CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-842

APPROVAL LETTER(S)

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-842

Takeda Global Research & Development Center, Inc.
Attention: Mary Jo Pritza, MPH, PharmD
Manager, Regulatory Affairs
475 Half Day Road
Lincolnshire, IL 60069

Dear Ms. Pritza:

Please refer to your new drug application (NDA) dated October 27, 2004, received October 29, 2004, submitted under section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Actoplus Met™ (pioglitazone HCl and metformin HCl) fixed-dose combination Tablets, 15mg/500 mg and 15 mg/850 mg.

We acknowledge receipt of your submissions dated January 13, February 18, March 11, April 1, June 28, and 30, July 11, and 12, and August 5, 9, 10, 17, and 22, 2005.

This new drug application provides for the use of Actoplus Met as an adjunct to diet and exercise to improve glycemic control in patients with type 2 diabetes who are already treated with a combination of pioglitazone and metformin or whose diabetes is not adequately controlled with metformin alone, or for those patients who have initially responded to pioglitazone alone and require additional glycemic control.

We completed our review of this application, as amended. It 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 submitted labeling (package insert labeling submitted on August 26, 2005, patient package insert submitted on August 8, 2005, immediate carton and container labels submitted on August 22, 2005. Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

Please submit an electronic version of the FPL 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 but no more than 30 days after it is printed. Individually mount 15 of the copies on heavy-weight paper or similar material. For administrative purposes, designate this submission "**FPL for approved NDA 21-842.**" Approval of this submission by FDA is not required before the labeling is used.

All applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred. We are waiving the pediatric study requirement for this application.

In addition, submit three copies of the introductory promotional materials that you propose to use for this product. Submit all proposed materials in draft or mock-up form, not final print. Send one copy to this Division/The Division of Metabolism and Endocrinology Products (DMEP) and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising,
and Communications, (DDMAC) HFD-42
Food and Drug Administration
5901-B Ammendale Road
Beltsville, Maryland 20705-1266

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 Health 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 and Research

Enclosures: (package insert, patient package insert, immediate container labels, carton labels).

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/s/

David Orloff
8/29/2005 05:30:45 PM