



NDA 021071/S-045
NDA 021410/S-034
NDA 021700/S-016

SUPPLEMENT APPROVALS

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

Dear Dr. Kreider:

Please refer to your Supplemental New Drug Applications (sNDAs) dated and received April 22, 2013, 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 July 18 and August 15, 2013, your risk evaluation and mitigation strategy (REMS) assessment, and agreed-upon labeling emailed to us on September 6, 2013.

These "Prior Approval" supplemental new drug applications propose to change the description of the tablets in the package insert and Medication Guide to reflect a change in the imprint on the tablets from "SB" to "GSK" for all tablet strengths of Avandia.

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 and Medication Guide), with the addition of any labeling changes in pending "Changes Being Effectuated" (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 that includes labeling changes 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 AVANDIA (rosiglitazone maleate) was originally approved on May 8, 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 January 25, 2013. The REMS consists of a Medication Guide, elements to assure safe use, implementation system, and a timetable for submission of assessments of the REMS. Your proposed modification to the REMS consists of a revised package insert and Medication Guide to change the description of the tablets to reflect a change in the imprint on the tablets from “SB” to “GSK” for all tablet strengths of Avandia.

Your proposed modified REMS, emailed on September 6, 2013, and appended to this letter, is approved.

The timetable for submission of assessments of the REMS will remain the same as that approved on January 25, 2013.

There are no changes to the REMS assessment plan described in our January 25, 2013, letter.

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 1 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, call Raymond Chiang, Regulatory Project Manager, at (301) 796-1940.

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

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
09/16/2013