



NDA 022068/S-019

**SUPPLEMENT APPROVAL
FULFILLMENT OF POSTMARKETING
COMMITMENT**

Novartis Pharmaceuticals Corporation
Attention: Margaret M. Woo, PharmD
Senior Associate Director, Drug Regulatory Affairs
One Health Plaza
East Hanover, NJ 07936-1080

Dear Dr. Woo:

Please refer to your Supplemental New Drug Application (sNDA) dated March 28, 2014, received March 28, 2014, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for TASIGNA[®] (nilotinib) capsules, 150 and 200 mg.

We acknowledge receipt of your amendments dated May 13; August 14; and September 10 and 17, 2014.

This “Prior Approval” supplemental new drug application provides for updates to the Drug Interactions section of the package insert based on final results of Study CAMN107A2128 entitled “*An open-label, two-period, fixed-sequence study to evaluate the effects of multiple doses of nilotinib on the pharmacokinetics of midazolam in CML patients who are resistant and/or intolerant against at least one prior therapy with a BCR-ABL tyrosine kinase inhibitor.*”

APPROVAL & LABELING

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.

WAIVER OF HIGHLIGHTS SECTION

Please note that we have previously granted a waiver of the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of prescribing information.

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, Medication Guide), 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 that include labeling changes 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.

FULFILLMENT OF POSTMARKETING COMMITMENT

We have received your submission dated March 28, 2014, containing the final report for the following postmarketing commitment listed in the October 27, 2007 approval letter.

- 1225-4 Conduct a clinical study or studies to evaluate whether multiple doses of nilotinib alter the metabolism of a sensitive CYP2C9 substrate (for example, S-warfarin). If a significant interaction is demonstrated, additional clinical studies may be needed to evaluate whether multiple doses of nilotinib alter the metabolism of a sensitive CYP2C8 substrate (for example, repaglinide) and/or a sensitive CYP3A4 substrate (for example, midazolam).

Protocol Submission: by July 2008

Study Start: by September 2008
Final Report Submission: by June 2009

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

This completes all of your postmarketing requirements and postmarketing commitments listed in the October 29, 2007 approval letter.

We remind you that there is a postmarketing requirement listed in the June 17, 2010 approval letter that is 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
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/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf>.

Information and Instructions for completing the form can be found at

<http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf>. 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>.

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, please Patricia Garvey, Regulatory Project Manager Team Leader, at (301) 796-8493.

Sincerely,

{See appended electronic signature page}

Robert C. Kane, MD
Deputy Director for Safety
Division of Hematology Products
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/

ROBERT C KANE
09/25/2014