CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

022410Orig1s000

RISK ASSESSMENT and RISK MITIGATION REVIEW(S)

INTERIM REMS REVIEW COMMENTS

Drug Name:	**BLA/NDA:**	**Date:** 8/6/10
SUBOXONE Sublingual Film (buprenorphine HCL and naloxone) (b) (4)	#22-410	**Comment Set # 1**
DRISK Scientific Leads: Jeanne Perla, Ph.D., Risk Management Analyst Megan Moncur, Risk Management Analyst		**Reviewers:** **DRISK** Gita Toyserkani, Pharm.D., Acting Team Leader Marcia Britt, Ph.D., Health Education Reviewer Brian Gordon, MA., Social Science Reviewer **DDMAC** Mathilda Fienkeng, Pharm.D., Regulatory Review Officer **OC** Agnes Plante, BSN, RN, Consumer Safety Officer
RCM #: 2010-970		

MATERIALS REVIEWED:

- General Advise Letter to applicant dated March 29, 2010
- SUBOXONE Sublingual Film NDA 22-410
  The following proposed REMS materials received April 30, 2010, were reviewed:
  1. Proposed REMS
  2. Proposed REMS Supporting Document
  3. REMS Instruction Letter to Prescribers
  4. REMS Introductory Letter to Pharmacists
  5. Appropriate Use Checklist
  6. Physician Brochure, “Important Information for Physicians- Frequently Asked Questions”
  7. Pharmacist Brochure, “Important Information for Pharmacists-Frequently Asked Questions”

(b) (4)

INTRODUCTION:

This interim REMS review is to provide preliminary comments on the proposed REMS submitted on April 23, 2010 for SUBOXONE sublingual film (NDA 22-410),

(b) (4)

On October 8, 2002 SUBUTEX and SUBOXONE sublingual tablets were approved for the treatment of opioid dependence with a Risk Management Plan. On October 20, 2008, Reckitt Benckiser submitted a REMS for NDA 22-410. The proposed indication for SUBOXONE sublingual film is for the maintenance treatment of opioid dependence.

(b) (4)

On August 21, 2009, Reckitt Benckiser received a Complete Response Letter for NDA 22-410 stating the proposed REMS was not sufficient to ensure the benefits outweighed the risk. In the CR letter the sponsor was notified that each patient using the drug be subject to certain clinical monitoring under section 5050(f)(3)(E) of the FDCA to ensure

that 1) each patient is receiving the psychosocial support necessary for safe use and effective use of [redacted] (b) (4) SUBOXONE, 2) each patient adheres to the conditions of safe use explained to him/her, and 3) each patient is using [redacted] (b) (4) SUBOXONE appropriately and making adequate progress towards treatment goals.

The sponsor requested a meeting and submitted questions in the meeting background package on October 5, 2009 to discuss their proposed REMS submitted on [redacted] (b) (4) November 24, 2009, (NDA 22410). Based on the review of the proposed REMS, the Agency provided responses in a General Advice letter to the questions and provided additional comments on the proposed REMS documents.

In the General Advice letter the sponsor was notified that based on the Agencies understanding of the risks of buprenorphine, it was determined that the REMS must include a Medication Guide, elements to assure safe use under 505-1(f)(3)(D) and 505-1(f)(3)(E), an implementation system, and a timetable for the submission of assessments of the REMS. A communication plan was not required as an element of the REMS.

Furthermore, because the risks of buprenorphine for the treatment of opioid dependence are the same, the sponsor was informed that the REMS for the three applications can be the same; however, the Medication Guide may be product specific and not all three products have to share the same Medication Guide. Additionally, the sponsor was informed that the goals of the REMS should be changed to the following: 1) to mitigate the risk of accidental overdose, misuse and abuse and 2) to inform patients of the serious risks associated with the use of SUBOXONE sublingual film [redacted] (b) (4)

The comments below are OSE/OC/DDMAC's preliminary review of the amended proposed REMS submitted by Reckitt Benckiser on April 23, 2010, which incorporates the goals and the elements as recommended in the General Advice letter of March 29, 2010.

COMMENTS FOR THE SPONSOR

The following comments are on the proposed REMS, appended material and Supporting Document submitted for NDA 22-410. [redacted] (b) (4) Please incorporate the changes for all three applications and submit all revised materials within 2 weeks.

1. **General Comments**
    a. Comments are provided based on the draft Product Labeling (PI). Revise all REMS materials to be consistent with the final agreed upon PI.
    b. Ensure the approved name of each drug is consistent with the PI in all of the REMS material.
    c. Replace [redacted] (b) (4) with *Reckitt Benckiser* throughout REMS and REMS Supporting Document.

d. Once the REMS and appended material are agreed upon, submit a final REMS with all appended materials and the REMS Supporting Document for each application.
e. Provide a track changes and clean version of all revised materials and documents.
f. All REMS documents should be dated and paginated to facilitate reviewer document control.
g. Remove the word (b) (4) from the final documents.
h. Please submit your revised proposed REMS and other materials in WORD format. It makes review of these materials more efficient and it is easier for the web posting staff to make the document 508 compliant. If certain documents are only in PDF format, they may be submitted as such, but any revisions will need to be identified (e.g. using the PDF Comment & Markup Tool).

2. REMS Goals and Objectives:

The goals of the REMS have been reviewed and found to be acceptable. The separate section titled (b) (4) has been removed from the REMS document but may remain in the Supporting Document.

3. Medication Guide:

a. Detailed information on the (b) (4) dispensing of the Medication Guide has been deleted from your REMS document, and should be included in your Supporting Document.
b. The Medication Guide for NDA 22-410 submitted on July 14, 2010 was reviewed and found to be acceptable.

(b) (4)

4. Elements to Assure Safe Use (ETASU):

a. Revisions were made to the following documents. See appended redline and clean versions:
   i. **Appendix A** (**Appendix B** – clean version) for revisions to the proposed REMS document. Please incorporate the changes. The REMS document may continue to undergo revisions by the Agency as the REMS goes through the internal clearance process.
   ii. **Attachment C** (**Appendix D** – clean Copy) for revisions to the REMS Instruction Letter to Prescribers
   iii. **Attachment E** (**Appendix F** – clean Copy) for revisions to the REMS Introductory Letter to Pharmacists
   iv. Insert headings (e.g., Obtaining Eligibility to Prescribe Suboxone, REMS, The Impact of a REMS on Prescribing Tradename) in the prescriber and pharmacist brochure to delineate the different sections being described. As currently written, the guide does not flow well.

DOCKET ALARM

Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts

Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research

With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips

Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS
Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS
Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS
Sync your system to PACER to automate legal marketing.