: July 31, 2002 (in progress)
Study Report Submission: November 30, 2010

111-2. To complete the ongoing clinical trial entitled "A single phase III randomized double-blind study of adjuvant imatinib versus placebo in patients who had complete gross resection of their primary gastrointestinal stromal tumor (GIST)" and provide a report and datasets at five years of follow-up for relapse-free survival.

Protocol Submission: NA
Trial Start Date: July 31, 2002 (in progress)
Report and Dataset Submission: November 30, 2011

111-3. To complete the ongoing clinical trial entitled "A single phase III randomized double-blind study of adjuvant imatinib versus placebo in patients who had complete gross resection of their primary gastrointestinal stromal tumor (GIST)" and provide a report and datasets after collection of 5 years of overall survival data.

Protocol Submission: NA
Trial Start Date: July 31, 2002 (in progress)
Report and Dataset Submission: November 30, 2011

111-4. To complete the clinical trial entitled "Short (12 months) versus long (36 months) duration of adjuvant treatment with the tyrosine kinase inhibitor imatinib mesylate of operable GIST with a high risk of recurrence (SSG XVIII/AIO)" and provide a report and datasets.

Protocol Submission: NA
Trial Start Date: February 2004 (in progress)
Report and Dataset Submission: November 30, 2011

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

We remind you that there are postmarketing commitments listed in the March 25, 2011, postapproval postmarketing commitment letter that are still open.

POSTMARKETING COMMITMENTS SUBJECT TO THE REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitment:

1870-1 Submit the per protocol overall survival follow-up (data cut-off date will be at least 5 years from the date of the last patient randomized) for Trial SSGXVIII/AIO entitled "Short (12 months) versus long (36 months) duration of adjuvant treatment with the tyrosine kinase inhibitor imatinib mesylate of operable GIST with a high risk for recurrence (SSG XVIII/AIO)". Updated OS results including datasets will be provided as an addendum to the full clinical trial report (dated 27-June-2011).

The timetable you submitted on January 30, 2012 (by e-mail) states that you will conduct this trial according to the following schedule:

Final Protocol Submission:	08/11
Survival Data Cutoff Date:	01/14
Final Report Submission:	03/15
Dataset Submission:	03/15

Submit clinical protocols to your IND 055666 for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all final reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii) you should include a status summary of each commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies/trials, number of patients entered into each study/trial. All submissions, including supplements, relating to these postmarketing commitments should be prominently labeled "**Postmarketing Commitment Protocol**," "**Postmarketing Commitment Final Report**," or "**Postmarketing Commitment Correspondence**."

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
Office of Prescription Drug Promotion (OPDP)
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 Office of Prescription Drug Promotion (OPDP), 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, R.N., MSHA, Regulatory Project Manager, at (301) 796-2850.

Sincerely,

{See appended electronic signature page}

Patricia Keegan, M.D.
Director
Division of Oncology Products 2
Office of Hematology and Oncology Products
Center for Drug Evaluation and Research

Robert L. Justice, M.D., M.S.
Director
Division of Oncology Products 1
Office of Hematology and Oncology Products
Center for Drug Evaluation and Research

ENCLOSURE:
Content of Labeling

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

/s/

JOSEPH E GOOTENBERG on behalf of PATRICIA KEEGAN
01/31/2012

ROBERT L JUSTICE
01/31/2012