DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 021071/S-044
NDA 021410/S-032
NDA 021700/S-015

SUPPLEMENTS APPROVAL

SmithKline Beecham (Cork) Ltd d/b/a GlaxoSmithKline
Attention: Margaret Kreider, Ph.D.
Senior 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 (sNDA) dated and received May 18, 2012, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for AVANDIA (rosiglitazone maleate) Tablets, AVANDAMET (rosiglitazone maleate and metformin hydrochloride) Tablets, and AVANDARYL (rosiglitazone maleate and glimepiride) Tablets.

We acknowledge receipt of your amendments dated June 29, July 18, September 7, 10, and 19, and November 7, and 16, 2012, and January 8, and 11, 2013 and your risk evaluation and mitigation strategy (REMS) assessments dated May 18, 2012.

These "Prior Approval" supplemental new drug applications propose modifications to the approved REMS for AVANDIA (rosiglitazone maleate) Tablets, AVANDAMET (rosiglitazone maleate and metformin hydrochloride) Tablets, and AVANDARYL (rosiglitazone maleate and glimepiride) Tablets. The proposed modifications allow for conversion of the GlaxoSmithKline REMS for rosiglitazone medicines entitled, "Avandia-Rosiglitazone Medicines Access Program," into a single shared REMS program that includes generic rosiglitazone-containing medicines.

We have completed our review of these supplemental applications, as amended. They are approved, effective on the date of this letter, for use as recommended in the enclosed, agreed-upon labeling text.

RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS

The REMS for AVANDIA (rosiglitazone maleate) was originally approved on May 18, 2011; the REMS for AVANDAMET (rosiglitazone maleate and metformin hydrochloride) and AVANDARYL (rosiglitazone maleate and glimepiride) were originally approved on December 2, 2008. The most recent REMS modification for the three rosiglitazone-containing products was approved on May 30, 2012. 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 modification to the REMS consists of conversion of the approved REMS for AVANDIA (rosiglitazone maleate), AVANDAMET (rosiglitazone maleate and metformin hydrochloride), and AVANDARYL (rosiglitazone maleate and glimepiride) to a single shared REMS program that includes generic rosiglitazone-containing medicines.

Your proposed modified REMS, submitted on January 8, 2013, and appended to this letter, is approved.

This REMS will use a single shared system for the elements to assure safe use and the implementation system. This single shared system, known as the Rosiglitazone REMS Program, currently includes the following products:

NDA 021071	Avandia (rosiglitazone maleate)
NDA 021410	Avandamet (rosiglitazone maleate and metformin hydrochloride)
NDA 021700	Avandaryl (rosiglitazone maleate and glimepiride)
ANDA 076747	Rosiglitazone maleate

Other products may be added in the future if additional NDAs or ANDAs are approved.

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.

The timetable for submission of assessments of the REMS will remain the same as that approved on May 18, 2011.

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

1. Number of prescribers ever enrolled in the Rosiglitazone REMS Program (during the reporting period and cumulative).

2. Number of specially certified distributors contracted to participate in the Rosiglitazone REMS Program.

3. Number of certified pharmacies for this program (during the reporting period and cumulative).

4. Number of patients ever enrolled:

    a. Number of patients new to rosiglitazone medicines therapy at time of enrollment (during the reporting period and cumulative).

b. Number of patients continuing rosiglitazone medicines therapy at time of enrollment (during the reporting period and cumulative).

5. The total number of prescriptions dispensed during the reporting period for each rosiglitazone medicine.

6. Metric on dispensing within or outside the REMS ETASU

7. Number of identified instances in which one of the distributors has shipped rosiglitazone medicines to non-certified pharmacies.

8. Number of certified pharmacies that dispense rosiglitazone medicines to patients who are not enrolled in the program, and number of instances of this type of unauthorized dispensing for individual mail-order pharmacies.

9. Number of certified pharmacies that dispense rosiglitazone medicines using a prescription written by a prescriber who is not enrolled in the program, and number of instances of this type of unauthorized dispensing for individual specific certified pharmacies.

10. Number of prescribers who are not enrolled in the program and who wrote one or more prescriptions for rosiglitazone medicines, and number of prescriptions written by each un-enrolled prescriber.

11. Number of enrolled prescribers who wrote a prescription for a patient not yet enrolled and number of instances in which this occurred by prescriber.

12. Number of prescribers de-enrolled from the program for non-compliance.

13. The results of surveys to evaluate prescribers' and patients' understanding of the risks associated with rosiglitazone medicines and their safe use.

14. A report on periodic assessments of the distribution and dispensing of the Medication Guide in accordance with 21 CFR 208.24.

The requirements for assessments of an approved REMS under section 505-1(g)(3) include with respect to each goal included in the strategy, an assessment of the extent to which the approved strategy, including each element of the strategy, is meeting the goal or whether one or more such goals or such elements should be modified.

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 the FDCA.

If the assessment instruments and methodology for your REMS assessments are not included in the REMS supporting document, or if you propose changes to the submitted assessment instruments or methodology, you should update the REMS supporting document to include specific assessment instrument and methodology information at least 90 days before the assessments will be conducted. Updates to the REMS supporting document may be included in a new document that references previous REMS supporting document submission(s) for unchanged portions. Alternatively, updates may be made by modifying the complete previous REMS supporting document, with all changes marked and highlighted.

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 021071/NDA 021410/NDA 021700 REMS CORRESPONDENCE
***insert concise description of content in bold capital letters, e.g.*,**
UPDATE TO REMS SUPPORTING DOCUMENT - ASSESSMENT METHODOLOGY

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 021071/NDA 021410/NDA 021700 REMS ASSESSMENT

NEW SUPPLEMENT FOR NDA 021071/NDA 021410/NDA 021700
PROPOSED REMS MODIFICATION

NEW SUPPLEMENT (NEW INDICATION FOR USE)
FOR NDA 021071/NDA 021410/NDA 021700
REMS ASSESSMENT
PROPOSED REMS MODIFICATION (if included)

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

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}

Amy G. Egan, M.D., M.P.H.
Deputy Director for Safety
Division of Metabolism & Endocrinology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research
Food and Drug Administration

ENCLOSURES:
REMS
Avandia Content of Labeling (previously approved on February 3, 2011 for S-038)
Avandamet Content of Labeling (previously approved on February 3, 2011 for S-026)
Avandaryl Content of Labeling (previously approved on February 3, 2011 for S-010)

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

/s/

AMY G EGAN
01/25/2013