NDA 20-733
SUBOXONE® (buprenorphine and naloxone) sublingual tablet CIII

Buprenorphine (opioid partial agonist-antagonist)

Naloxone (opioid antagonist)

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RISK EVALUATION AND MITIGATION STRATEGY (REMS)

This REMS does not apply to SUBOXONE tablets dispensed to patients admitted to an Opioid Treatment Program under 42 CFR Part 8.

I. GOAL(S):

The goals of the SUBOXONE tablet risk evaluation and mitigation strategy are to:

- Mitigate the risks of accidental overdose, misuse, and abuse
- Inform patients of the serious risks associated with SUBOXONE tablets

II. REMS ELEMENTS:

A. Medication Guide

A Medication Guide will be dispensed with each SUBOXONE tablet prescription in accordance with 21 CFR 208.24.

B. Elements to Assure Safe Use

1. Safe use conditions

a. SUBOXONE tablet 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. Reckitt Benckiser Pharmaceuticals Inc. will ensure that within 30 days of FDA approval of the SUBOXONE Tablet REMS, a REMS Instruction Letter to Prescribers will be mailed to all physicians 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, as well as the need to appropriately monitor patients and document safe use conditions. Annual mailings will occur in September of each year thereafter.
d. Reckitt Benckiser Pharmaceuticals Inc. will, on a monthly basis, identify any newly DATA 2000-certified physicians and mail the applicable documents to them. The following materials will be appended to the Prescriber Instruction Letter: Medication Guide, Full Prescribing Information, Physician Brochure, and the Appropriate Use Checklist.
e. To further reinforce safe use conditions, Reckitt Benckiser Pharmaceuticals Inc. will ensure that within 30 days of FDA approval of the SUBOXONE Tablet REMS, a REMS Introductory Letter for

Pharmacists will be mailed to all retail pharmacies authorized by DEA to handle schedule 3 controlled substances on a national mailing list from the National Technical Information Service. The following materials will be appended to the Introductory Pharmacist Letter: Medication Guide, Full Prescribing Information and the Pharmacist Brochure. Annual mailings will occur in September of each year thereafter.

f. Reckitt Benckiser Pharmaceuticals 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 product website.

2. Monitoring

a. Each patient using SUBOXONE tablet 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:

- SUBOXONE tablet Medication Guide
- REMS Instruction Letter to Prescribers
- REMS Introductory Letter to Pharmacists
- Appropriate Use Checklist
- Physician Brochure, *"Important Information for Physicians-Frequently Asked Questions"*
- Pharmacist Brochure, *"Important Information for Pharmacists-Frequently Asked Questions"*

C. Implementation System

The Implementation System includes the following:

1. Reckitt Benckiser Pharmaceuticals Inc. will ensure that all DATA 2000-certified physicians receive the Instruction Letter with the appended materials.
2. Reckitt Benckiser Pharmaceuticals 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. Reckitt Benckiser Pharmaceuticals 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

Reckitt Benckiser Pharmaceuticals Inc. will submit the first REMS assessment to FDA by August 31, 2012, the second REMS assessment by February 28, 2013, the third REMS assessment by August 31, 2013, and 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. Reckitt Benckiser Pharmaceuticals Inc. will submit each assessment so it will be received by the FDA on or before the due date.

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