CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

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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:	December 03, 2010
To:	Thomas Laughren, MD, Director **Division of Psychiatry Products (DPP)**
Through:	Claudia Karwoski PharmD, Director **Division of Risk Management (DRISK)**
From:	Shawna Hutchins, MPH, BSN RN Patient Labeling Reviewer **Division of Risk Management (DRISK)**
Subject:	DRISK Review of Proposed Risk Evaluation and Mitigation Strategy (REMS)
Drug Name(s):	vilazodone HCL tablets
Application Type/Number:	NDA 22-567
Applicant/sponsor:	PGxHealth, LLC
OSE RCM #:	2010-784

1. INTRODUCTION

This review is written in response to a request by the Division of Psychiatry Products (DPP) for the Division of Risk Management (DRISK) to review the Applicant's proposed Risk Evaluation and Mitigation Strategy (REMS) and REMS Supporting Document for vilazodone hydrochloride (HCL) tablets. The trade name for this NDA is currently under review.

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 DRISK review of the Medication Guide will be provided under a separate cover. The DRISK review of the methodology and survey instruments to be submitted by the Applicant to evaluate the REMS will be provided under separate cover.

2. BACKGROUND

On March 22, 2010 PGxHealth, LLC, submitted a New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for vilazodone (HCL) 10 mg, 20 mg, and 40 mg tablets for the treatment of major depressive disorder (MDD).

Section 505-1 of the FDCA authorizes FDA to require the submission of a risk evaluation and mitigation strategy (REMS), if FDA determines that such a strategy is necessary to ensure that the benefits of the drug outweigh the risks [section 505-1(a)]. In accordance with section 505-1 of FDCA, the FDA determined that a REMS is necessary for vilazodone HCL tablets to ensure the benefits of the drug outweigh the increased risk of suicidality in children, adolescents, and young adults as observed in short-term studies of major depressive disorder (MDD) and other psychiatric disorders. The components of the REMS include a Medication Guide (MG) and a timetable for submission of assessments.

3. MATERIAL REVIEWED

- vilazodone HCL tablets Risk Evaluation and Mitigation Strategy (REMS) Notification Letter dated November 01, 2010.
- Proposed vilazodone HCL tablets Risk Evaluation and Mitigation Strategy (REMS) and REMS Supporting Document, submitted on March 22, 2010, and received by DRISK on November 23, 2010.

4. RESULTS OF REVIEW

In our review of the proposed REMS, we have:

- Ensured it includes the elements outlined in the REMS Notification Letter.
- Ensured it meets the statutory requirements under the Food and Drug Administration Amendments Act (FDAAA) of 2007.

5. CONCLUSIONS AND RECOMMENDATIONS

DRISK concurs with the elements of the proposed REMS.

Please note, the timetable for submission of the assessment 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 PGxHealth, LLC:

See the appended vilazodone HCL tablets 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 this REMS is to inform patients about the serious risk associated with the use of vilazodone HCL tablets.

b. Your Medication Guide distribution plan appears to be 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.

- We remind you that under 21 CFR 208.24, you are responsible for ensuring that sufficient numbers of Medication Guides are provided with the product such that a dispenser can provide one Medication Guide with each new or refilled prescription.
- We remind you that under 21 CFR 208.24, you are responsible for ensuring that the vilazodone HCL tablets carton or container label contains a prominent statement that the Medication Guide should be dispensed to each patient. We recommend one of the following statements, depending upon whether the Medication Guide accompanies the product or is enclosed in the carton (for example, unit of use):
  - "Dispense the enclosed Medication Guide to each patient." Or
  - "Dispense the accompanying Medication Guide to each patient."
- See our editorial comments on this section of the proposed REMS (see Appendix A).

c. Your proposed timetable for submission of assessments (18 months, 3 years and 7 years) is acceptable.

We have some editorial comments in this section of the REMS.

d. Regarding your REMS Assessment Plan

We acknowledge that you provided a brief description of the REMS Assessment Plan. We recommend that you submit for review the detailed plan you propose to use to evaluate patients' understanding about the safe use of vilazodone HCL tablets. You may submit the proposed plan after approval of the REMS, however submit it at least 90 days before you conduct the evaluation. Code the submission "REMS Correspondence." Make sure the submission includes all methodology and instruments used to evaluate the knowledge about the risks associated with and safe use of vilazodone HCL tablets.

If you plan to use a survey to conduct the assessment, we offer the following guidance 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).

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 vilazodone HCL tablets or have taken the drug in the past 3 months
   - Not currently participating in a clinical trial involving vilazodone HCL tablets
   - 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.

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