

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

022567Orig1s000

**ADMINISTRATIVE and CORRESPONDENCE
DOCUMENTS**

EXCLUSIVITY SUMMARY

NDA # 022567

SUPPL #

HFD # 130

Trade Name Viibryd

Generic Name vilazodone hydrochloride

Applicant Name Trovis Pharmaceuticals LLC (formerly PGxHealth, LLC)

Approval Date, If Known January 21, 2011

PART I IS AN EXCLUSIVITY DETERMINATION NEEDED?

1. An exclusivity determination will be made for all original applications, and all efficacy supplements. Complete PARTS II and III of this Exclusivity Summary only if you answer "yes" to one or more of the following questions about the submission.

a) Is it a 505(b)(1), 505(b)(2) or efficacy supplement?

YES NO

If yes, what type? Specify 505(b)(1), 505(b)(2), SE1, SE2, SE3,SE4, SE5, SE6, SE7, SE8

505(b)(1)

c) Did it require the review of clinical data other than to support a safety claim or change in labeling related to safety? (If it required review only of bioavailability or bioequivalence data, answer "no.")

YES NO

If your answer is "no" because you believe the study is a bioavailability study and, therefore, not eligible for exclusivity, EXPLAIN why it is a bioavailability study, including your reasons for disagreeing with any arguments made by the applicant that the study was not simply a bioavailability study.

N/A

If it is a supplement requiring the review of clinical data but it is not an effectiveness supplement, describe the change or claim that is supported by the clinical data:

N/A

d) Did the applicant request exclusivity?

YES NO

If the answer to (d) is "yes," how many years of exclusivity did the applicant request?

Five years

e) Has pediatric exclusivity been granted for this Active Moiety?

YES NO

If the answer to the above question in YES, is this approval a result of the studies submitted in response to the Pediatric Written Request?

N/A

IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS AT THE END OF THIS DOCUMENT.

2. Is this drug product or indication a DESI upgrade?

YES NO

IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8 (even if a study was required for the upgrade).

PART II FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES

(Answer either #1 or #2 as appropriate)

1. Single active ingredient product.

Has FDA previously approved under section 505 of the Act any drug product containing the same active moiety as the drug under consideration? Answer "yes" if the active moiety (including other esterified forms, salts, complexes, chelates or clathrates) has been previously approved, but this particular form of the active moiety, e.g., this particular ester or salt (including salts with hydrogen or coordination bonding) or other non-covalent derivative (such as a complex, chelate, or clathrate) has not been approved. Answer "no" if the compound requires metabolic conversion (other than deesterification of an esterified form of the drug) to produce an already approved active moiety.

YES NO

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA#

NDA#

NDA#

2. Combination product.

If the product contains more than one active moiety(as defined in Part II, #1), has FDA previously approved an application under section 505 containing any one of the active moieties in the drug product? If, for example, the combination contains one never-before-approved active moiety and one previously approved active moiety, answer "yes." (An active moiety that is marketed under an OTC monograph, but that was never approved under an NDA, is considered not previously approved.)

YES NO

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA#

NDA#

NDA#

IF THE ANSWER TO QUESTION 1 OR 2 UNDER PART II IS "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8. (Caution: The questions in part II of the summary should only be answered "NO" for original approvals of new molecular entities.)

IF "YES," GO TO PART III.

PART III THREE-YEAR EXCLUSIVITY FOR NDAs AND SUPPLEMENTS

To qualify for three years of exclusivity, an application or supplement must contain "reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant." This section should be completed only if the answer to PART II, Question 1 or 2 was "yes."

1. Does the application contain reports of clinical investigations? (The Agency interprets "clinical investigations" to mean investigations conducted on humans other than bioavailability studies.) If the application contains clinical investigations only by virtue of a right of reference to clinical investigations in another application, answer "yes," then skip to question 3(a). If the answer to 3(a) is "yes" for any investigation referred to in another application, do not complete remainder of summary for that investigation.

YES NO

IF "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

2. A clinical investigation is "essential to the approval" if the Agency could not have approved the application or supplement without relying on that investigation. Thus, the investigation is not essential to the approval if 1) no clinical investigation is necessary to support the supplement or application in light of previously approved applications (i.e., information other than clinical trials, such as bioavailability data, would be sufficient to provide a basis for approval as an ANDA or 505(b)(2) application because of what is already known about a previously approved product), or 2) there are published reports of studies (other than those conducted or sponsored by the applicant) or other publicly available data that independently would have been sufficient to support approval of the application, without reference to the clinical investigation submitted in the application.

(a) In light of previously approved applications, is a clinical investigation (either conducted by the applicant or available from some other source, including the published literature) necessary to support approval of the application or supplement?

YES NO

If "no," state the basis for your conclusion that a clinical trial is not necessary for approval AND GO DIRECTLY TO SIGNATURE BLOCK ON PAGE 8:

(b) Did the applicant submit a list of published studies relevant to the safety and effectiveness of this drug product and a statement that the publicly available data would not independently support approval of the application?

YES NO

(1) If the answer to 2(b) is "yes," do you personally know of any reason to disagree with the applicant's conclusion? If not applicable, answer NO.

YES NO

If yes, explain:

(2) If the answer to 2(b) is "no," are you aware of published studies not conducted or sponsored by the applicant or other publicly available data that could independently demonstrate the safety and effectiveness of this drug product?

YES NO

If yes, explain:

- (c) If the answers to (b)(1) and (b)(2) were both "no," identify the clinical investigations submitted in the application that are essential to the approval:

Studies comparing two products with the same ingredient(s) are considered to be bioavailability studies for the purpose of this section.

3. In addition to being essential, investigations must be "new" to support exclusivity. The agency interprets "new clinical investigation" to mean an investigation that 1) has not been relied on by the agency to demonstrate the effectiveness of a previously approved drug for any indication and 2) does not duplicate the results of another investigation that was relied on by the agency to demonstrate the effectiveness of a previously approved drug product, i.e., does not redemonstrate something the agency considers to have been demonstrated in an already approved application.

- a) For each investigation identified as "essential to the approval," has the investigation been relied on by the agency to demonstrate the effectiveness of a previously approved drug product? (If the investigation was relied on only to support the safety of a previously approved drug, answer "no.")

Investigation #1 YES NO

Investigation #2 YES NO

If you have answered "yes" for one or more investigations, identify each such investigation and the NDA in which each was relied upon:

- b) For each investigation identified as "essential to the approval", does the investigation duplicate the results of another investigation that was relied on by the agency to support the effectiveness of a previously approved drug product?

