DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 204242/S-005

SUPPLEMENT APPROVAL

Orexo US, Inc.
150 Headquarters Plaza
East Tower 5th Floor
Morristown, NJ 07960

Attention: Alfred W. Schweikert, PhD, RAC
Head of Regulatory Affairs, US

Dear Dr. Schweikert:

Please refer to your Supplemental New Drug Application (sNDA) amendment dated and received December 13, 2013, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Zubsolv (buprenorphine and naloxone sublingual tablets).

We acknowledge receipt of your amendments dated March 25, May 21, July 28, August 15, and November 1, 2014, and January 8, 2015.

This "Prior Approval" supplemental new drug application provides for modifications to the approved REMS for Zubsolv, which is part of the waiver-granted shared system REMS, the Buprenorphine-containing Transmucosal products for Opioid Dependence (BTOD) REMS Program.

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 system BTOD REMS was originally approved on February 22, 2013. Your REMS for Zubsolv was originally approved on July 3, 2013, and modified on September 4, 2013, incorporating Zubsolv into the BTOD REMS.

The REMS consists of a Medication Guide, 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:

- Addition of two new strengths of Zubsolv: 8.6 mg buprenorphine/ 2.1 mg naloxone and 11.4 mg buprenorphine/ 2.9 mg naloxone

- Addition of Bunavail (buprenorphine/naloxone) buccal film product information

- A change to the indication for Suboxone (buprenorphine and naloxone) sublingual film to include the use of Suboxone (buprenorphine and naloxone) sublingual film in all phases of treatment for opioid dependence
    - Limitations of use in initial treatment to patients physically dependent on heroin or other short-acting opioids

- A new warning regarding use in patients with hepatic impairment

- Updated language on use in pregnancy, nursing mothers, and patients with hepatic impairment

Your proposed REMS, submitted on January 8, 2015, and appended to this letter, is approved.

The BTOD REMS currently includes the products listed on the FDA REMS website, available at http://www.fda.gov/downloads/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/UCM340947.pdf.

Other products may be added to the BTOD REMS in the future if additional BTOD NDAs or ANDAs are approved.

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 September 4, 2013, letter.

In addition to the assessments submitted according to the timetable included in the approved REMS, you must submit a REMS assessment when you submit a supplemental application for a new indication for use as described in section 505-1(g)(2)(A) of the FDCA. Also, under section 505-1(g)(2)(C), FDA can require the submission of a REMS assessment if FDA determines an assessment is needed to evaluate whether the REMS should be modified to ensure the benefits of the drug outweigh the risks or to minimize the burden on the healthcare delivery system of complying with the REMS.

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 Swati Patwardhan, Regulatory Project Manager, at (301) 796-4085.

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
02/12/2015