



NDA 022068/S-013

**SUPPLEMENT APPROVAL/
RELEASE REMS REQUIREMENT/
REMS ASSESSMENT ACKNOWLEDGMENT**

Novartis Pharmaceuticals Corporation
Attention: Katie Chon
Drug Regulatory Affairs
One Health Plaza
East Hanover, NJ 07936-1080

Dear Ms. Chon:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Tasigna[®] (nilotinib) 150 and 200 mg Capsules.

We also refer to your risk evaluation and mitigation strategy (REMS) assessment dated March 15, 2013. After consultation between the Office of Surveillance and Epidemiology and the Office of New Drugs, we found the REMS assessment to be complete.

We acknowledge receipt of your proposal to eliminate the requirement for the approved Tasigna[®] (nilotinib) REMS, also included in your March 15, 2013, submission. We consider this proposal to be a supplemental application to your NDA.

We have completed our review of this supplemental application. It is approved, effective on the date of this letter.

RISK EVALUATION AND MITIGATION STRATEGY (REMS) REQUIREMENT

The REMS for Tasigna[®] (nilotinib) was approved on March 15, 2010 and the most recent REMS modification was approved on October 26, 2011. The REMS consists of a Medication Guide, communication plan, and a timetable for submission of assessments of the REMS.

You propose that FDA no longer require a REMS for Tasigna[®] (nilotinib).

We have determined that maintaining the Medication Guide as part of the approved labeling is adequate to address the serious and significant public health concern and meets the standard in 21 CFR 208.1. Therefore, it is no longer necessary to include the Medication Guide as an element of the approved REMS to ensure that the benefits of Tasigna[®] (nilotinib) outweigh its risks.

Because the assessment demonstrates that the communication plan has been completed and has met its goals, we have determined that it is no longer necessary to include it as an element of the approved REMS to ensure that the benefits of the drug outweigh the risks.

Therefore, we agree with your proposal, and a REMS for Tasigna[®] (nilotinib) is no longer required.

We remind you that the Medication Guide will continue to be part of the approved labeling in accordance with 21 CFR 208.

OTHER

We request that you perform, as a component of your periodic postmarket safety reporting (i.e., in your Periodic Safety Update Report (PSUR) or, if applicable, the Periodic Benefit-Risk Evaluation Report (PBRER)), an analysis of the post-marketing cases of QT prolongation, ventricular arrhythmias, sudden death, or syncope reported in association with Tasigna[®] (nilotinib) to Novartis Pharmaceutical Corporation (during the reporting period and cumulatively). The analysis should include possible factors that prolonged the QT interval (e.g., dosing with food, dosing outside of the 12 hour frequency, interacting medication initiated, change in patient's health status, failure to adjust dose, lack of ECG monitoring, lack of electrolyte monitoring, etc.).

In addition, we request that you perform follow-up of serious cases of QT prolongation, ventricular arrhythmia, sudden death, and syncope received from spontaneous reporting, post marketing surveillance, and global clinical trials, using a targeted questionnaire/checklist.

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.

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

We remind you that, as stated in our October 29, 2007, approval letter, in addition to the usual postmarketing reporting of adverse drug experiences (21 CFR 314.80(c)), you will initiate a 15-day Alert report and follow-up for each of the following:

1. Medication errors involving dosing outside of the Tassigna (nilotinib) labeled recommendations including, but not limited to:
 - dosing with food
 - dosing outside of the recommended 12 hour frequency
 - taking more tablets than prescribed or recommended by the sponsor
 - or administration with other drug products potentially affecting the absorption or metabolism of nilotinib (e.g. CYP3A4 inhibitor)
2. QTc prolongation. These reports will include information and follow-up as to whether the event was the result of a medication error (e.g., dosing with food, dosing outside of the 12 hr frequency, etc).

If you have any questions, call Mrs. Diane Leaman, Safety Regulatory Project Manager, at (301) 796-1424.

Sincerely,

{See appended electronic signature page}

Robert C. Kane, M.D.
Deputy Director for Safety
Division of Hematology Products
Office of Hematology and Oncology Products
Center for Drug Evaluation and Research

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
05/17/2013