Investigation #1 YES NO

Investigation #2 YES NO

If you have answered "yes" for one or more investigation, identify the NDA in which a similar investigation was relied on:

Investigation #2

!

YES

!

! NO

Explain:

! Explain:

(c) Notwithstanding an answer of "yes" to (a) or (b), are there other reasons to believe that the applicant should not be credited with having "conducted or sponsored" the study? (Purchased studies may not be used as the basis for exclusivity. However, if all rights to the drug are purchased (not just studies on the drug), the applicant may be considered to have sponsored or conducted the studies sponsored or conducted by its predecessor in interest.)

YES

NO

If yes, explain:

=====

Name of person completing form: Bill Bender
Title: Senior Regulatory Project Manager
Date: 01/24/2011

Name of Office/Division Director signing form: Thomas Laughren, M.D.
Title: Director, Division of Psychiatry Products

Form OGD-011347; Revised 05/10/2004; formatted 2/15/05

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

/s/

WILLIAM H BENDER
01/24/2011

THOMAS P LAUGHREN
01/24/2011

ACTION PACKAGE CHECKLIST

APPLICATION INFORMATION ¹		
NDA # 022567 BLA #	NDA Supplement # BLA STN #	If NDA, Efficacy Supplement Type:
Proprietary Name: Viibryd Established/Proper Name: vilazodone hydrochloride Dosage Form: Tablets		Applicant: Trovis LLC Agent for Applicant (if applicable):
RPM: Bill Bender		Division: Division of Psychiatry Products
<p>NDA: NDA Application Type: <input checked="" type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2) Efficacy Supplement: <input type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2)</p> <p>(A supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2). Consult page 1 of the 505(b)(2) Assessment or the Appendix to this Action Package Checklist.)</p>		<p>505(b)(2) Original NDAs and 505(b)(2) NDA supplements: Listed drug(s) relied upon for approval (include NDA #(s) and drug name(s)):</p> <p>Provide a brief explanation of how this product is different from the listed drug.</p> <p>If no listed drug, explain.</p> <p><input type="checkbox"/> This application relies on literature. <input type="checkbox"/> This application relies on a final OTC monograph. <input type="checkbox"/> Other (explain)</p> <p><u>Two months prior to each action, review the information in the 505(b)(2) Assessment and submit the draft to CDER OND IO for clearance. Finalize the 505(b)(2) Assessment at the time of the approval action.</u></p> <p><u>On the day of approval, check the Orange Book again for any new patents or pediatric exclusivity.</u></p> <p><input type="checkbox"/> No changes <input type="checkbox"/> Updated Date of check:</p> <p>If pediatric exclusivity has been granted or the pediatric information in the labeling of the listed drug changed, determine whether pediatric information needs to be added to or deleted from the labeling of this drug.</p>
❖ Actions		
<ul style="list-style-type: none"> • Proposed action • User Fee Goal Date is <u>January 22, 2011</u> 		<input checked="" type="checkbox"/> AP <input type="checkbox"/> TA <input type="checkbox"/> CR
<ul style="list-style-type: none"> • Previous actions (<i>specify type and date for each action taken</i>) 		<input checked="" type="checkbox"/> None
❖ If accelerated approval or approval based on efficacy studies in animals, were promotional materials received? Note: Promotional materials to be used within 120 days after approval must have been submitted (for exceptions, see http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm069965.pdf). If not submitted, explain _____		<input type="checkbox"/> Received

¹ The **Application Information** section is (only) a checklist. The **Contents of Action Package** section (beginning on page 5) lists the documents to be included in the Action Package.

❖ Application Characteristics ²	
<p>Review priority: <input checked="" type="checkbox"/> Standard <input type="checkbox"/> Priority Chemical classification (new NDAs only):</p> <p><input type="checkbox"/> Fast Track <input type="checkbox"/> Rx-to-OTC full switch <input type="checkbox"/> Rolling Review <input type="checkbox"/> Rx-to-OTC partial switch <input type="checkbox"/> Orphan drug designation <input type="checkbox"/> Direct-to-OTC</p> <p>NDAs: Subpart H BLAs: Subpart E <input type="checkbox"/> Accelerated approval (21 CFR 314.510) <input type="checkbox"/> Accelerated approval (21 CFR 601.41) <input type="checkbox"/> Restricted distribution (21 CFR 314.520) <input type="checkbox"/> Restricted distribution (21 CFR 601.42)</p> <p>Subpart I Subpart H <input type="checkbox"/> Approval based on animal studies <input type="checkbox"/> Approval based on animal studies</p> <p><input type="checkbox"/> Submitted in response to a PMR REMS: <input checked="" type="checkbox"/> MedGuide <input type="checkbox"/> Submitted in response to a PMC <input type="checkbox"/> Communication Plan <input type="checkbox"/> Submitted in response to a Pediatric Written Request <input type="checkbox"/> ETASU <input type="checkbox"/> REMS not required</p> <p>Comments:</p>	
❖ BLAs only: Ensure <i>RMS-BLA Product Information Sheet for TBP</i> and <i>RMS-BLA Facility Information Sheet for TBP</i> have been completed and forwarded to OPI/OBI/DRM (Vicky Carter)	<input type="checkbox"/> Yes, dates
❖ BLAs only: Is the product subject to official FDA lot release per 21 CFR 610.2 (<i>approvals only</i>)	<input type="checkbox"/> Yes <input type="checkbox"/> No
❖ Public communications (<i>approvals only</i>)	
• Office of Executive Programs (OEP) liaison has been notified of action	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
• Press Office notified of action (by OEP)	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
• Indicate what types (if any) of information dissemination are anticipated	<input type="checkbox"/> None <input checked="" type="checkbox"/> HHS Press Release <input type="checkbox"/> FDA Talk Paper <input type="checkbox"/> CDER Q&As <input type="checkbox"/> Other

² Answer all questions in all sections in relation to the pending application, i.e., if the pending application is an NDA or BLA supplement, then the questions should be answered in relation to that supplement, not in relation to the original NDA or BLA. For example, if the application is a pending BLA supplement, then a new *RMS-BLA Product Information Sheet for TBP* must be completed.

