



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration  
Rockville, MD 20857

NDA 21-410/S-005 and S-006  
NDA 21-071/S-009

SM Pharmco Puerto Rico, Ind. (d/b/a GlaxoSmithKline)  
Attention: Willa B. Phyll, Ph.D.  
Director, U.S. Regulatory Affairs  
One Franklin Plaza; P.O. Box 7929  
Philadelphia, PA 19101-7929

Dear Dr. Phyll:

Please refer to the following supplemental new drug applications submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for:

NDA 21-410 (Avandamet) for supplement 005 submitted November 26, 2003, and supplement 006 submitted February 6, 2004.

NDA 21-071 (Avandia) for supplement 009, submitted February 6, 2004.

We acknowledge receipt of your submissions dated February 4, 2004, (S-005), and February 13, and April 30, 2004, (S-009), both submitted to NDA 21-071.

Supplement 005 was submitted as a "Changes Being Effected" supplemental new drug application, and provided for changes to the **WARNINGS** section, **Cardiac Failure and Other Cardiac Effects** subsection of the Avandamet™ package insert label that would make it consistent with the approved label for Avandia®. In addition, numerous editorial changes were also implemented.

Supplements 006 and 009 provided for revisions to the **PRECAUTIONS** sections of the package inserts for the respective applications to provide for consistency.

We completed our review of these applications, as amended. These applications are approved, effective on the date of this letter, for use as recommended in the submitted labeling.

The final printed labeling (FPL) must be identical to the submitted labeling (text for the package inserts dated February 6, 2004, to NDA 21-071 and NDA 21-410, and February 4, 2004, to NDA 21-071, for the patient package inserts).

Please submit the FPL electronically according to the guidance for industry titled Providing Regulatory Submissions in Electronic Format – NDA. Alternatively, you may submit 20 paper copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount 15 of the copies on heavy-weight paper or similar material. For administrative purposes, these submissions should be designated "FPL for approved supplements 21-071/S-009 and 21-410/S-005 and S-006." Approval of these submissions by FDA is not required before the labeling is used.

NDA 21-410/S-005 and S-006

NDA 21-071/S-009

Page 2

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

MEDWATCH, HFD-410  
FDA  
5600 Fishers Lane  
Rockville, MD 20857

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 301-827-6422.

Sincerely,

*{See appended electronic signature page}*

David G. Orloff, M.D.  
Director  
Division of Metabolic and Endocrine Drug Products  
Office of Drug Evaluation II Center for Drug Evaluation

Enclosure (package insert label for  
NDA 21-071 and NDA 21-410)

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**This is a representation of an electronic record that was signed electronically and  
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/s/

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David Orloff  
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