RISK EVALUATION AND MITIGATION STRATEGY (REMS)

This REMS does not apply to SUBOXONE sublingual film, Authorized Generic of SUBOXONE sublingual film, SUBOXONE sublingual tablets, and SUBUTEX sublingual tablets dispensed to patients admitted to an Opioid Treatment Program (OTP) under 42 CFR Part 8 because the care of OTP patients is subject to specific requirements under those regulations.

I. GOAL(S):

The goals of the REMS for SUBOXONE sublingual film, Authorized Generic of SUBOXONE sublingual film, SUBOXONE sublingual tablets, and SUBUTEX sublingual tablets are to:

- Mitigate the risks of accidental overdose, misuse and abuse
- Inform prescribers, pharmacists, and patients of the serious risks associated with SUBOXONE sublingual film, Authorized Generic of SUBOXONE sublingual film, SUBOXONE sublingual tablets, and SUBUTEX sublingual tablets
II. REMS ELEMENTS:

A. Medication Guide
A Medication Guide will be dispensed with each SUBOXONE sublingual film, Authorized Generic of SUBOXONE sublingual film, SUBOXONE sublingual tablets, and SUBUTEX sublingual tablets prescription in accordance with 21 CFR 208.24. The Medication Guides for buprenorphine-containing products are part of the SUBOXONE sublingual film, Authorized Generic of SUBOXONE sublingual film, SUBOXONE sublingual tablets, and SUBUTEX sublingual tablets REMS and will be provided with the product and is also available by going online to www.suboxoneREMS.com or calling 1-866-463-4846.

B. Elements to Assure Safe Use

1. Safe use conditions
   a. SUBOXONE sublingual film, Authorized Generic of SUBOXONE sublingual film, SUBOXONE sublingual tablets, and SUBUTEX sublingual tablets will only be dispensed by the prescriber or prescribed to patients with documentation of the following safe use conditions:
      i. Verification that the patient meets the diagnostic criteria for opioid dependence.
      ii. Risks described in the professional labeling and the Medication Guide have been discussed with the patient.
      iii. Safe storage of the medication has been explained and reviewed with the patient.
      iv. After appropriate induction, the patient is prescribed a limited amount of medication at the first visit.
   b. Prescribers will document safe use conditions for each patient by using the ‘Appropriate Use Checklist,’ or by using another method (e.g. electronic health record) specific to the prescriber’s office practice.
   c. Indivior Inc. will ensure that within 30 days of FDA approval of the SUBOXONE sublingual film, Authorized Generic of SUBOXONE sublingual film, SUBOXONE sublingual tablets, and SUBUTEX sublingual tablets REMS, a Dear Prescriber Letter will be mailed to all providers certified to treat opioid dependence under the Drug Addiction Treatment Act of 2000 (DATA 2000). This letter is designed to convey and reinforce the risks of accidental overdose, misuse, and abuse of SUBOXONE sublingual film, Authorized Generic of SUBOXONE sublingual film, SUBOXONE sublingual tablets, and SUBUTEX sublingual tablets, as well as the need to appropriately monitor patients and document safe use conditions. The prescriber brochure, Office-Based Buprenorphine Therapy for Opioid Dependence: Important Information for Prescribers, and the Appropriate Use Checklist will be appended to the

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Dear Prescriber Letter. The letter will provide instructions on where to obtain copies of the Full Prescribing Information and Medication Guide. Mailings will occur annually thereafter.

d. Indivior Inc. will, on a monthly basis, identify any newly DATA 2000-certified providers and mail the applicable documents to them. The prescriber brochure, *Office-Based Buprenorphine Therapy for Opioid Dependence: Important Information for Prescribers*, will be appended to the Dear Prescriber Letter as well as the Medication Guide, Full Prescribing Information, and the Appropriate Use Checklist.

e. To further reinforce safe use conditions, Indivior Inc. will ensure that within 30 days of FDA approval of the SUBOXONE sublingual film, Authorized Generic of SUBOXONE sublingual film, SUBOXONE sublingual tablets, and SUBUTEX sublingual tablets REMS, a Dear Pharmacist Letter will be mailed to all pharmacists on a national mailing list of all retail pharmacies authorized by DEA to handle Schedule 3 controlled substances on a national mailing list from the National Technical Information Service. The pharmacist brochure, *Office-Based Buprenorphine Therapy for Opioid Dependence: Important Information for Pharmacists*, will be appended to the Dear Pharmacist Letter as well as the Medication Guide and Full Prescribing Information. Mailings will occur annually thereafter.

f. Indivior Inc. will make the letters and all materials that are appended to the letters available through its toll-free information line, through its field personnel, and on the SUBOXONE and SUBUTEX REMS website.

2. Monitoring

a. Each patient using SUBOXONE sublingual film, Authorized Generic of SUBOXONE sublingual film, SUBOXONE sublingual tablets, and SUBUTEX sublingual tablets will be subject to the following monitoring:
   i. Return visits are scheduled at intervals commensurate with patient stability. Weekly, or more frequent, visits are recommended for the first month.
   ii. Assessment and reinforcement of patient’s compliance with the prescribed medication.
   iii. Assessment of appropriateness of dosage prescribed.
   iv. Assessment of whether patient is receiving the necessary psychosocial support.
   v. Assessment of whether patient is making adequate progress towards treatment goals.

b. Prescribers will document that each patient has received the required clinical monitoring using the ‘Appropriate Use Checklist,’ or by using another method/system (e.g. electronic health record) specific to the prescriber’s office practice.

The following materials are part of the REMS and are appended to the REMS document:

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C. Implementation System
   The Implementation System includes the following:
   1. Indivior Inc. will ensure that all DATA 2000-certified providers receive the Dear Prescriber Letter with the appended materials.
   2. Indivior Inc. will monitor compliance with the requirements to document prescribing and dispensing with documentation of safe use conditions through surveys of patients and prescribers, evaluations of health care utilization databases, and ongoing surveillance (sources including, but not limited to, internet, street ethnography, national databases, and surveys conducted at substance abuse treatment programs).
   3. Indivior Inc. will monitor and evaluate the implementation of the elements to assure safe use provided for under Sections B1, above, and in the manner described in the REMS supporting document, and will take reasonable steps to improve implementation of these elements to meet the goals of the REMS.

D. Timetable for Submission of Assessments
   Indivior Inc. will submit REMS Assessments to FDA at 6 months and at 12 months for the first year from the date of approval of the REMS, then annually thereafter. To facilitate inclusion of as much information as possible, while allowing reasonable time to prepare the submission, the reporting interval covered by each assessment will conclude no earlier than 60 days before the submission date for that assessment. Indivior Inc. will submit each assessment so it will be received by the FDA on or before the due date.