❖ Exclusivity	
<ul style="list-style-type: none"> Is approval of this application blocked by any type of exclusivity? 	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes
<ul style="list-style-type: none"> NDA and BLAs: Is there existing orphan drug exclusivity for the “same” drug or biologic for the proposed indication(s)? <i>Refer to 21 CFR 316.3(b)(13) for the definition of “same drug” for an orphan drug (i.e., active moiety). This definition is NOT the same as that used for NDA chemical classification.</i> 	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If, yes, NDA/BLA # and date exclusivity expires:
<ul style="list-style-type: none"> (b)(2) NDAs only: Is there remaining 5-year exclusivity that would bar effective approval of a 505(b)(2) application? <i>(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)</i> 	<input type="checkbox"/> No <input type="checkbox"/> Yes If yes, NDA # and date exclusivity expires:
<ul style="list-style-type: none"> (b)(2) NDAs only: Is there remaining 3-year exclusivity that would bar effective approval of a 505(b)(2) application? <i>(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)</i> 	<input type="checkbox"/> No <input type="checkbox"/> Yes If yes, NDA # and date exclusivity expires:
<ul style="list-style-type: none"> (b)(2) NDAs only: Is there remaining 6-month pediatric exclusivity that would bar effective approval of a 505(b)(2) application? <i>(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)</i> 	<input type="checkbox"/> No <input type="checkbox"/> Yes If yes, NDA # and date exclusivity expires:
<ul style="list-style-type: none"> NDAs only: Is this a single enantiomer that falls under the 10-year approval limitation of 505(u)? <i>(Note that, even if the 10-year approval limitation period has not expired, the application may be tentatively approved if it is otherwise ready for approval.)</i> 	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If yes, NDA # and date 10-year limitation expires:
❖ Patent Information (NDAs only)	
<ul style="list-style-type: none"> Patent Information: Verify that form FDA-3542a was submitted for patents that claim the drug for which approval is sought. If the drug is an old antibiotic, skip the Patent Certification questions. 	<input checked="" type="checkbox"/> Verified <input type="checkbox"/> Not applicable because drug is an old antibiotic.
<ul style="list-style-type: none"> Patent Certification [505(b)(2) applications]: Verify that a certification was submitted for each patent for the listed drug(s) in the Orange Book and identify the type of certification submitted for each patent. 	21 CFR 314.50(i)(1)(i)(A) <input type="checkbox"/> Verified 21 CFR 314.50(i)(1) <input type="checkbox"/> (ii) <input type="checkbox"/> (iii)
<ul style="list-style-type: none"> [505(b)(2) applications] If the application includes a paragraph III certification, it cannot be approved until the date that the patent to which the certification pertains expires (but may be tentatively approved if it is otherwise ready for approval). 	<input type="checkbox"/> No paragraph III certification Date patent will expire
<ul style="list-style-type: none"> [505(b)(2) applications] For each paragraph IV certification, verify that the applicant notified the NDA holder and patent owner(s) of its certification that the patent(s) is invalid, unenforceable, or will not be infringed (review documentation of notification by applicant and documentation of receipt of notice by patent owner and NDA holder). <i>(If the application does not include any paragraph IV certifications, mark “N/A” and skip to the next section below (Summary Reviews)).</i> 	<input checked="" type="checkbox"/> N/A (no paragraph IV certification) <input type="checkbox"/> Verified

- [505(b)(2) applications] For **each paragraph IV** certification, based on the questions below, determine whether a 30-month stay of approval is in effect due to patent infringement litigation.

Answer the following questions for **each** paragraph IV certification:

- (1) Have 45 days passed since the patent owner's receipt of the applicant's notice of certification?

Yes No

(Note: The date that the patent owner received the applicant's notice of certification can be determined by checking the application. The applicant is required to amend its 505(b)(2) application to include documentation of this date (e.g., copy of return receipt or letter from recipient acknowledging its receipt of the notice) (see 21 CFR 314.52(e)).

If "Yes," skip to question (4) below. If "No," continue with question (2).

- (2) Has the patent owner (or NDA holder, if it is an exclusive patent licensee) submitted a written waiver of its right to file a legal action for patent infringement after receiving the applicant's notice of certification, as provided for by 21 CFR 314.107(f)(3)?

Yes No

If "Yes," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip the rest of the patent questions.

If "No," continue with question (3).

- (3) Has the patent owner, its representative, or the exclusive patent licensee filed a lawsuit for patent infringement against the applicant?

Yes No

(Note: This can be determined by confirming whether the Division has received a written notice from the (b)(2) applicant (or the patent owner or its representative) stating that a legal action was filed within 45 days of receipt of its notice of certification. The applicant is required to notify the Division in writing whenever an action has been filed within this 45-day period (see 21 CFR 314.107(f)(2)).

If "No," the patent owner (or NDA holder, if it is an exclusive patent licensee) has until the expiration of the 45-day period described in question (1) to waive its right to bring a patent infringement action or to bring such an action. After the 45-day period expires, continue with question (4) below.

- (4) Did the patent owner (or NDA holder, if it is an exclusive patent licensee) submit a written waiver of its right to file a legal action for patent infringement within the 45-day period described in question (1), as provided for by 21 CFR 314.107(f)(3)?

Yes No

If "Yes," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next section below (Summary Reviews).

If "No," continue with question (5).

<p>(5) Did the patent owner, its representative, or the exclusive patent licensee bring suit against the (b)(2) applicant for patent infringement within 45 days of the patent owner's receipt of the applicant's notice of certification?</p> <p>(Note: This can be determined by confirming whether the Division has received a written notice from the (b)(2) applicant (or the patent owner or its representative) stating that a legal action was filed within 45 days of receipt of its notice of certification. The applicant is required to notify the Division in writing whenever an action has been filed within this 45-day period (see 21 CFR 314.107(f)(2)). If no written notice appears in the NDA file, confirm with the applicant whether a lawsuit was commenced within the 45-day period).</p> <p><i>If "No," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next section below (Summary Reviews).</i></p> <p><i>If "Yes," a stay of approval may be in effect. To determine if a 30-month stay is in effect, consult with the OND ADRA and attach a summary of the response.</i></p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> No</p>
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CONTENTS OF ACTION PACKAGE

❖ Copy of this Action Package Checklist ³	yes
Officer/Employee List	
❖ List of officers/employees who participated in the decision to approve this application and consented to be identified on this list (<i>approvals only</i>)	<input checked="" type="checkbox"/> Included
Documentation of consent/non-consent by officers/employees	<input checked="" type="checkbox"/> Included
Action Letters	
❖ Copies of all action letters (<i>including approval letter with final labeling</i>)	Action(s) and date(s) Approval , January 22, 2011
Labeling	
❖ Package Insert (<i>write submission/communication date at upper right of first page of PI</i>)	
<ul style="list-style-type: none"> • Most recent draft labeling. If it is division-proposed labeling, it should be in track-changes format. 	
<ul style="list-style-type: none"> • Original applicant-proposed labeling 	March 22, 2010
<ul style="list-style-type: none"> • Example of class labeling, if applicable 	

