**NDA 21-842 ACTOPLUS MET** (pioglitazone hydrochloride and metformin hydrochloride) tablets

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**RISK EVALUATION AND MITIGATION STRATEGY (REMS)**

**I. GOAL:**

The goal of this REMS is to ensure that patients understand the risks of heart failure in patients being treated with pioglitazone containing products.

**II. REMS ELEMENTS:**

**A. Medication Guide**

A Medication Guide will be dispensed with each ACTOPLUS MET prescription. The Medication Guide will be included at the end of the prescribing information as a perforated attachment. Each packaging configuration including bottles, sample cards, and trays will contain a Medication Guide.

Because the Medication Guide is included as part of the packaging and provided by additional means for ACTOPLUS MET, Takeda has met the requirements of 21 CFR 208.24 for distribution and dispensing of the Medication Guide.

**B. Timetable for Submission of Assessments**

The Timetable for Assessments is as follows:

1st Assessment: 18 months from approval of REMS (May 12, 2009)
2nd Assessment: 3 years from approval of REMS (May 12, 2009)
3rd Assessment: 7 years from approval of REMS (May 12, 2009)

To facilitate inclusion of as much information as possible while allowing reasonable time to prepare the submission, the reporting interval covered by each assessment should conclude no earlier than 60 days before the submission date for that assessment. Takeda will submit each assessment so that it will be received by the FDA on or before the due date.