DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 205637/S-004

SUPPLEMENT APPROVAL

BioDelivery Science International
801 Corporate Center Drive, Suite 210
Raleigh, NC 27607

Attention: Chris Prue, RPh, MBA
VP, Regulatory Affairs

Dear Mr. Prue:

Please refer to your Supplemental New Drug Application (sNDA) dated and received January 8, 2015, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Bunavail (buprenorphine and naloxone) buccal film.

We acknowledge receipt of your amendment dated January 27, 2015, and your risk evaluation and mitigation strategy (REMS) assessment dated January 8, 2015.

This "Prior Approval" supplemental new drug application provides for modifications to the approved REMS for Bunavail, 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, as amended. 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 Bunavail was originally approved on June 6, 2014, as part of 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.

We also refer to our letter dated December 11, 2014, notifying you that in order to ensure the benefits of buprenorphine-containing transmucosal products for opioid dependence outweigh their risks, we determined that you were required to make REMS modifications to reflect information about a new indication for Suboxone (buprenorphine and naloxone) sublingual film; new approved strengths for Zubsolv (buprenorphine and naloxone sublingual tablets); and updated information about use of buprenorphine in certain patient populations.

Your proposed modification to the BTOD REMS, including appended REMS materials as applicable, consists of the following changes that are consistent with our December 11, 2014 letter:

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

- 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 June 6, 2014, 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 205637 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 205637 REMS ASSESSMENT

NEW SUPPLEMENT FOR NDA 205637
PROPOSED REMS MODIFICATION

NEW SUPPLEMENT (NEW INDICATION FOR USE)
FOR NDA 205637

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