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APPROVAL PACKAGE FOR:

APPLICATION NUMBER

21-335/S-004

Approval Letter(s)

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-335/S-004

Novartis Pharmaceuticals Corporation
One Health Plaza, Building 105/2W200
Hanover, New Jersey 07936-1080

Attention: Robert A. Miranda, Associate Director
Drug Regulatory Affairs

Dear Mr. Miranda:

Please refer to your supplemental new drug application dated June 28, 2002, received June 28, 2002, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Gleevec™ (imatinib mesylate). 100 mg capsules.

We acknowledge receipt of your submissions dated July 23; August 15, 26 and 30; September 4; November 20 and 21; December 19, 2002.

This new drug application provides for the use of Gleevec™ (imatinib mesylate), 100 mg capsules for the treatment of newly diagnosed adult patients with Philadelphia chromosome positive chronic myeloid leukemia (CML). Follow-up is limited.

We have completed the review of this supplemental application, as amended, according to the regulations for accelerated approval, and have concluded that adequate information has been presented to approve Gleevec™ (imatinib mesylate) 100 mg capsules for use as recommended in the agreed upon enclosed labeling text. Accordingly, the application is approved under 21 CFR 314 Subpart H. Approval is effective on the date of this letter. Marketing of this drug product and related activities are to be in accordance with the substance and procedures of the referenced accelerated approval regulations.

The final printed labeling (FPL) must be identical to the enclosed labeling.

Please submit 20 paper copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please mount individually ten of the copies on heavy-weight paper or similar material. Alternatively, you may submit the FPL electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format – NDAs* (January 1999). For administrative purposes, this submission should be designated "FPL for approved NDA 21-335/S-004." Approval of this submission by FDA is not required before the labeling is used.

Products approved under the accelerated approval regulations, 21 CFR 314.510, require further adequate and well-controlled studies to verify and describe clinical benefit. We remind you of your post marketing study (Subpart H Phase 4 commitments) specified in your submission dated December 19, 2002. The commitment, along with any completion dates agreed upon, is listed below.

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 expected January 2004 and annually thereafter until January 2009.

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 Commitments."

In addition, we note your following Phase 4 commitment, specified in your submission dated December 19. 2002, that is not a condition of the accelerated approval. This commitment, along with any completion dates agreed upon, is:

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.

Protocols, data, and final reports should be submitted to your IND for this product and a copy of the cover letter sent to this NDA. If an IND not be required to meet your Phase 4 commitments, please submit protocol, data, and final reports to this NDA as correspondences. For administrative purposes, all submissions, including labeling supplements, relating to these Phase 4 commitments must be clearly designated "Phase 4 Commitments."

Additionally, we refer to prior accelerated approval commitments and phase 4 commitments as stated in the approval letters dated May 10, 2001 and February 1, 2002.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, call Ann Staten, Regulatory Project Manager, at (301) 594-0490.

Sincerely,

{See appended electronic signature page}

/S/

Richard Pazdur, M.D.
Director
Division of Oncology Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

Enclosure

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

/s/

Richard Pazdur
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