³ Fill in blanks with dates of reviews, letters, etc.
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❖ Medication Guide/Patient Package Insert/Instructions for Use/Device Labeling (<i>write submission/communication date at upper right of first page of each piece</i>)	<input checked="" type="checkbox"/> Medication Guide <input checked="" type="checkbox"/> Patient Package Insert <input type="checkbox"/> Instructions for Use <input type="checkbox"/> Device Labeling <input type="checkbox"/> None
<ul style="list-style-type: none"> Most-recent draft labeling. If it is division-proposed labeling, it should be in track-changes format. 	
<ul style="list-style-type: none"> Original applicant-proposed labeling 	March 22, 2010
<ul style="list-style-type: none"> Example of class labeling, if applicable 	
❖ Labels (full color carton and immediate-container labels) (<i>write submission/communication date on upper right of first page of each submission</i>)	
<ul style="list-style-type: none"> Most-recent draft labeling 	January 19, 2011
❖ Proprietary Name <ul style="list-style-type: none"> Acceptability/non-acceptability letter(s) (<i>indicate date(s)</i>) Review(s) (<i>indicate date(s)</i>) 	11/17/2010 Acceptability
❖ Labeling reviews (<i>indicate dates of reviews and meetings</i>)	<input type="checkbox"/> RPM <input type="checkbox"/> DMEPA <input checked="" type="checkbox"/> DRISK MedGuide 12/26/2010 REMS Review 12/03/2010 <input checked="" type="checkbox"/> DDMAC 12/14/2010 <input checked="" type="checkbox"/> CSS 01/05/2011 <input type="checkbox"/> Other reviews
Administrative / Regulatory Documents	
❖ Administrative Reviews (<i>e.g., RPM Filing Review⁴/Memo of Filing Meeting</i>) (<i>indicate date of each review</i>) ❖ All NDA (b)(2) Actions: Date each action cleared by (b)(2) Clearance Cmte ❖ NDA (b)(2) Approvals Only: 505(b)(2) Assessment (<i>indicate date</i>)	RPM Filing Review 07/08/2010 Regulatory Filing Letter 05/28/2010 <input checked="" type="checkbox"/> Not a (b)(2) <input checked="" type="checkbox"/> Not a (b)(2)
❖ NDAs only: Exclusivity Summary (<i>signed by Division Director</i>)	<input checked="" type="checkbox"/> Included
❖ Application Integrity Policy (AIP) Status and Related Documents http://www.fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/default.htm	
<ul style="list-style-type: none"> Applicant is on the AIP 	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<ul style="list-style-type: none"> This application is on the AIP <ul style="list-style-type: none"> If yes, Center Director's Exception for Review memo (<i>indicate date</i>) If yes, OC clearance for approval (<i>indicate date of clearance communication</i>) 	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> Not an AP action
❖ Pediatrics (<i>approvals only</i>) <ul style="list-style-type: none"> Date reviewed by PeRC <u>December 1, 2010</u> If PeRC review not necessary, explain: _____ Pediatric Page/Record (<i>approvals only, must be reviewed by PERC before finalized</i>) 	<input type="checkbox"/> Included
❖ Debarment certification (original applications only): verified that qualifying language was not used in certification and that certifications from foreign applicants are cosigned by U.S. agent (<i>include certification</i>)	<input checked="" type="checkbox"/> Verified, statement is acceptable

⁴ Filing reviews for scientific disciplines should be filed behind the respective discipline tab.
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❖ Outgoing communications (<i>letters (except action letters), emails, faxes, telecons</i>)	
❖ Internal memoranda, telecons, etc.	
❖ Minutes of Meetings	
• Regulatory Briefing (<i>indicate date of mtg</i>)	<input type="checkbox"/> No mtg
• If not the first review cycle, any end-of-review meeting (<i>indicate date of mtg</i>)	<input type="checkbox"/> N/A or no mtg
• Pre-NDA/BLA meeting (<i>indicate date of mtg</i>)	<input type="checkbox"/> No mtg 06/17/2009; 07/31/2009
• EOP2 meeting (<i>indicate date of mtg</i>)	<input type="checkbox"/> No mtg
• Other milestone meetings (e.g., EOP2a, CMC pilots) (<i>indicate dates of mtgs</i>)	
❖ Advisory Committee Meeting(s)	<input checked="" type="checkbox"/> No AC meeting
• Date(s) of Meeting(s)	
• 48-hour alert or minutes, if available (<i>do not include transcript</i>)	
Decisional and Summary Memos	
❖ Office Director Decisional Memo (<i>indicate date for each review</i>)	<input type="checkbox"/> None 01/21/2011
Division Director Summary Review (<i>indicate date for each review</i>)	<input type="checkbox"/> None 01/18/2011
Cross-Discipline Team Leader Review (<i>indicate date for each review</i>)	<input type="checkbox"/> None 01/05/2011
PMR/PMC Development Templates (<i>indicate total number</i>)	<input type="checkbox"/> None 11
Clinical Information⁵	
❖ Clinical Reviews	
• Clinical Team Leader Review(s) (<i>indicate date for each review</i>)	01/05/2011
• Clinical review(s) (<i>indicate date for each review</i>)	01/20/2011
• Social scientist review(s) (if OTC drug) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
❖ Financial Disclosure reviews(s) or location/date if addressed in another review OR If no financial disclosure information was required, check here <input type="checkbox"/> and include a review/memo explaining why not (<i>indicate date of review/memo</i>)	12/03/2010
❖ Clinical reviews from immunology and other clinical areas/divisions/Centers (<i>indicate date of each review</i>)	<input type="checkbox"/> None Ophthalmology 01/07/2011 and CardioRenal QT- IRT review 09/15/2010
❖ Controlled Substance Staff review(s) and Scheduling Recommendation (<i>indicate date of each review</i>)	<input type="checkbox"/> Not applicable 01/05/2011
❖ Risk Management	
• REMS Documents and Supporting Statement (<i>indicate date(s) of submission(s)</i>)	11/18/2010
• REMS Memo(s) and letter(s) (<i>indicate date(s)</i>)	01/04/2011
• Risk management review(s) and recommendations (including those by OSE and CSS) (<i>indicate date of each review and indicate location/date if incorporated into another review</i>)	<input type="checkbox"/> None 12/03/2010
❖ DSI Clinical Inspection Review Summary(ies) (<i>include copies of DSI letters to investigators</i>)	<input type="checkbox"/> None requested 09/15/2010; 09/21/2010; 09/30/2010; 10/4/2010; 10/5/2010

