DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-700/S-008

SB Pharmco Puerto Rico, Inc (d/b/a GlaxoSmithKline)
Attention: Michael Capone, MS
Associate Director, Global Regulatory Affairs
One Franklin Plaza; 200 N. 16th Street
Philadelphia, PA 19102

Dear Mr. Capone:

Please refer to your supplemental new drug application dated December 11, 2007, received December 11, 2007, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for AVANDARYL (rosiglitazone maleate + glimepiride) Tablets.

We acknowledge receipt of your submissions dated March 4, August 27, September 9, and September 26, 2008.

This supplemental application proposes for the conversion of the package insert to the format prescribed by the Physician Labeling Rule (PLR), and conversion of the approved Patient Information to a Medication Guide (dated March 4, 2008). These changes are to be consistent with, but not identical to the changes approved for Avandia (rosiglitazone maleate) Tablets.

We completed our review of this application, as amended. This application is **approved**, effective on the date of this letter, for use as recommended in the agreed-upon labeling text.

The final printed labeling (FPL) must be identical to the attached labeling (text for the package insert and Medication Guide) submitted September 9, 2008.

As soon as possible, but no later than 14 days from the date of this letter, please submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format as described at http://www.fda.gov/oc/datacouncil/spl.html that is identical to the enclosed labeling (text for the package insert and Medication Guide), submitted September 9, 2008). Upon receipt, we will transmit this version to the National Library of Medicine for public dissemination. For administrative purposes, please designate this submission **"SPL for approved NDA 21-700/S-008."**

RISK EVALUATION AND MITIGATION STRATEGY

Title IX, Subtitle A, Section 901 of the Food and Drug Administration Amendments Act of 2007 (FDAAA) amends the FDCA to authorize FDA to require the submission of a Risk Evaluation and Mitigation Strategy (REMS) for an approved drug if FDA becomes aware of new safety information and makes a determination that such a strategy is necessary to ensure that the benefits of the drug outweigh the risks (section 505-1(a)). This provision took effect on March 25, 2008.

Since AVANDARYL was approved on November 23, 2005, for the treatment of adult patients with type 2 diabetes mellitus to improve glycemic control, FDA has become aware of new safety information. We have conducted a meta-analysis of all clinical trial data that shows an increased risk of ischemic cardiovascular events in certain patients receiving rosiglitazone-containing products. This information was not available when AVANDARYL was granted marketing authorization. We consider the meta-analysis to be "new safety information" as defined in FDAAA.

In accordance with section 505-1 of FDCA, as one element of a REMS, FDA may require the development of a Medication Guide as provided for under 21 CFR Part 208. Pursuant to 21 CFR Part 208, FDA has determined that AVANDARYL poses a serious and significant public health concern requiring distribution of a Medication Guide. FDA has determined that AVANDARYL is a product that has serious risks of which patients should be made aware because information concerning the risks could affect patients' decisions to use, or continue to use AVANDARYL. Under 21 CFR 208, you are responsible for ensuring that the Medication Guide is available for distribution to patients who are dispensed AVANDARYL.

Your proposed REMS, submitted on September 26, 2008, and appended to this letter, is **approved.** The REMS consists of a Medication Guide included in this letter and the timetable for submission of assessments of the REMS included in your September 26, 2008, submission.

Your assessment of the REMS should include the following:

a. An evaluation of patients' understanding of the serious risks of AVANDARYL.

Prominently identify submissions related to the approved REMS with the following wording in bold capital letters at the top of the first page of the submission:

NDA 21-700 REMS ASSESSMENT
NDA 21-700 PROPOSED REMS MODIFICATION

REPORTING REQUIREMENTS

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

HEALTH CARE PROFESSIONAL LETTER

If you issue a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH
Food and Drug Administration
5515 Security Lane
HFD-001, Suite 5100
Rockville, MD 20852

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 & Endocrinology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

Enclosures: REMS, package insert and Medication Guide labeling

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

/s/

Mary Parks

12/2/2008 12:22:28 PM