IMPORTANT DRUG WARNING

Subject: Risk Evaluation and Mitigation Strategy (REMS) for SUBOXONE® (buprenorphine and naloxone) Sublingual Film CIII, SUBOXONE® (buprenorphine and naloxone) Sublingual Tablets CIII, and SUBUTEX® (buprenorphine) Sublingual Tablets CIII for opioid dependence due to risks of accidental overdose, misuse, and abuse.

<DATE>

Dear Prescriber:

You are receiving this letter because you are a prescriber certified to treat opioid dependence under the Drug Addiction Treatment Act of 2000 (DATA 2000).

The purpose of this letter is to inform you of a Risk Evaluation and Mitigation Strategy (REMS) for SUBOXONE sublingual film, SUBOXONE sublingual tablets, SUBUTEX sublingual tablets, and the generic equivalent products, hereafter collectively called buprenorphine-containing products. This REMS does not apply to buprenorphine-containing products that are dispensed to patients in an Opioid Treatment Program (OTP) under 42 CFR Part 8 because the care of OTP patients is subject to specific requirements under those regulations.

The FDA has determined that a REMS is necessary to ensure that the benefits of buprenorphine-containing products for opioid dependence outweigh the potential risks of accidental overdose, misuse, and abuse. Please be aware that:

› SUBOXONE sublingual film is indicated for the treatment of opioid dependence.
› SUBOXONE sublingual tablets, including generic equivalents, Zubsolv sublingual tablets, and Bunavail buccal film are indicated for the maintenance treatment of opioid dependence after initial induction.
› SUBUTEX sublingual tablets and generic equivalents are indicated for the treatment of opioid dependence.
› Patients physically dependent on heroin or other short-acting opioids may initiate treatment (induct) with either SUBOXONE sublingual film or with a buprenorphine-only sublingual product.
› SUBUTEX sublingual tablets and generic equivalent buprenorphine-only tablets are preferred for induction for patients physically dependent on methadone or long-acting opioids taken as per approved labeling.
› SUBOXONE sublingual film or tablets are preferred over buprenorphine-only products for unsupervised administration.

› All of these products are used as part of a complete treatment plan, including counseling and/or psychosocial support.

**Serious Risks of Buprenorphine-containing Products**

Please communicate the following key messages to patients about the risks of accidental overdose, misuse, and abuse while taking buprenorphine-containing products:

› Warn patients that it is extremely dangerous to self-administer non-prescribed benzodiazepines or other central nervous system (CNS) depressants (including alcohol) with these products. Caution patients prescribed benzodiazepines or other CNS depressants to use them only as directed by their prescriber.

› Instruct patients to keep buprenorphine-containing products in a secure place and out of the sight and reach of children. Accidental or deliberate ingestion by a child may cause respiratory depression that can result in death. If a child is exposed to one of these products, medical attention should be sought immediately.

› Advise patients that buprenorphine-containing products contain an opioid that can be a target for people who abuse prescription medications or street drugs. Caution patients to keep their products in a safe place, and to protect them from theft.

› Instruct patients never to give buprenorphine-containing products to anyone else, even if he or she has the same signs and symptoms. It may cause harm or death.

› Advise patients that selling or giving away buprenorphine-containing products is against the law.

**Prescriber Action**

You are encouraged to read the enclosed educational brochure entitled *Office-Based Buprenorphine Therapy for Opioid Dependence: Important Information for Prescribers*. Under the SUBOXONE sublingual film, SUBOXONE sublingual tablets, and SUBUTEX sublingual tablets REMS program, prescribers are strongly encouraged to perform and document all of the following actions:

› Verify the patient meets diagnostic criteria for opioid dependence

› Discuss the risks associated with these products, including those described in the professional labeling and the Medication Guide

› Provide induction doses under appropriate supervision

› Prescribe a limited amount of medication to the patient that will last until the next visit

› Explain how to safely store the medication out of reach of children

› Schedule patient appointments commensurate with patient stability (weekly or more frequent visits recommended for the first month)

› Consider “pill/film count”/dose reconciliation

› Assess whether the patient is receiving the counseling/psychosocial support considered necessary for treatment

› Assess whether the patient is making progress toward treatment goals, including, as appropriate, urine toxicology testing

› Continually assess appropriateness of maintenance dose

› Continually assess benefits of treatment outweigh the risks

Reference ID: 3822165
Patient Monitoring and Appropriate Dosing Info

An Appropriate Use Checklist is enclosed to assist you in performing and documenting the above prescriber actions of the SUBOXONE sublingual film, SUBOXONE sublingual tablets, and SUBUTEX sublingual tablets REMS. You may use the enclosed checklist or other means (e.g., electronic health record) specific to your office practice to document that the above actions have been completed for each patient.

Medication Guide

The SUBOXONE sublingual film, SUBOXONE sublingual tablets, and SUBUTEX sublingual tablets REMS include product specific Medication Guides on the safe and effective use of SUBOXONE sublingual film, SUBOXONE sublingual tablets, and SUBUTEX sublingual tablets. A Medication Guide will be dispensed with each prescription of SUBOXONE sublingual film, SUBOXONE sublingual tablets, and SUBUTEX sublingual tablets. Please review this important information with your patients or their caregivers. Please also discuss the importance of participating in a complete treatment program that may include counseling, behavioral therapy, and/or psychosocial support.

Reporting Adverse Events

To report SUSPECTED ADVERSE EVENTS contact:

› Indivior Inc. at 1-877-782-6966 or

› FDA MedWatch program by phone at 1-800-FDA-1088 or online at www.fda.gov/medwatch/report.htm

This letter is not a comprehensive description of the risks associated with the use of buprenorphine-containing products. Additional important safety information can be found in the Office-Based Buprenorphine Therapy for Opioid Dependence: Important Information for Prescribers educational brochure and Full Prescribing Information.


Sincerely,

<NAME>

<TITLE>

Indivior Inc.

Enclosures:

Appropriate Use Checklist
Prescriber Brochure: “Office-Based Buprenorphine Therapy for Opioid Dependence: Important Information for Prescribers”