⁵ Filing reviews should be filed with the discipline reviews.
Version: 8/25/10

Clinical Microbiology <input checked="" type="checkbox"/> None	
❖ Clinical Microbiology Team Leader Review(s) (<i>indicate date for each review</i>)	<input type="checkbox"/> None
Clinical Microbiology Review(s) (<i>indicate date for each review</i>)	<input type="checkbox"/> None
Biostatistics <input type="checkbox"/> None	
❖ Statistical Division Director Review(s) (<i>indicate date for each review</i>)	<input type="checkbox"/> None
Statistical Team Leader Review(s) (<i>indicate date for each review</i>)	<input type="checkbox"/> None
Statistical Review(s) (<i>indicate date for each review</i>)	<input type="checkbox"/> None Clinical 12/03/2010
Clinical Pharmacology <input type="checkbox"/> None	
❖ Clinical Pharmacology Division Director Review(s) (<i>indicate date for each review</i>)	<input type="checkbox"/> None
Clinical Pharmacology Team Leader Review(s) (<i>indicate date for each review</i>)	<input type="checkbox"/> None
Clinical Pharmacology review(s) (<i>indicate date for each review</i>)	<input type="checkbox"/> None 12/08/2010; Amended 12/10/2010
❖ DSI Clinical Pharmacology Inspection Review Summary (<i>include copies of DSI letters</i>)	<input checked="" type="checkbox"/> None
Nonclinical <input type="checkbox"/> None	
❖ Pharmacology/Toxicology Discipline Reviews	
• ADP/T Review(s) (<i>indicate date for each review</i>)	<input type="checkbox"/> None 01/14/2011
• Supervisory Review(s) (<i>indicate date for each review</i>)	<input type="checkbox"/> None 01/12/2011
• Pharm/tox review(s), including referenced IND reviews (<i>indicate date for each review</i>)	<input type="checkbox"/> None 12/22/2010
❖ Review(s) by other disciplines/divisions/Centers requested by P/T reviewer (<i>indicate date for each review</i>)	<input type="checkbox"/> None
❖ Statistical review(s) of carcinogenicity studies (<i>indicate date for each review</i>)	<input type="checkbox"/> No carc Carcinogenicity 11/09/2010
❖ ECAC/CAC report/memo of meeting	<input type="checkbox"/> None Included in P/T review, page
❖ DSI Nonclinical Inspection Review Summary (<i>include copies of DSI letters</i>)	<input checked="" type="checkbox"/> None requested
Product Quality <input type="checkbox"/> None	
❖ Product Quality Discipline Reviews	
• ONDQA/OBP Division Director Review(s) (<i>indicate date for each review</i>)	<input type="checkbox"/> None 01/07/2011
• Branch Chief/Team Leader Review(s) (<i>indicate date for each review</i>)	<input type="checkbox"/> None
• Product quality review(s) including ONDQA biopharmaceutics reviews (<i>indicate date for each review</i>)	<input type="checkbox"/> None 11/03/2010; 12/06/2010; Biopharmaceutics 12/10/2010
❖ Microbiology Reviews <input type="checkbox"/> NDAs: Microbiology reviews (sterility & pyrogenicity) (OPS/NDMS) (<i>indicate date of each review</i>) <input type="checkbox"/> BLAs: Sterility assurance, microbiology, facilities reviews (DMPQ/MAPCB/BMT) (<i>indicate date of each review</i>)	<input checked="" type="checkbox"/> Not needed
❖ Reviews by other disciplines/divisions/Centers requested by CMC/quality reviewer (<i>indicate date of each review</i>)	<input checked="" type="checkbox"/> None

❖ Environmental Assessment (check one) (original and supplemental applications)	
<input checked="" type="checkbox"/> Categorical Exclusion (<i>indicate review date</i>)(<i>all original applications and all efficacy supplements that could increase the patient population</i>)	
<input type="checkbox"/> Review & FONSI (<i>indicate date of review</i>)	
<input type="checkbox"/> Review & Environmental Impact Statement (<i>indicate date of each review</i>)	
❖ Facilities Review/Inspection	
<input type="checkbox"/> NDAs: Facilities inspections (include EER printout) (<i>date completed must be within 2 years of action date</i>) (<i>only original NDAs and supplements that include a new facility or a change that affects the manufacturing sites⁶</i>)	Date completed: 06/02/2010 <input checked="" type="checkbox"/> Acceptable <input type="checkbox"/> Withhold recommendation <input type="checkbox"/> Not applicable
<input type="checkbox"/> BLAs: TB-EER (<i>date of most recent TB-EER must be within 30 days of action date</i>) (<i>original and supplemental BLAs</i>)	Date completed: <input type="checkbox"/> Acceptable <input type="checkbox"/> Withhold recommendation
❖ NDAs: Methods Validation (<i>check box only, do not include documents</i>)	<input checked="" type="checkbox"/> Completed <input type="checkbox"/> Requested <input type="checkbox"/> Not yet requested <input type="checkbox"/> Not needed (per review)

⁶ I.e., a new facility or a change in the facility, or a change in the manufacturing process in a way that impacts the Quality Management Systems of the facility.

Appendix to Action Package Checklist

An NDA or NDA supplemental application is likely to be a 505(b)(2) application if:

- (1) It relies on published literature to meet any of the approval requirements, and the applicant does not have a written right of reference to the underlying data. If published literature is cited in the NDA but is not necessary for approval, the inclusion of such literature will not, in itself, make the application a 505(b)(2) application.
- (2) **Or** it relies for approval on the Agency's previous findings of safety and efficacy for a listed drug product and the applicant does not own or have right to reference the data supporting that approval.
- (3) **Or** it relies on what is "generally known" or "scientifically accepted" about a class of products to support the safety or effectiveness of the particular drug for which the applicant is seeking approval. (Note, however, that this does not mean *any* reference to general information or knowledge (e.g., about disease etiology, support for particular endpoints, methods of analysis) causes the application to be a 505(b)(2) application.)

Types of products for which 505(b)(2) applications are likely to be submitted include: fixed-dose combination drug products (e.g., heart drug and diuretic (hydrochlorothiazide) combinations); OTC monograph deviations (see 21 CFR 330.11); new dosage forms; new indications; and, new salts.

