NDA 020732/S-025
NDA 020733/S-029
NDA 022410/S-044

SUPPLEMENT APPROVAL

Indivior Inc.
10710 Midlothian Turnpike
Suite 125
North Chesterfield, VA 23235

Attention: Rachel Capone, MSHS
Manager, Regulatory Affairs

Dear Ms. Capone:

Please refer to your supplemental new drug applications (sNDAs) dated and received August 19, 2021, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for the following products:

NDA #	Product	Supplement #
020732	Subutex (buprenorphine) sublingual tablets	025
020733	Suboxone (buprenorphine and naloxone) sublingual tablets	029
022410	Suboxone (buprenorphine and naloxone) sublingual film	044

These Changes Being Effected sNDAs provide for proposed modification to the approved Suboxone/Subutex Risk Evaluation and Mitigation Strategy (REMS).

We have completed our review of these supplemental applications, as amended. They are approved effective on the date of this letter.

RISK EVALUATION AND MITIGATION STRATEGY (REMS) REQUIREMENTS

The REMS for Suboxone (buprenorphine and naloxone) sublingual film was originally approved on August 30, 2010. The REMS for Subutex (buprenorphine) sublingual tablets and the REMS for Suboxone (buprenorphine and naloxone) sublingual tablets were originally approved on December 22, 2011. Each REMS was modified on September 22, 2015, to consolidate the three product-specific REMS into a single REMS. The most recent modification was approved on March 2, 2020. 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 modifications to the REMS consist of removal of references to the authorized generic of Suboxone sublingual film, alignment with the updated Department of Health and Human Services (HHS) guidelines for prescribers of buprenorphine for Opioid Use Disorder (OUD)[1], and addressing feedback from a routine FDA compliance inspection in July 2021, which included clarifying acceptable methods for documentation of required safe use conditions (e.g., checklist or other means, such as within a patient's electronic health record).

In accordance with section 505-1 of the FDCA, we have determined that the following REMS modifications are necessary to ensure the benefits of the drug outweigh the risks: update the REMS materials to conform with a safety labeling change (SLC) approved on March 4, 2021. The SLC required language regarding healthcare providers discussing the availability of naloxone, assessing each patient's need for a naloxone prescription, and co-prescribing naloxone if appropriate.[2]

Your proposed modified REMS, submitted on August 19, 2021, amended and appended to this letter, is approved.

The timetable for submission of assessments of the REMS remains the same as that approved on August 30, 2010.

There are no changes to the REMS assessment plan described in our March 2, 2020 letter.

We remind you that in addition to the REMS assessments submitted according to the timetable in the approved REMS, you must include an adequate rationale to support a proposed REMS modification for the addition, modification, or removal of any goal or element of the REMS, as described in section 505-1(g)(4) of the FDCA.

We also remind you that 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. This assessment should include:

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[1] Practice Guidelines for the Administration of Buprenorphine for Treating Opioid Use Disorder, 86 FR 22439, 22439-22440, April 28, 2021, accessed April 28, 2021, https://www.federalregister.gov/documents/2021/04/28/2021-08961/practice-guidelines-for-the-administration-of-buprenorphine-for-treating-opioid-use-disorder.

[2] U.S. Food and Drug Administration, Drug Safety Communication: FDA recommends health care professionals discuss naloxone with all patients when prescribing opioid pain relievers or medicines to treat opioid use disorder, July 23, 2020, accessed October 8, 2021, https://www.fda.gov/drugs/drug-safety-and-availability/fda-recommends-health-care-professionals-discuss-naloxone-all-patients-when-prescribing-opioid-pain.

a) An evaluation of how the benefit-risk profile will or will not change with the new indication;

b) A determination of the implications of a change in the benefit-risk profile for the current REMS;

c) *If the new indication for use introduces unexpected risks*: A description of those risks and an evaluation of whether those risks can be appropriately managed with the currently approved REMS.

