DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 021073/S-045
NDA 021842/S-016
NDA 022024/S-009
NDA 021925/S-012

SUPPLEMENT APPROVAL
RELEASE REMS REQUIREMENT

Takeda Global Research & Development Center, Inc.
Attention: Jessie Y. Lee, Ph.D., RAC
Manager, Regulatory Affairs
One Takeda Parkway
Deerfield, IL 60015-2235

Dear Dr. Lee:

Please refer to your New Drug Applications (NDAs) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for:

• ACTOS (pioglitazone hydrochloride) Tablets,
• ACTOPLUS MET (pioglitazone hydrochloride and metformin hydrochloride) fixed-dose combination Tablets,
• ACTOPLUS MET XR (pioglitazone hydrochloride and metformin hydrochloride extended-release) fixed-dose combination Tablets, and
• DUETACT (pioglitazone hydrochloride and glimepiride) fixed-dose combination Tablets.

We acknowledge receipt of your amendments dated April 5 and 6, and May 1 and 9, 2012, and your risk evaluation and mitigation strategy (REMS) assessment dated February 1, 2012. After consultation between the Office of New Drugs (OND) and the Office of Surveillance and Epidemiology (OSE), we have found the REMS assessment to be adequate.

These supplemental new drug applications propose to eliminate the requirement for the approved REMS for these pioglitazone-containing products.

RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS

A REMS for ACTOS (pioglitazone hydrochloride) and DUETACT (pioglitazone hydrochloride and glimepiride) was originally approved on September 9, 2009; a REMS for ACTOPLUS MET (pioglitazone hydrochloride and metformin hydrochloride) was originally approved on September 14, 2009; and a REMS for ACTOPLUS MET XR (pioglitazone hydrochloride and

metformin hydrochloride extended-release) was originally approved on May 12, 2009. The most recent REMS modification for all four pioglitazone-containing products was approved on August 4, 2011. The REMS consists of a Medication Guide and a timetable for submission of assessments of the REMS.

You propose that FDA no longer require a REMS for these pioglitazone-containing products.

We have determined that maintaining the Medication Guide as part of the approved labeling is adequate to address the serious and significant public health concern and meets the standard in 21 CFR 208.1. Therefore, it is no longer necessary to include the Medication Guide as an element of the approved REMS to ensure that the benefits of these pioglitazone-containing products outweigh the risks.

Therefore, we agree with your proposal, and a REMS for these pioglitazone-containing products is no longer required.

We remind you that the Medication Guide will continue to be part of the approved labeling in accordance with 21 CFR 208.

REPORTING REQUIREMENTS

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 contact Jena Weber, Regulatory Project Manager, at (301) 796-1306.

Sincerely,

{See appended electronic signature page}

Amy G. Egan, M.D., M.P.H.
Deputy Director for Safety
Division of Metabolism & Endocrinology Products
Center for Drug Evaluation and Research
Food and Drug Administration

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

/s/

AMY G EGAN
05/17/2012