DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-997 **NDA APPROVAL**

DJA Global Pharma LLC
For Orexo AB, Sweden
115 Commons Ct.
Chadds Ford, PA 19317

Attention: Demaris DeGraft-Johnson, R.Ph., MSc., Med. Chem.
President

Dear Ms. DeGraft-Johnson:

Please refer to your new drug application (NDA) dated May 14, 2008, received May 14, 2008, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Edluar, (zolpidem tartrate), sublingual tablets, 5 and 10 mg.

We acknowledge receipt of your submissions dated June 13, 2008, August 15, 2008, September 19, 2008, October 10, 2008, November 6 and 12, 2008, December 16, 18, 19, and 30, 2008, January 12, 2009, February 20, and 27, 2009, and March 6 and 12, 2009.

This new drug application provides for the use of Edluar (zolpidem tartrate) sublingual tablets, 5 and 10 mg for the treatment of insomnia.

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

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, text for the patient package insert, Medication Guide). 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 21-997."

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the

product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are waiving the pediatric study requirement for this application because there is evidence strongly suggesting that Edular (zolpidem tartrate) sublingual tablets, 5 and 10 mg would be ineffective and unsafe in the pediatric age group 6 to 17 years, and because studies are impossible or highly impractical in the pediatric age group 0 to <6 years. The waiver is granted based, in part, on data submitted to the Agency included in the Ambien® (zolpidem tartrate) pediatric efficacy supplement 022, where administration of oral zolpidem tartrate to attention-deficit/hyperactivity disorder (ADHD) children ages 6 to 17 years did not establish efficacy and showed significant safety concerns in the pediatric age group 6 to 17 years.

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 Federal Food, Drug, and Cosmetic Act (FDCA) to authorize FDA to require the submission of a REMS if FDA determines that such a strategy is necessary to ensure that the benefits of the drug outweigh the risks (section 505-1(a)). This provision took effect on March 25, 2008.

We have determined that a REMS is necessary for Edluar® (zolpidem tartrate, sl) to ensure the benefits of the drug outweigh the risks of complex sleep-related behaviors, such as sleep-driving and sleep-eating, and severe anaphylactic reactions.

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 Edluar (zolpidem tartrate) sublingual tablets, 5 and 10 mg poses a serious and significant public health concern requiring distribution of a Medication Guide. The Medication Guide is necessary for patients' safe and effective use of Edluar (zolpidem tartrate) sublingual tablets, 5 and 10 mg. FDA has determined that Edluar (zolpidem tartrate) sublingual tablets, 5 and 10 mg, 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 Edluar (zolpidem tartrate) sublingual tablets, 5 and 10 mg. FDA has also determined that Edluar (zolpidem tartrate) sublingual tablets, 5 and 10 mg 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 Edluar (zolpidem tartrate) sublingual tablets, 5 and 10 mg .

Your proposed REMS, submitted on February 27, 2009, 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 February 27, 2009 submission.

Your assessment of the REMS should include an evaluation of patients' understanding of the serious risks of Edluar (zolpidem tartrate) sublingual tablets, 5 and 10 mg.

Prominently identify submissions containing REMS assessments or proposed modifications of the REMS with the following wording in bold capital letters at the top of the first page of the submission:

- **NDA 21-997 REMS ASSESSMENT**

- **NEW SUPPLEMENT for NDA 21-997**
  PROPOSED REMS MODIFICATION
  REMS ASSESSMENT (if included)

If you do not submit electronically, please send 5 copies of submissions containing REMS assessments or proposed modifications of your REMS.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the package insert(s) 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

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the package insert(s), at the time of initial dissemination or publication, accompanied by a Form FDA 2253. For instruction on completing the Form FDA 2253, see page 2 of the Form. For more information about submission of promotional materials to the Division of Drug Marketing, Advertising, and Communications (DDMAC), see www.fda.gov/cder/ddmac.

LETTERS TO HEALTH CARE PROFESSIONALS

If you issue a letter communicating important safety related information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit an electronic copy of the letter to both this NDA and to the following address:

MedWatch
Food and Drug Administration
Suite 12B05
5600 Fishers Lane
Rockville, MD 20857

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

We acknowledge your March 4, 2009 commitment to expedited reporting of "Events of Interest" based upon the following MedDRA preferred terms: Drug administered at inappropriate site, Drug administration error, Incorrect dose administered, Incorrect route of drug administration, Wrong technique in drug usage process, Intentional drug misuse, Accidental exposure, Accidental overdose, Intentional overdose, Multiple drug overdose, Multiple drug overdose accidental, Multiple drug overdose intentional, Overdose, Drug abuser, Substance abuser, Dependence, Drug dependence, Drug tolerance, Drug tolerance decreased, Drug tolerance increased.

We acknowledge your commitment to include a discussion in your quarterly periodic report and annual report based upon the Standardized MedDRA Query: "Drug Abuse, Dependence and Withdrawal". We acknowledge that you plan to review data from the Drug Abuse Warning Network (DAWN) and the Toxic Exposure Surveillance System (TESS) report prepared by the National Poison Data System, and commit to submitting analysis of this information in your quarterly periodic report and annual report, with analysis based on both individual cases and aggregate analysis. Events of interest from DAWN and TESS would be those that involve a sublingual formulation or an unknown formulation of zolpidem.

If you have any questions, call Cathleen Michaloski, MPH, Regulatory Project Manager, at (301) 796-1123.

Sincerely,

{See appended electronic signature page}

Russell Katz, M.D.
Director
Division of Neurology Products
Office of Drug Evaluation 1
Center for Drug Evaluation and Research

Enclosure: labeling
REMS document

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

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