CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

201194Orig1s000

RISK ASSESSMENT and RISK MITIGATION REVIEW(S)

Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Surveillance and Epidemiology

Date:	January 20, 2011
To:	Bob Rappaport, MD, Division Director **Division of Analgesics and Anesthetics Products (DAAP)**
Through:	Claudia Karwoski, PharmD, Director **Division of Risk Management (DRISK)**
From:	Steve L. Morin, RN, BSN Patient Labeling Reviewer **Division of Risk Management**
Subject:	DRISK Review of Proposed Risk Evaluation and Mitigation Strategy (REMS)
Drug Name(s):	Oxycodone Hydrochloride Oral Solution (5mg/5mL)
Application Type/Number:	NDA 201-194
Therapeutic Class:	Opioid Agonist
Applicant/sponsor:	VistaPharm, Inc.
OSE RCM #:	2010-1379

1 Introduction

This memorandum is in response to a request by the Division of Analgesics and Anesthetics Products (DAAP) for the Division of Risk Management (DRISK) to review the proposed Risk Evaluation and Mitigation Strategy (REMS) for Oxycodone Hydrochloride Oral Solution.

2 Background

VistaPharm, Inc. submitted a New Drug Application (NDA) on May 4, 2010 (received May 5, 2010) under section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Oxycodone Oral Solution.

Section 505-1 of the FDCA authorizes the FDA to require the submission of a REMS if FDA determines that such a strategy is necessary to ensure that the benefits of the drug outweigh the risks. In accordance with section 505-1 of the FDCA, the FDA determined that a REMS is necessary for Oxycodone Hydrochloride Oral Solution (5mg/5mL) to ensure the benefits of the drug outweigh the risk of medication errors, which may result in overdose.

Please send these comments to the Applicant and request a response within two weeks of receipt. Let us know if you would like a meeting to discuss these comments before sending to the Applicant. The Medication Guide is being reviewed by DRISK and will be provided under separate cover.

2 Material Reviewed

- Proposed Oxycodone Hydrochloride Oral Solution (5mg/5mL) Risk Evaluation and Mitigation Strategy (REMS) submitted on January 13, 2011

3 CONCLUSIONS AND RECOMMENDATIONS

DRISK concurs with the elements of the REMS as proposed by the Applicant.

Please note, the timetable for submission of the assessments is required to be approved as part of the REMS, but not the Applicant's proposed information about the details of the REMS evaluation (methodology/instruments). The methodology and instruments **do not** need to be reviewed or approved prior to approval of the REMS.

We have the following comments and recommendations for the Applicant with regard to the proposed REMS.

Comments to VistaPharm, Inc:

See the appended Oxycodone Hydrochloride Oral Solution (5mg/5mL) REMS proposal (Appendix A of this memo) for track changes corresponding to comments in this review.

a. GOAL

Revise your goal as follows:

The goal of the REMS is to inform patients about the serious risks associated with the use of Oxycodone Hydrochloride Oral Solution.

b. Your Medication Guide Distribution plan is acceptable. Your detailed plan for how you plan to distribute the Medication Guide in accordance with 21 CFR 208.24 is more appropriate for the REMS Supporting Document.

c. Your proposed timetable for submission of assessments is acceptable. We have some editorial comments in this section of the proposed REMS.

d. REMS Assessment Plan: We request that you submit for review the detailed plan you propose to evaluate patients' understanding about the serious risks and safe use of Oxycodone Hydrochloride Oral Solution at least 90 days before you conduct the evaluation. Code the submission "REMS" Correspondence." If the plan is to conduct the required assessment using a survey, make sure the submission includes all methodology and instruments used to evaluate the patients' knowledge about the risks associated with and safe use of Oxycodone Hydrochloride Oral Solution. We offer the following guidance, if you plan to use a survey, as you develop your proposal.

1. Recruit respondents using a multi-modal approach. For example, you might recruit respondents through physicians' offices, pharmacies, managed care providers, consumer panels, or on-line.

   Explain how often you perform non-respondent follow-up or reminders.

   If you use an incentive or honorarium, provide details on what is offered and the estimated dollar value.

   Explain how you select recruitment sites.

   Submit for review any recruitment advertisements.

2. Describe the rationale for your sample size. Report the 95% confidence interval around the expected level(s) of patient knowledge for each key risk(s).

3. Define the expected number of people to be contacted to obtain the proposed sample size, and how the sample is determined (selection criteria).

4. Ensure the sample is demographically representative of the population who use the drug (patients), regardless of the condition for which they use it.

5. When possible and appropriate, ensure the sample is diverse in terms of age, race, ethnicity, sex, socio-economic status, education level, and geographically.

6. List the inclusion criteria. For example, eligible patient respondents must be:
   - Age 18 or older
   - Currently taking Oxycodone Hydrochloride Oral Solution or have taken the drug in the past 3 months
   - Not currently participating in a clinical trial involving Oxycodone Hydrochloride Oral Solution
   - Not a healthcare provider

Submit any screener instruments, and describe any quotas of sub-populations used.

