DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-782/S-008, S-009, S-010

Takeda Global Research and Development Center, Inc.
One Takeda Parkway
Deerfield, IL 60015-2235

Attention: Timothy Farber
Product Manager, Regulatory Affairs

Dear Mr. Farber:

Please refer to your supplemental new drug applications (NDA) dated December 19, 2007, received December 20, 2007, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Rozerem® (ramelteon) Tablets 8 mg.

Application	Submitted on:	Received on:	Provides for:
SE8 S-008	December 19, 2007	December 20, 2007	Efficacy Study: Long term safety and efficacy to support an increase in duration for up to 6 months
SE8 S-009	December 19, 2007	December 20, 2007	Clinical Study Labeling Supplement - Study 01-05-TL-375-060- Balance in elderly insomnia patients
SE8 S-010	December 19, 2007	December 20, 2007	Clinical Study Labeling Supplement – Study 01-05-TL-375-068- Depressant effects in COPD patients

We acknowledge receipt of your submission dated August 28, 2008.

These supplemental new drug applications provide for the use of Rozerem (ramelteon) 8 mg Tablets for the treatment of insomnia.

We completed our review of these supplemental applications as amended. These applications are approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling text.

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert, Medication Guide, and immediate carton and container labels) submitted October 20, 2008.

Other Supplements

Additionally, we note the following labeling supplements have been submitted as described below, and have been superseded with the approval of this application. These labeling supplements will be retained in our files.

1. S-003 Prior Approval Supplement dated March 13, 2007, and amended April 27, 2007 included Class Labeling changes as requested by the Agency in correspondences dated February 14, 2006, December 20, 2006 and March 14, 2007. These labeling revisions pertain to the risk for complex sleep behaviors and anaphylaxis. Changes appear in the **WARNINGS and PRECAUTIONS,** and **PATIENT COUNSELING INFORMATION, and MEDICATION GUIDE** sections.

2. S-007 Prior Approval Supplements (Medication Guide) submitted September 7, 2007 in response to Agency Letters dated March 14, 2007 and April 27, 2007; prescribing information was revised as well as Class Labeling changes. Changes appear in the section 17 for the institution of a **MEDICATION GUIDE** provided at the end of the Package Insert.

RISK EVALUATION AND MITIGATION STRATEGIES (REMS) REQUIREMENTS

Title IX, Subtitle A, Section 901 of the Food and Drug Administration Amendments Act of 2007 (FDAAA) amends the FDCA to authorize FDA to require the submission of a REMS for an approved drug if the FDA becomes aware of new safety information and makes a determination that such a strategy is necessary to ensure that the benefits of the drug outweigh the risks (section 505-1(a)(2)). This provision took effect on March 25, 2008.

Since Rozerem (ramelteon) was approved in 2005 for the treatment of insomnia, FDA has become aware of reports of complex sleep-related behaviors, such as sleep-driving and sleep-eating, and anaphylaxis/angioedema in patients who take sedative hypnotics. This information was not available at the time Rozerem (ramelteon) was granted marketing authorization. Therefore, we consider this information to be "new safety information" as defined in FDAAA.

In accordance with section 505-1 of FDCA, as one element of a REMS, FDA may require the development of a Medication Guide as provided for under 21 CFR Part 208. Pursuant to 21 CFR Part 208, FDA has determined that Rozerem (ramelteon) poses a serious a significant public health concern requiring distribution of a Medication Guide. The Medication Guide is necessary for patients' safe and effective use of Rozerem (ramelteon). FDA has determined that Rozerem (ramelteon) is a product that has serious risks of which patients should be made aware because information concerning the risks could affect patients' decisions to use, or continue to use Rozerem (ramelteon). FDA has also determined that Rozerem (ramelteon) is a product for which patient labeling could help prevent serious adverse events. Under 21 CFR 208, you are responsible for ensuring that the Medication Guide is available for distribution to patients who are dispensed Rozerem.

Your proposed REMS, submitted on October 17, 2008, and appended to this letter, is approved. The REMS consists of the Medication Guide included with this letter and the timetable for submission of assessments of the REMS included in your July 29, 2008, submission.

Information needed for assessment of the REMS may include but may not be limited to:

a. A survey of patients' understanding of the serious risks of Rozerem

b. A report on periodic assessments of the distribution and dispensing of the Medication Guide in accordance with 21 CFR 208.24
c. A report on failures to adhere to distribution and dispensing requirements, and corrective actions taken to address noncompliance.

Use the following designator to prominently label all submissions, including supplements, relating to this REMS:

NDA 21-782 REMS ASSESSMENT
NDA 21-782 PROPOSED REMS MODIFICATION

CONTENT OF LABELING

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, Medication Guide) and submitted on July 18, 2008. 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 21-782/S-008/S-009/S-010".

PROMOTIONAL MATERIALS

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 Neurology Products and two copies of both the promotional materials and the package insert(s) directly to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications
5901-B Ammendale Road
Beltsville, MD 20705-1266

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
Suite 12B05
5600 Fishers Lane
Rockville, MD 20857

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, call Cathleen Michaloski, MPH, Regulatory Project Manager, at (301) 796-1123.

Sincerely,

{See appended electronic signature page}
Russell G. Katz, M.D.
Director, Division of Neurology Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

Enclosure:
REMS
Labeling (Package Insert including Medication Guide)

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

/s/

Russell Katz

10/20/2008 05:15:29 PM