DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 022291/S-006

SUPPLEMENT APPROVAL
REMOVE REMS ELEMENTS
REMS MODIFICATION

GlaxoSmithKline
Attention: Dennis R. Williams, Pharm.D.
Associate Director, Regulatory Affairs, Oncology
1250 South Collegeville Road
P.O. Box 5089
Collegeville, PA 19426

Dear Dr. Williams:

Please refer to your Supplemental New Drug Application (sNDA) dated January 11, 2011, received January 11, 2011, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Promacta® (eltrombopag) Tablets.

We acknowledge receipt of your amendments dated March 16, 2011, September 8, 2011, October 31, 2011, November 8, 14, and 18, 2011 and December 2, 2011 and your risk evaluation and mitigation strategy (REMS) assessment dated November 30, 2010.

We also refer to our REMS modification notification letter dated November 12, 2010; the teleconference held on February 11, 2011 between the Division of Hematology Products and GlaxoSmithKline when we discussed the REMS for Promacta; and our REMS advice letter dated July 25, 2011.

This "Prior Approval" supplemental new drug application proposes revisions to the labeling (package insert and Medication Guide) for Promacta® (eltrombopag) Tablets; modifications to the Promacta® (eltrombopag) REMS to eliminate the elements to assure safe use (ETASU), the Medication Guide, and the implementation system; and the addition to the Promacta® REMS of a communication plan to provide for the dissemination of information about the REMS modification eliminating the requirement for the ETASU, about how to obtain Promacta® (eltrombopag) Tablets, and reminding prescribers about the serious risks associated with Promacta® (eltrombopag) and appropriate patient selection.

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, text for the 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 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).

We request that the labeling approved today be available on your website within 10 days of receipt of this letter.

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.

RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS

The REMS for Promacta® (eltrombopag) Tablets was originally approved on November 20, 2008, and the most recent REMS modification was approved on March 5, 2010. The REMS consists of a Medication Guide, ETASU, an implementation system, and a timetable for submission of assessments of the REMS.

Your proposed modification to the REMS consists of eliminating the requirement for the Medication Guide, the ETASU, and the implementation system as elements of the REMS; adding a communication plan; and revising the timetable for submission of assessments of the REMS.

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. We have also determined that the revised product labeling and the addition of the communication plan to the REMS will be adequate to address the serious risks associated with the use of Promacta® (eltrombopag). Therefore, it is no longer necessary to include the Medication Guide, ETASU, and implementation system as elements of the approved REMS to ensure that the benefits of Promacta® (eltrombopag) outweigh its risks. We remind you that the Medication Guide will continue to be part of the approved labeling for Promacta® (eltrombopag) in accordance with 21 CFR part 208.

Your proposed modified REMS, submitted on December 2, 2011, and appended to this letter, is approved.

The modified REMS consists of a communication plan and a revised timetable for submission of assessments of the REMS. We remind you that the timetable for submission of assessments was revised to June 30, 2012, June 30, 2015, and June 30, 2019.

At least 90 days before the assessments will be conducted, you should update the REMS supporting document to include revised assessment instrument and methodology information. Prominently identify the submission containing the assessment instruments and methodology with the following wording in bold capital letters at the top of the first page of the submission:

> **NDA 022291 REMS CORRESPONDENCE**
> **(insert concise description of content in bold capital letters, e.g.,**
> **UPDATE TO REMS SUPPORTING DOCUMENT - ASSESSMENT METHODOLOGY)**

The revised REMS assessment plan should include, but is not limited to, the following:

1. An evaluation of healthcare providers' understanding of the serious risks associated with the use of Promacta.

2. Only for the REMS assessment due by June 30, 2012, provide the following information about the revised communication plan:
    - The date of the launch of the revised communication plan
    - Number of recipients of the Dear Health Care Provider (DHCP) letter
    - Number of DHCP letters returned
    - Number of electronic DHCP letters opened
    - Source of recipient lists
    - Number of Dear Professional Society letters sent

- Number of Dear Professional Society letters returned

3. Information on the status of any postapproval study or clinical trial required under section 505(o)(3) or otherwise undertaken to investigate a safety issue. With respect to any such postapproval study, you must include the status of such study, including whether any difficulties completing the study have been encountered. With respect to any such postapproval clinical trial, you must include the status of such clinical trial, including whether enrollment has begun, the number of participants enrolled, the expected completion date, whether any difficulties completing the clinical trial have been encountered, and registration information with respect to requirements under subsections (i) and (j) of section 402 of the Public Health Service Act. You can satisfy these requirements in your REMS assessments by referring to relevant information included in the most recent annual report required under section 506B and 21 CFR 314.81(b)(2)(vii) and including any material or significant updates to the status information since the annual report was prepared. Failure to comply with the REMS assessments provisions in section 505-1(g) could result in enforcement action.

In addition to the assessments submitted according to the timetable included in the approved REMS, you must submit a REMS assessment and may propose a modification to the approved REMS when you submit a supplemental application for a new indication for use as described in section 505-1(g)(2)(A) of FDCA.

An authorized generic drug under this NDA must have an approved REMS prior to marketing. Should you decide to market, sell, or distribute an authorized generic drug under this NDA, contact us to discuss what will be required in the authorized generic drug REMS submission.

Prominently identify the submission containing the REMS assessments or proposed modifications of the REMS with the following wording in bold capital letters at the top of the first page of the submission as appropriate:

NDA 022291 REMS ASSESSMENT

NEW SUPPLEMENT FOR NDA 022291
PROPOSED REMS MODIFICATION
REMS ASSESSMENT

NEW SUPPLEMENT (NEW INDICATION FOR USE)
FOR NDA 22291
REMS ASSESSMENT
PROPOSED REMS MODIFICATION (if included)

If you do not submit electronically, please send 5 copies of REMS-related submissions.

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
Division of Drug Marketing, Advertising, and Communications
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 Division of Drug Marketing, Advertising, and Communications (DDMAC), 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, call Mara Miller, Regulatory Project Manager, at (301) 796-0683.

Sincerely,

{See appended electronic signature page}

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

ENCLOSURE(S):
Content of Labeling
REMS

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
12/06/2011