



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-588/S020

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

Attention: Jeremy Brace
Senior Associate Director
Drug Regulatory Affairs

Dear Mr. Brace:

Please refer to your supplemental new drug application dated July 31, 2006, received August 1, 2006, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Gleevec (imatinib mesylate) 100 and 400 mg tablets.

We acknowledge receipt of your submissions dated December 5, 2006; May 11, 2007; July 13, 2007; and August 22, 2007.

Your submission of July 13, 2007 constituted a complete response to our May 31, 2007 action letter.

This supplemental new drug application provides for the updating of the labeling to include the 60- month data from Study 106 for newly diagnosed Philadelphia positive chronic myeloid leukemia (CML) .

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

We are waiving the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of prescribing information. This waiver applies to all future supplements containing revised labeling unless we notify you otherwise.

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)] 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). Upon receipt, we will transmit that version to the National Library of Medicine for public dissemination. For administrative purposes, please designate this submission, "SPL for approved NDA 21-588/S020."

We note your request to consider fulfilled commitment #7, stated below, and thereby convert this indication to full approval. We have considered your request and have determined that follow-up on Study 106 should continue for the agreed-upon additional two years. We will reconsider your request when the final data through January 2009 is submitted.

7. To provide interval follow-up safety and efficacy information on study 106 annually, for three additional years, and survival data and serious adverse event data thereafter for another three years. Timeline: First interval report submitted on December 22, 2003 and to be submitted annually thereafter until January 2009.

We remind you of your other postmarketing study commitments as listed below.

Prior commitment required for accelerated approval of Gleevec for newly diagnosed Philadelphia positive CML in pediatric patients (NDA 21-588/016 submitted March 27, 2006 and approved September 27, 2006):

1. To provide 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 re-assessed following the submission of the March 2008 study status report and will depend on the number of patients still on study at that time.

We refer to your submission of May 4, 2007 regarding this commitment. This submission is under review by FDA.

Prior commitments required for accelerated approval of Gleevec for GIST patients (NDA 21-335/001 submitted October 15, 2001 and approved February 1, 2002):

4. Submit data from the two ongoing multicenter trials of imatinib that are testing 400 mg/day versus 800 mg/day in patients with GIST (EORTC and NCI sponsored trials). Response rate, duration of response, safety and survival data should be submitted. The data should be submitted in a timeline consistent with the statistical analysis plan of each respective protocol.

We note that this study is ongoing.

7. To provide interval follow-up safety and efficacy information on study 106 annually, for three additional years, and survival data and serious adverse event data thereafter for another three years. Timeline: First interval report submitted on December 22, 2003 and to be submitted annually thereafter until January 2009.

See above FDA comment.

Final study reports should be submitted to this NDA as a supplemental application. For administrative purposes, all submissions relating to this Phase 4 commitment must be clearly designated "**Subpart H Phase 4 Commitment.**"

Prior commitments which are not a condition of accelerated approval of Gleevec for CML patients (NDA 21-335/000 submitted February 1, 2001 and approved May 10, 2001):

11. To conduct the appropriate study to assess the potential drug interaction between Gleevec and a substrate of CYP2D6 and to submit the final study report.

We refer to your submission of December 15, 2006 regarding this commitment. This submission is under review by FDA.

14. To evaluate the etiology and treatment of the fluid retention syndrome associated with imatinib treatment.

We refer to your submission of September 5, 2006 regarding this commitment. This submission is under review by FDA.

Prior commitment which is not a condition of accelerated approval of Gleevec for GIST patients (NDA 21-335/001 submitted October 15, 2001 and approved February 1, 2002):

15. Submit the PK/PD data from the comparison of 400 mg/day versus 800 mg/day in GIST patients in the two ongoing multicenter trials of imatinib (EORTC and NCI sponsored trials).

We note that this study is ongoing.

Prior commitment which is not a condition of accelerated approval of Gleevec for newly diagnosed CML patients (NDA 21-335/004 submitted June 28, 2002 and approved December 20, 2002):

18. To conduct a prospective study performed in patients receiving both Gleevec and a potent CYP3A4 inducer such as phenytoin, phenobarbital, or carbamazepine and submit a final study report. The purpose of this study is to determine the dose of Gleevec that is necessary to produce similar AUCs in these patients on enzyme inducers to those achieved in adult patients receiving the usual recommended dose (400 mg/day). Timeline: Protocol submission June 2003; study start date December 2003; and final report December 2004.

We refer to your submission of December 15, 2006 regarding this commitment. This submission is under review by FDA.

Submit clinical protocols to your IND for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all study 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, number of patients entered into each study. All submissions, including supplements, relating to these postmarketing study commitments must be prominently labeled "Postmarketing Study Commitment Protocol", "Postmarketing Study Commitment Final Report", or "Postmarketing Study Commitment Correspondence."

In addition, submit three copies of the introductory promotional materials that you propose to use for this product. Submit all proposed materials in draft or mock-up form, not final print. Send two copies of both the promotional materials and the package insert directly 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

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

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 Dotti Pease, Regulatory Project Manager, at (301) 796-1434.

Sincerely,

{See appended electronic signature page}

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

Enclosure : Labeling

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

/s/

Ann Farrell
9/13/2007 10:26:53 AM