7. Explain how you administer surveys and the intended frequency.

   Offer respondents multiple options for completing the survey. Be sure to include an option for the lower literacy population. For example, respondents might complete surveys online or through email, in writing or by mail, over the phone, and in person.

   Explain how you train surveyors.

8. Explain how you control for limitations or bias associated with the methodology and survey instrument(s).

9. Submit for review the introductory text used to inform respondents about the purpose of the survey.

   Tell potential respondents that their answers will not affect their ability to receive or take (patients) the drug, and that their answers and personal information will be kept confidential and anonymous.

10. Clarify in your methodology that respondents are eligible for one wave of the survey only.

11. The assessment evaluates the effectiveness of the REMS in achieving the goal by evaluating patients' knowledge of the serious risks associated with use of the drug. The assessment does not evaluate consumer comprehension of the Medication Guide.

    According to regulation (21 CFR 208.24), patients receive the Medication Guide at the time the prescription is filled/dispensed. Do not offer respondents an opportunity to read or see the Medication Guide, Package Insert, or any other related educational materials again prior to taking the survey.

12. Submit for review the survey instruments (questionnaires and/or moderator's guide), including any background information on testing survey questions and correlation to the messages in the Medication Guide.

13. Ensure the patient knowledge survey includes questions that ask about the specific risks or safety information conveyed in the Medication Guide to determine if the patient understands the information and knows what to do if they experience an adverse event.

    Derive the risk-specific questions from information located in the "What is the Most Important Information I should know about Oxycodone Hydrochloride Oral Solution?" section of the Medication Guide.

    Ensure the risk-specific questions are not biased or leading, and that multiple choice questions include an instruction to "select all that apply." Ensure that each question has an "I don't know" answer option.

    Randomize the order of the multiple choice responses on each survey.

14. Order questions so the risk-specific questions are asked first, followed by questions about receipt of the Medication Guide. Collect demographic questions last or as part of any screener questions.

    Do not allow respondents the opportunity or ability to go back to previous questions in the survey.

    Explain if and when any education will be offered for incorrect responses.

15. Include questions about receipt of the Medication Guide in the patient survey as a way to fulfill the obligation to report on the distribution of the Medication Guide.

16. Prior to the questions about receipt of the Medication Guide, include text that describes a Medication Guide. For example,

    Now we are going to ask you some questions about the Medication Guide you may have received with Oxycodone Hydrochloride Oral Solution. The Medication Guide is a paper handout that contains important information about the risks associated with use of Oxycodone Hydrochloride Oral Solution and how to use Oxycodone Hydrochloride Oral Solution safely. Medication Guides always include the title "Medication Guide" followed by the word Oxycodone Hydrochloride Oral Solution and its pronunciation. The Medication Guide usually has sections titled "What is the most important information I should know about Oxycodone Hydrochloride Oral Solution," "What is Oxycodone Hydrochloride Oral Solution," and "Who should not take Oxycodone Hydrochloride Oral Solution."

17. Use the following (or similar) questions to assess receipt and use of the Medication Guide.

    - Who gave you the Medication Guide for Oxycodone Hydrochloride Oral Solution? (Select all that apply)
        a) My doctor or someone in my doctor's office
        b) My pharmacist or someone at the pharmacy
        c) Someone else - please explain: _____
        d) I did not get a Medication Guide for Oxycodone Hydrochloride Oral Solution

    - Did you read the Medication Guide?
        a) All,
        b) Most,
        c) Some,
        d) None

    - Did you understand what you read in the Medication Guide?
        a) All,
        b) Most,
        c) Some,
        d) None

    - Did someone offer to explain to you the information in the Medication Guide?
        a) Yes, my doctor or someone in my doctor's office

b) Yes, my pharmacist or someone at the pharmacy
c) Yes, someone else – please explain: _____
d) No

- Did you accept the offer? Yes or No
- Did you understand the explanation that was given to you?
  a) All,
  b) Most,
  c) Some,
  d) None
- Did or do you have any questions about the Medication Guide? Yes or No (If Yes, list your question(s) below) Note: Group/code this open text field prior to submitting to FDA

18. Analyze results on an item-by-item or variable-by-variable basis. You may present the date using descriptive statistics, such as sample size, mean, standard deviation, median, minimum and maximum (for continuous variables), and frequency distributions (for categorical variables).

    You may stratify the data by any relevant demographic variable, and presented in aggregate. Submit with your assessments all methodology and instruments utilized.

Please let us know if you have any questions.

14 Page(s) has been Withheld in Full as b4 (CCI/TS) immediately following this page

---

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

STEVE L MORIN
01/25/2011

CLAUDIA B KARWOSKI
01/26/2011
concur