DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration Silver Spring, MD 20993

NDA 021071/S-038
NDA 021410/S-026
NDA 021700/S-010

SUPPLEMENT APPROVAL

SmithKline Beecham (Cork) Ltd (d/b/a/GlaxoSmithKline)
Attention: Margaret M. Kreider, Ph.D.
Sr. Director, Regulatory Affairs
2301 Renaissance Blvd.; Mail Code 0420
King of Prussia, PA 19406-2772

Dear Dr. Kreider:

Please refer to your Supplemental New Drug Applications (sNDAs) dated and received October 22, 2010, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Avandia (rosiglitazone maleate) Tablets, 2 mg, 4 mg and 8 mg, Avandamet (rosiglitazone maleate/metformin hydrochloride) Tablets, 2 mg/500 mg, 4 mg/500 mg, 2 mg/1,000 mg, and 4 mg/1,000 mg, and Avandaryl (rosiglitazone maleate/glimepiride) Tablets, 4 mg/1 mg, 4 mg/2 mg, 4 mg/4 mg, 8 mg/2 mg, and 8 mg/4 mg.

We acknowledge receipt of your amendments dated November 1, and December 13, 2010, and January 5, 21, and 24, 2011, to NDA 021071/S-038, and November 1, 2010, to NDAs 021410/S-026, and 021700/S-010.

We also refer to our letter dated September 23, 2010, notifying you, under Section 505(o)(4) of the FDCA, of new safety information that needs to be included in the labeling for Avandia (rosiglitazone maleate), Avandamet (rosiglitazone maleate/metformin hydrochloride), and Avandaryl (rosiglitazone maleate/glimepiride). This information pertains to the potential for an increased risk of ischemic cardiovascular events associated with the use of rosiglitazone.

These supplemental new drug applications provide for revisions to the prescribing information and Medication Guides for Avandia (rosiglitazone maleate), Avandamet (rosiglitazone maleate/metformin hydrochloride), and Avandaryl (rosiglitazone maleate/glimepiride), as required in our September 23, 2010, letter. (b) (4)

We have completed our review of these supplemental applications, NDA 021071/S-038, NDA 021410/S-026, NDA 021700/S-010. They are **approved**, effective on the date of this letter, for use as recommended in the agreed-upon revisions (see attachment detailing labeling revisions for Avandia), and as recommended in the enclosed, agreed-upon labeling text (see attachments for labeling text for all three products, and labeling revisions for Avandamet (rosiglitazone maleate/metformin hydrochloride), and Avandaryl (rosiglitazone maleate/glimepiride) in "track changes" format).

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

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit, using the FDA automated drug registration and listing system (eLIST), the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format, as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm, that is identical to the enclosed labeling (text for the package inserts and text for the Medication Guide) and include the labeling changes proposed in any pending "Changes Being Effected" (CBE) supplements and any 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 these NDAs, 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 these supplemental applications.

We acknowledge your January 14, 2011, submission (sent via electronic mail) that contained final printed carton and container labels.

Please submit these labels electronically according to the guidance for industry titled "Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (June 2008)." Alternatively, you may submit 12 paper copies, with 6 of the copies individually mounted on heavy-weight paper or similar material. For administrative purposes, designate this submission "**Product Correspondence – Final Printed Carton and Container Labels for approved NDA 021071/S-038, NDA 021410/S-026, and NDA 021700/S-010."** Approval of these submissions by FDA is not required before the labeling is used.

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(s) must be promptly revised to be consistent with the labeling changes approved in these supplements, 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.

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 call Ms. Jena Weber, Regulatory Project Manager, at 301-796-1306.

Sincerely,

{See appended electronic signature page}

Mary H. Parks, M.D.
Director
Division of Metabolism and Endocrinology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

ENCLOSURES: Summary of Avandia labeling changes, Avandia labeling (clean), Avandamet labeling (tracked and clean), Avandaryl labeling (tracked and clean).

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

/s/

MARY H PARKS
02/03/2011