DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 204242/S-002

SUPPLEMENT APPROVAL

Orexo AB
c/o DJA Global Pharmaceuticals, Inc.
115 Commons Court
Chadds Ford, PA 19317

Attention: Damaris DeGraft-Johnson, RPh, MSc. Med. Chem.
President, DJA Global Pharmaceuticals, Inc.

Dear Ms. DeGraft-Johnson:

Please refer to your Supplemental New Drug Application (sNDA) dated August 28, 2013, received August 28, 2013, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Zubsolv (buprenorphine and naloxone sublingual tablets), 1.4 mg/0.36 mg and 5.7 mg/1.4 mg.

This "Prior Approval" supplemental new drug application proposes modification to the REMS document and applicable appended materials including the Appropriate Use Checklist, Prescriber Brochure- "Office-Based Buprenorphine Therapy for Opioid Dependence: Important Information for Prescribers", Pharmacist Brochure- "Office-Based Buprenorphine Therapy for Opioid Dependence: Important Information for Pharmacists", and the Buprenorphine-containing Transmucosal products for Opioid Dependence (BTOD) REMS Website.

We have completed our review of this supplemental application. It is approved, effective on the date of this letter.

RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS

The waiver-granted shared REMS for the Buprenorphine-containing Transmucosal products for Opioid Dependence (BTOD) was originally approved on February 22, 2013. Your REMS was originally approved on July 3, 2013. We also refer to your June 27, 2013, email stating your agreement to join the waiver-granted shared REMS for BTOD. This modified REMS incorporates Zubsolv into this REMS.

The REMS consists of a Medication Guide for each product covered under the REMS, elements to assure safe use, an implementation system, and a timetable for submission of assessments of the REMS.

Your proposed modification to the BTOD REMS, including appended REMS materials as applicable, consists of the following:

- a minor revision to one of the goals to include informing prescribers and pharmacists of the serious risks associated with buprenorphine-containing products,
- the addition of a timetable for submission of assessments for the NDA holder(s) of the BTOD REMS, and
- updated REMS materials to reflect the addition of a new product to the BTOD REMS including information on how the new product differs from the currently available products, how to switch between products, and recommended dosing.

We remind you that section 505-1(f)(8) of FDCA prohibits holders of an approved covered application with elements to assure safe use from using any element to block or delay approval of an application under section 505(b)(2) or (j). A violation of this provision in 505-1(f) could result in enforcement action.

There are no changes to the REMS assessment plan described in our July 3, 2013, letter. We also note that as part of the waiver-granted shared REMS for BTOD, your REMS now has a timetable for assessments.

In addition to the assessments submitted according to the timetable included in the approved REMS, you must submit a REMS assessment and may propose a modification to the approved REMS when you submit a supplemental application for a new indication for use as described in section 505-1(g)(2)(A) of the FDCA.

If the assessment instruments and methodology for your REMS assessments are not included in the REMS supporting document, or if you propose changes to the submitted assessment instruments or methodology, you should update the REMS supporting document to include specific assessment instrument and methodology information at least 90 days before the assessments will be conducted. Updates to the REMS supporting document may be included in a new document that references previous REMS supporting document submission(s) for unchanged portions. Alternatively, updates may be made by modifying the complete previous REMS supporting document, with all changes marked and highlighted. Prominently identify the submission containing the assessment instruments and methodology with the following wording in bold capital letters at the top of the first page of the submission:

> **NDA 204242 REMS CORRESPONDENCE**
> **(insert concise description of content in bold capital letters, e.g.,**
> **UPDATE TO REMS SUPPORTING DOCUMENT - ASSESSMENT METHODOLOGY**

An authorized generic drug under this NDA must have an approved REMS prior to marketing. Should you decide to market, sell, or distribute an authorized generic drug under this NDA, contact us to discuss what will be required in the authorized generic drug REMS submission.

Prominently identify the submission containing the 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 as appropriate:

NDA 204242 REMS ASSESSMENT

NEW SUPPLEMENT FOR NDA 204242
PROPOSED REMS MODIFICATION

NEW SUPPLEMENT (NEW INDICATION FOR USE)
FOR NDA 204242
REMS ASSESSMENT
PROPOSED REMS MODIFICATION (if included)

If you do not submit electronically, please send 5 copies of REMS-related submissions.

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, call Matt Sullivan, Senior Regulatory Project Manager, at (301) 796-1245.

Sincerely,

{See appended electronic signature page}

Judith A. Racoosin, M.D., M.P.H.
Deputy Director for Safety
Division of Anesthesia, Analgesia, and
Addiction Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

ENCLOSURE:
REMS

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

/s/

JUDITH A RACOOSIN
09/04/2013