An efficacy supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2).

An efficacy supplement is a 505(b)(1) supplement if the supplement contains all of the information needed to support the approval of the change proposed in the supplement. For example, if the supplemental application is for a new indication, the supplement is a 505(b)(1) if:

- (1) The applicant has conducted its own studies to support the new indication (or otherwise owns or has right of reference to the data/studies).
- (2) **And** no additional information beyond what is included in the supplement or was embodied in the finding of safety and effectiveness for the original application or previously approved supplements is needed to support the change. For example, this would likely be the case with respect to safety considerations if the dose(s) was/were the same as (or lower than) the original application.
- (3) **And** all other "criteria" are met (e.g., the applicant owns or has right of reference to the data relied upon for approval of the supplement, the application does not rely for approval on published literature based on data to which the applicant does not have a right of reference).

An efficacy supplement is a 505(b)(2) supplement if:

- (1) Approval of the change proposed in the supplemental application would require data beyond that needed to support our previous finding of safety and efficacy in the approval of the original application (or earlier supplement), and the applicant has not conducted all of its own studies for approval of the change, or obtained a right to reference studies it does not own. For example, if the change were for a new indication AND a higher dose, we would likely require clinical efficacy data and preclinical safety data to approve the higher dose. If the applicant provided the effectiveness data, but had to rely on a different listed drug, or a new aspect of a previously cited listed drug, to support the safety of the new dose, the supplement would be a 505(b)(2).
- (2) **Or** the applicant relies for approval of the supplement on published literature that is based on data that the applicant does not own or have a right to reference. If published literature is cited in the supplement but is not necessary for approval, the inclusion of such literature will not, in itself, make the supplement a 505(b)(2) supplement.
- (3) **Or** the applicant is relying upon any data they do not own or to which they do not have right of reference.

If you have questions about whether an application is a 505(b)(1) or 505(b)(2) application, consult with your ODE's ADRA.

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/s/

WILLIAM H BENDER
01/24/2011

Bender, William

From: Bender, William
Sent: Thursday, January 20, 2011 5:50 PM
To: 'Fabrizio, Kimberly'

As we discussed today during our telephone conversation, we have separated the initial PMR regarding metabolite M17 into 2 PMRs as follows:

1723-5 Assess the reproductive toxicity of metabolite M17 by conducting an embryo-fetal study in either rats or rabbits in which M17 is administered by a route that will produce systemic exposure equal to or greater than the exposure in humans at the MRHD.

The timetable as agreed upon on a January 19, 2011 communication, states that you will conduct this study according to the following schedule:

Final Protocol Submission Date:	Not applicable
Study Completion Date:	November 30, 2012
Final Report Submission:	January 31, 2013

1723-6 Assess the reproductive toxicity of metabolite M17 by demonstrating that the original rabbit study was adequate to assess the embryo-fetal toxicity of M17. This will require data demonstrating that the systemic exposure to M17 in rabbits in that study was equal to or greater than that in humans at the MRHD.

The timetable as agreed upon on a January 19, 2011 communication, states that you will conduct this study according to the following schedule:

Final Protocol Submission Date:	Not applicable
Study Completion Date:	November 30, 2012
Final Report Submission:	January 31, 2013

If you provide adequate data to fulfill PMR 1723-6, then you will be released from PMR 1723-5.

Thank you,
Bill

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/s/

WILLIAM H BENDER
01/20/2011

Bender, William

From: Fabrizio, Kimberly [KFabrizio@pgxhealth.com]
Sent: Wednesday, January 19, 2011 9:55 AM
To: Bender, William
Subject: NDA 22567 Vilazodone PMR/PMC

Hi Bill,

We agree to the PMR/PMCs as noted in your email below with one exception. As was agreed upon during our teleconference on 06Jan2011, we will study a dose of 20 mg/day but with the study design to be determined at a later date. The Division agreed this was acceptable provided we adhere to the timelines outlined below.

Best regards,

Kimberly Fabrizio

Vice President Regulatory Affairs

PGxHealth™, a Division of Clinical Data®

5 Science Park

New Haven, CT 06511 (USA)

Phone: +1 (203) 786-3502 x2502

Email: kfabrizio@pgxhealth.com

Web: <http://www.pgxhealth.com>

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From: Bender, William [mailto:William.Bender2@fda.hhs.gov]
Sent: Wednesday, January 19, 2011 9:04 AM
To: Fabrizio, Kimberly
Subject: NDA 22567 Vilazodone PMR/PMC

Hi Kim,

Attached are the final PMR/PMCs. Please email me back with your agreement.

Thanks,
Bill

Post Marketing Requirements

red pediatric study under PREA for the treatment of major depressive disorder in pediatric patients ages 7 to 17 years-old. A study to obtain pharmacokinetic, safety, and tolerability data and provide information pertinent to dosing of vilazodone in the relevant pediatric population.

Reference ID: 2893799

1/20/2011

Final Protocol Submission Date: January 31, 2012
 Study Completion Date: February 28, 2013
 Final Report Submission: January 31, 2016

Deferred pediatric study under PREA for the treatment of major depressive disorder in pediatric patients ages 7 to 17 years-old. A study to obtain data on the efficacy and safety of vilazodone in the relevant pediatric population. This must be a placebo-controlled and active-controlled (fluoxetine) study. This study must be a fixed-dose study.

Final Protocol Submission Date: May 31, 2013
 Study Completion Date: July 31, 2015
 Final Report Submission: January 31, 2016

Deferred pediatric study under PREA for the treatment of major depressive disorder in pediatric patients aged 7 to 17 years-old. A second study to obtain data on the efficacy and safety of vilazodone in the relevant pediatric population. This must be a placebo-controlled and active-controlled (fluoxetine) study. This study may be a fixed-dose study.

Final Protocol Submission Date: May 31, 2013
 Study Completion Date: July 31, 2015
 Final Report Submission: January 31, 2016

To support the use of vilazodone in children less than 13 years of age, you must conduct a study to assess the safety of vilazodone in juvenile rats. This study must include evaluation of neurological/behavioral development and reproductive development. You should submit the protocol for our comments prior to initiating the study.

