DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-073/S-029
NDA 21-842/S-003

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 supplemental new drug applications dated June 29, 2006, received June 30, 2006, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for:

Actos (pioglitazone HCl): NDA 21-073/S-029
ActoPlus Met (pioglitazone HCl plus metformin HCl): NDA 21-842/S-003

These supplemental applications propose labeling changes to the **PRECAUTIONS** section, **Carcinogenicity, Mutagenesis, Impairment of Fertility,** *pioglitazone hydrochloride* subsection of the package insert, to include information regarding reports of bladder cancer in patients taking pioglitazone.

We completed our review of these applications. These applications are 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 (text for each package insert sent electronic mail) on September 27, 2006.

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 these submissions "**FPL for approved supplements NDA 21-073/S-029 and NDA 21-842/S-003.** Approval of these submissions by FDA is not required before the labeling is used.

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 inserts)

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

9/28/2006 08:39:12 PM