d) *If a REMS assessment was submitted in the 18 months prior to submission of the supplemental application for a new indication for use*: A statement about whether the REMS was meeting its goals at the time of that last assessment and if any modifications of the REMS have been proposed since that assessment.

e) *If a REMS assessment has not been submitted in the 18 months prior to submission of the supplemental application for a new indication for use:* Provision of as many of the currently listed assessment plan items as is feasible.

f) *If you propose a REMS modification based on a change in the benefit-risk profile or because of the new indication of use, submit an adequate rationale to support the modification, including*: Provision of the reason(s) why the proposed REMS modification is necessary, the potential effect on the serious risk(s) for which the REMS was required, on patient access to the drug, and/or on the burden on the health care delivery system; and other appropriate evidence or data to support the proposed change. Additionally, include any changes to the assessment plan necessary to assess the proposed modified REMS. *If you are not proposing REMS modifications*, provide a rationale for why the REMS does not need to be modified.

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 020732
NDA 020733
NDA 022410 REMS ASSESSMENT METHODOLOGY
(insert concise description of content in bold capital letters, e.g., ASSESSMENT METHODOLOGY, PROTOCOL, SURVEY METHODOLOGIES, AUDIT PLAN, DRUG USE STUDY)

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.

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.

Prominently identify any 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 020732
NDA 020733
NDA 022410 REMS ASSESSMENT

or

NEW SUPPLEMENTS FOR
NDA 020732/S-000/ NDA 020733/S-000/ NDA 022410/S-000/
CHANGES BEING EFFECTED IN 30 DAYS
PROPOSED MINOR REMS MODIFICATION

or

NEW SUPPLEMENTS FOR
NDA 020732/S-000/ NDA 020733/S-000/ NDA 022410/S-000/
PRIOR APPROVAL SUPPLEMENTS
PROPOSED MAJOR REMS MODIFICATION

or

**NEW SUPPLEMENTS FOR
NDA 020732/S-000/ NDA 020733/S-000/ NDA 022410/S-000/
PRIOR APPROVAL SUPPLEMENTS
PROPOSED REMS MODIFICATIONS DUE TO SAFETY LABELING CHANGES SUBMITTED IN SUPPLEMENTS NDA 020732/S-000/ NDA 020733/S-000/ NDA 022410/S-000/**

or

**NEW SUPPLEMENTS (NEW INDICATION FOR USE) FOR
NDA 020732/S-000/ NDA 020733/S-000/ NDA 022410/S-000/
REMS ASSESSMENT
PROPOSED REMS MODIFICATION (if included)**

Should you choose to submit a REMS revision, prominently identify the submission containing the REMS revisions with the following wording in bold capital letters at the top of the first page of the submission:

**REMS REVISIONS FOR
NDA 020732
NDA 020733
NDA 022410**

To facilitate review of your submission, we request that you submit your proposed modified REMS and other REMS-related materials in Microsoft Word format. If certain documents, such as enrollment forms, or website screenshots are only in PDF format, they may be submitted as such, but Word format is preferred.

SUBMISSION OF REMS DOCUMENT IN SPL FORMAT

FDA can accept the REMS document in Structured Product Labeling (SPL) format. If you intend to submit the REMS document in SPL format, as soon as possible, but no later than 14 days from the date of this letter, submit the REMS document in SPL format using the FDA automated drug registration and listing system (eLIST).

For more information on submitting REMS in SPL format, please email FDAREMSwebsite@fda.hhs.gov.

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 LCDR Jessica Voqui, PharmD, MS, Associate Director for Postmarket Regulatory Science, at 301-796-2915.

Sincerely,

{See appended electronic signature page}

CDR Mark A. Liberatore, PharmD, RAC
Deputy Director for Safety
Division of Anesthesiology, Addiction Medicine, and Pain Medicine
Office of Neuroscience
Center for Drug Evaluation and Research

ENCLOSURE:

- REMS

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

MARK A LIBERATORE
11/19/2021 03:26:00 PM