Final Protocol Submission Date: January 30, 2012
 Study Completion Date: January 30, 2014
 Final Report Submission: January 30, 2015

Assess the reproductive toxicity of metabolite M17 by conducting an embryo-fetal study in either rats or rabbits in which M17 is administered by a route that will produce systemic exposure equal to or greater than the exposure in humans at the MRHD. Alternatively, since M17 was formed by isolated rabbit hepatocytes and may thus possibly be present in plasma of rabbits treated with vilazodone, justify that the original rabbit study was adequate to assess the embryo-fetal toxicity of M17 by providing data demonstrating that the systemic exposure to M17 in rabbits in that study was equal to or greater than that in humans at the MRHD

The timetable as agreed upon on a January 4, 2011 communication, states that you will conduct this study according to the following schedule:

Final Protocol Submission Date: Not applicable
 Study Completion Date: November 30, 2012
 Final Report Submission: January 31, 2013

PostMarketing Commitments

We remind you of your postmarketing commitments agreed upon in your communications dated January 5, 2011:

rolled trial to evaluate the longer-term (i.e., maintenance) efficacy of vilazodone in the treatment of adults with major depressive disorder. This trial must be placebo-controlled, utilize a randomized withdrawal design, and include an adequate period of stabilization with open-label treatment of vilazodone prior to double-blind randomization.

Final Protocol Submission: September 30, 2011
 Trial Completion Date: January 31, 2015
 Final Report Submission: January 31, 2016

It is apparent from the trials you have conducted in major depressive disorder that the lowest effective dose of vilazodone has been identified, because only one dose (40 mg/day) was studied. However, there are suggestions that 20 mg/day may be effective at least in some subjects. In one of the trials, those who did not tolerate 40 mg/day could continue in the trial on a dose of 20 mg/day, and some may have had a significant treatment effect. In addition, data from the phase 2 fixed-dose trials suggest that there may have been a signal of efficacy with the 20 mg/day dose, as measured by the secondary efficacy measure (MADRS). Moreover, some important adverse reactions are dose-related. Thus, we request that you further characterize the efficacy and safety of vilazodone in the treatment of adults with MDD using fixed doses of vilazodone (20 mg and 40 mg), an active control (for assay sensitivity), and placebo in an adequate and well controlled trial.

Final Protocol Submission: October 30, 2011
 Trial Completion: January 31, 2013
 Final Report Submission: January 31, 2014

Vilazodone is metabolized primarily by CYP3A4. Information on the effect of CYP3A4 induction on vilazodone exposure was not submitted. We request that you conduct a drug-drug interaction trial of vilazodone using a CYP3A4 inducer (carbamazepine) in healthy subjects.

Final Protocol Submission: July 30, 2011
 Trial Completion: July 31, 2012
 Final Report Submission: January 31, 2013

Vilazodone is extensively metabolized; however, the pharmacokinetics of vilazodone in patients with severe hepatic impairment has not been assessed. We request that you conduct a Phase 1 trial to evaluate the pharmacokinetics of vilazodone in patients with severe hepatic impairment.

Final Protocol Submission: July 31, 2011
 Trial Completion: July 31, 2012
 Final Report Submission: February 28, 2013

Information on the effect of P-gP on the pharmacokinetics of vilazodone and the effect of vilazodone on P-gP was not submitted. We request that you conduct an in vitro study to evaluate whether vilazodone is a substrate or inhibitor of P-gP.

Final Protocol Submission: July 31, 2011
 Study Completion: September 30, 2011
 Final Report Submission: December 31, 2011

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/s/

WILLIAM H BENDER
01/20/2011

Bender, William

From: Bender, William
Sent: Friday, January 14, 2011 3:38 PM
To: 'Fabrizio, Kimberly'
Subject: FW: NDA 22-567 Container Packaging Labels Response

Hi Kim,

We find the revisions to your container packaging labels acceptable.

Thanks,
Bill

From: Fabrizio, Kimberly [mailto:KFabrizio@pgxhealth.com]
Sent: Friday, January 14, 2011 12:59 PM
To: Griffith, Sandra J
Cc: Bender, William
Subject: NDA 22-567 Container Packaging Labels Response
Importance: High

Dear Sandra,

We have addressed all the Division's comments received yesterday (13 Jan 2011) and applied the requested changes to the attached labels. We have included the hospital unit dose labels for completeness but there have been no changes.

Please note that in regards to the comment B3, we were able to add the requested additional line spaces to all labels above 60cc. (b) (4)

Please feel free to contact me with any questions or concerns. Please call my cell to insure contact (203-823-0039).

Best regards,

Kimberly Fabrizio

Vice President Regulatory Affairs

PGxHealth™, a Division of Clinical Data®

5 Science Park

New Haven, CT 06511 (USA)

Phone: +1 (203) 786-3502 x2502

Email: kfabrizio@pgxhealth.com

Web: <http://www.pgxhealth.com>

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Reference ID: 2895009

1/21/2011

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/s/

WILLIAM H BENDER
01/21/2011

Bender, William

From: Bender, William
Sent: Friday, January 14, 2011 1:32 PM
To: 'Fabrizio, Kimberly'
Subject: FW: NDA 22-567 Response Language on MOA per teleconference

Hi Kim,

Attached is our final proposal regarding section 12. 1: Mechanism of Action for the label:

"The mechanism of the antidepressant effect of vilazodone is not fully understood but is thought to be related to its enhancement of serotonergic activity in the CNS through selective inhibition of serotonin reuptake. Vilazodone is also a partial agonist at serotonergic 5HT1A receptors; however, the net result of this action on serotonergic transmission and its role in vilazodone's antidepressant effect are unknown."

Please let us know if you agree/don't agree by Tuesday at noon.

Thanks,
Bill

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/s/

WILLIAM H BENDER
01/14/2011



NDA 22567

**ACKNOWLEDGE CORPORATE
NAME CHANGE**

Trovis Pharmaceuticals LLC
Attention: Kimberly Fabrizio
Vice President, Regulatory Affairs
Five Science Park
New Haven, CT 06511

Dear Ms. Fabrizio:

We acknowledge receipt on January 6, 2011 of your January 6, 2011 correspondence notifying the Food and Drug Administration that the corporate name has been changed from

PGxHealth LLC
Five Science Park
New Haven, CT 06511

to

Trovis Pharmaceuticals LLC
Five Science Park
New Haven, CT 06511

for the following new drug application:

NDA 22567 for Viibryd (vilazodone hydrochloride) tablets 10 mg, 20 mg and 40 mg for the treatment of Major Depressive Disorder.

We have revised our records to reflect this change.

We request that you notify your suppliers and contractors who have DMFs referenced by your application of the change so that they can submit a new letter of authorization (LOA) to their Drug Master File(s).

