NDA 022291/S-001

SUPPLEMENT APPROVAL

GlaxoSmithKline LLC
Attention: Dennis R. Williams, Pharm.D.
Associate Director
1250 South Collegeville Road, UP4110
Collegeville, PA 19426

Dear Dr. Williams:

Please refer to your Supplemental New Drug Application (sNDA) dated March 19, 2009, received March 19, 2009, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Promacta® (eltrombopag) 25 mg, 50 mg and 75 mg Tablets.

We acknowledge receipt of your amendments dated May 14, June 4, July 9 and 17, December 7, 2009; January 7, August 27, September 15, 20 and 29, October 18, November 10, December 7 and 22, 2010: January 18 and 25, and February 1, 2011, and your risk evaluation and mitigation strategy (REMS) assessment dated November 30, 2010.

The August 27, 2010, submission constituted a complete response to our January 15, 2010, action letter.

This supplemental new drug application provides for conversion of accelerated approval to full approval status, revised labeling, and proposed modifications to the approved REMS.

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, 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 with the revisions 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.

SUBPART H FULFILLED

We approved this NDA under the regulations at 21 CFR 314 Subpart H for accelerated approval of new drugs for serious or life-threatening illnesses. Approval of this supplement fulfills the requirements made under 21 CFR 314.510.

PMR 1196-1. To complete trial TRA102537 entitled, "A randomized, double-blind, placebo-controlled Phase 3 study, to evaluate the efficacy, safety and tolerability of eltrombopag, a thrombopoietin receptor agonist, administered for 6 months as oral tablets once daily in adult subjects with previously treated chronic idiopathic thrombocytopenic purpura (ITP)."

PMR 1196-2. To complete trial TRA108057 entitled, "An open-label repeat dosing study of eltrombopag olamine in adult subjects, with chronic idiopathic thrombocytopenic purpura (ITP)."

POSTMARKETING REQUIREMENTS UNDER 505(o)

We remind you that there are postmarketing requirements listed in the November 20, 2008 approval letter that are still open.

POSTMARKETING COMMITMENTS NOT SUBJECT TO THE REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitment:

PMC 1736-1 Develop and propose a 12.5 mg dosing form to allow for proper dose titration when eltrombopag needs to be co-administered in patients at risk for clinically relevant changes in eltrombopag exposure [e.g., East Asian patients with hepatic impairment and super responders (patients who exceeded 400,000 platelets per microliter at the lowest approved once daily dose)]. The 12.5 mg dosage form

should be sufficiently distinguishable from the 25 mg, 50 mg and 75 mg tablets. Full chemistry, manufacturing and controls (CMC) information for the 12.5 mg dosage form, including the batch data and stability data, labels, updated labeling, and updated environmental assessment section, is required. Provide the final report in a prior approval supplement to the NDA.

The timetable you submitted on January 10, 2011, states that you will conduct this study according to the following schedule:

Final Protocol Submission:	April 11, 2011
Study/Trial Completion:	Not Applicable
Final Report Submission:	October 11, 2011

Submit clinical protocols to your IND 063293 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/trials, number of patients entered into each study/trial. All submissions, including supplements, relating to these postmarketing commitments should be prominently labeled "**Postmarketing Commitment Protocol**," "**Postmarketing Commitment Final Report**," or "**Postmarketing Commitment Correspondence**."

RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS

The REMS for Promacta® (eltrombopag) Tablets was originally approved on November 20, 2008, and a REMS modification was approved on and March 5, 2010. The REMS consists of a Medication Guide, elements to assure safe use, an implementation system, and a timetable for submission of assessments of the REMS. Your proposed modifications to the REMS consist of elimination of the Prescriber Introductory letter and Pharmacy Introductory letter, as well as revisions to the Medication Guide, Overview for Healthcare Providers, Instructional Video (storyboard), Promacta Cares Website, Prescriber Enrollment Form, Overview for Patients and Patient Enrollment Form.

We remind you that section 505-1(f)(8) of FDCA prohibits holders of an approved covered application with elements to assure safe use from using any element to block or delay approval of an application under section 505(b)(2) or (j). A violation of this provision in 505-1(f) could result in enforcement action.

Your proposed modified REMS, submitted on February 1, 2011, and appended to this letter, is approved.

The timetable for submission of assessments of the REMS will remain the same as that approved on November 20, 2008.

There are no changes to the REMS assessment plan described in our November 20, 2008 letter.

We remind you that assessments of an approved REMS must also include, under section 505-1(g)(3)(B) and (C), information on the status of any postapproval study or clinical trial required under section 505(o) 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.

If you currently distribute or plan to distribute an authorized generic product under this NDA, you must submit a complete proposed REMS that relates only to the authorized generic product. Submit a proposed REMS, REMS supporting document, and any required appended documents as a prior approval supplement. Approval of the proposed REMS is required before you may market your authorized generic product.

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 022291
REMS ASSESSMENT
PROPOSED REMS MODIFICATION (if included)

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

As stated above, we acknowledge receipt of your November 30, 2010 REMS assessment. In accordance with Section 505-1(h)(2) of the FDCA, we notified you through a fax sent on January 27, 2011 that we were initiating discussions of your assessment. In follow-up to that fax, we have determined that the REMS assessment is adequate and only the modifications to your REMS described above are necessary.

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.

All promotional materials that include representations about your drug product must be promptly revised to be consistent with the labeling changes approved in this supplement, including any new safety information [21 CFR 314.70(a)(4)]. The revisions in your promotional materials should include prominent disclosure of the important new safety information that appears in the revised package labeling. Within 7 days of receipt of this letter, submit your statement of intent to comply with 21 CFR 314.70(a)(4) to the address above or by fax to 301-847-8444.

LETTERS TO HEALTH CARE PROFESSIONALS

If you decide to issue a letter communicating important safety-related information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit, at least 24 hours prior to issuing the letter, an electronic copy of the letter to this NDA to the following address:

MedWatch Program
Office of Special Health Issues
Food and Drug Administration
10903 New Hampshire Ave
Building 32, Mail Stop 5353
Silver Spring, MD 20993

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 Hyon-Zu Lee, Pharm.D., Regulatory Project Manager, at 301-796-2192.

Sincerely,

{See appended electronic signature page}

Ann Farrell, M.D.
Director (Acting)
Division of Hematology Products
Office of Oncology Drug Products
Center for Drug Evaluation and Research

ENCLOSURES:
Content of Labeling
REMS
REMS materials

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

/s/

ANN T FARRELL
02/25/2011