DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-842/S-005

Takeda Global Research & Development Center, Inc.
Attention: Mary Jo Pritza, MPH, PharmD
Associate Director, Regulatory Affairs
One Takeda Parkway
Deerfield, IL 60015

Dear Ms. Pritza:

Please refer to your supplemental new drug application dated September 14, 2007, received September 17, 2007, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Actoplus Met (pioglitazone HCl and metformin HCl) fixed-dose combination Tablets, 15 mg/500 mg and 15 mg/850 mg.

This supplemental new drug application provides for changes to conform to revisions to the package insert and patient package insert in accordance with recently approved language for NDA 21-073, Actos (pioglitazone HCl) package insert as follows:

> S-026, approved February 25, 2007: provided revisions to the **WARNINGS** and **ADVERSE REACTIONS** sections to add safety information generated by the cardiovascular outcome study (PROactive);
>
> S-031, approved August 14, 2007: provided for the addition of a **BOXED WARNING** to more prominently address the risks for congestive heart failure, a statement to the **CONTRAINDICATIONS** section to state that initiation of pioglitazone is contraindicated in patients with New York Heart Association (NYHA) Class III and IV heart failure, and to the **WARNINGS, PRECAUTIONS,** and **DOSAGE AND ADMINISTRATION** sections;
>
> S-030, approved September 6, 2007: provided revisions to the **PRECAUTIONS** section to include information from fracture cases in patients taking pioglitazone.

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

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 patient package insert) submitted September 14, 2007.

Upon receipt, we will transmit that version to the National Library of Medicine for public dissemination. For administrative purposes, please designate this submission, "SPL for approved NDA 21-842."

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

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}

Mary H. Parks, M.D.
Director
Division of Metabolism and Endocrinology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

Enclosure (package insert +
patient package insert)

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

9/26/2007 10:09:43 AM