Please cite the NDA number listed above at the top of the first page of all submissions to this application. Send all submissions, electronic or paper, including those sent by overnight mail or courier, to the following address:

NDA 22567

Page 2

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Psychiatry Products
5901-B Ammendale Road
Beltsville, MD 20705-1266

If you have any questions, please call me at (301) 796-2145.

Sincerely,

{See appended electronic signature page}

CDR Bill Bender
Senior Regulatory Project Manager
Division of Psychiatry Products
Office of Drug Evaluation 1
Center for Drug Evaluation and Research

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/s/

WILLIAM H BENDER
01/13/2011

Bender, William

From: Bender, William
Sent: Wednesday, January 12, 2011 1:39 PM
To: 'Fabrizio, Kimberly'
Subject: FW: Vilazodone - formatting Figures 1 and 2
Attachments: IntrinsicFactors.emf; ExtrinsicFactors.emf

Kim,

As promised, attached are the figures to incorporate into your label.

Please contact me with any questions.

Thanks,
Bill

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/s/

WILLIAM H BENDER
01/12/2011

Bender, William

From: Bender, William
Sent: Wednesday, January 12, 2011 1:06 PM
To: 'Fabrizio, Kimberly'
Subject: RE: NDA 22-567 Med Guide (final)
Attachments: 22567 Vilazodone Medication Guide_FDA_01122011final.doc

Hi Kim,

We are fine with you adding the below information to the MedGuide. Also, we agree with your breastfeeding change, and we added the yellow and red dye as you referred to in a previous email to be consistent with the PI. The attached MedGuide incorporates these changes. Please confirm that you agree with this final MedGuide.

Thanks,
Bill

From: Fabrizio, Kimberly [mailto:KFabrizio@pgxhealth.com]
Sent: Wednesday, January 12, 2011 11:22 AM
To: Bender, William
Subject: NDA 22-567 Med Guide

Bill,

Similarly to the PI, our legal council would like the following information added to the medication guide. Do you have a preference the order this is added at the very end or the additional of the text at all? I look forward to your response on this question and the breastfeeding note sent last night, in an effort to get this added to our final SPL.

VIIBRYD™ is a trademark of Trovis Pharmaceuticals, LLC.

© 2011 Trovis Pharmaceuticals LLC.

Product protected by U.S. Patent No. 5,532,241 and U.S. Patent No. 7,834,020.

Thank you and hope your not too snowed in!

Kimberly Fabrizio

Vice President Regulatory Affairs

PGxHealth™, a Division of Clinical Data®

5 Science Park

New Haven, CT 06511 (USA)

Phone: +1 (203) 786-3502 x2502

Email: kfabrizio@pgxhealth.com

Web: <http://www.pgxhealth.com>

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Reference ID: 2890761

1/12/2011

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/s/

WILLIAM H BENDER
01/12/2011

Bender, William

From: Bender, William
Sent: Wednesday, January 12, 2011 12:43 PM
To: 'Fabrizio, Kimberly'
Subject: FW: NDA 22-567 011211.doc

Attachments: NDA 22-567 011211.doc

Hi Kim,

Attached is the final label with our changes. Please let me know if you concur with this final label. You can then accept them and formally submit the final label officially to your NDA. As stated in this label, we will send the charts so you can make the modifications.



NDA 22-567
11211.doc (298 KB)

Please contact me with any questions.

Thanks,
Bill

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/s/

WILLIAM H BENDER
01/12/2011

Bender, William

From: Bender, William
Sent: Tuesday, January 11, 2011 1:51 PM
To: 'Fabrizio, Kimberly'
Subject: NDA 22567 Vilazodone MedGuide

Attachments: 22567 Vilazodone Medication Guide_FDA_011111.doc

Hi Kim,

As promised, attached is our response to the "MedGuide" label that you emailed to me on 1/6/2011. Please let me know if you concur with our changes via email. You can then formally submit the revised label officially to your NDA.

Thanks,
Bill



22567
done Medication

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/s/

WILLIAM H BENDER
01/11/2011

Bender, William

From: Bender, William
Sent: Thursday, January 06, 2011 12:16 PM
To: 'Fabrizio, Kimberly'
Subject: NDA 22567 container label comments

Hi Kim,

Attached are the container labeling comments:

A. General Comments for All Container Labels and Blister Carton Labeling

1. Ensure the established name is at least ½ the size of the proprietary name, taking into account all pertinent factors including typography, layout, contrast and other printing features [21 CFR 201.10(g)(2)].
2. The dosage form statement “Tablets” appears more prominent than the active ingredient statement. The dosage form statement is a part of the established name, therefore, ensure it is commensurate in size, font, etc. to the active ingredient statement.

B. Container Labels, 10 mg, 20 mg, and 40 mg (30-count, 90-count, and 500-count)

1. The net quantity statement is too prominent. Therefore, we request you decrease the prominence by unbolding the statement and reducing its size.
2. The Medication Guide statement is not prominent. Separate the Medication Guide statement from the Usual Dosage and “Dispense in...container” statements (e.g., use a line to separate these statements). Additionally, increase the prominence of the Medication Guide statement with the use of bold type.
3. The statement “Each tablet contains...” is located on the principal display panel and detracts from important product identifying information such as the proprietary name, established name, and strength. Relocate this statement to one of the side panels.

C. Blister Carton

1. The active ingredient statement “vilazodone HCl” is printed in a light grey color that lacks sufficient contrast against the white background and is, thus, difficult to see. Additionally, the dosage form statement “Tablets” appears more prominent than the active ingredient statement because it appears in a dark green font color. The active ingredient and dosage form statements make up the established name and, thus, ensure they appear in the same color and are commensurate in size, font, etc.
2. The statement of strength is left justified on the front and two side panels. For improved readability, center the statement of strength on these panels. In order to make space for this, relocate the “Each tablet contains...” statement to the back panel.

D. Blister Labels, 10 mg, 20 mg, and 40 mg (10-count unit dose blisters)

1. Increase the prominence of the proprietary name and established name.
2. Relocate the statement of strength to the usual position which is immediately below the established name. In its current position, it looks like the blister number rather than the product strength.
3. Decrease the prominence of the lot number and expiration date.
4. The blister labels look identical for all three strengths. Differentiate the strengths with the use of color, different box shapes, or some other means.
5. Delete the statement “Each tablet contains...” This statement crowds the label and it is not necessary because the label is too small.

E. Patient Starter Package and Physician Sample Package

1. As currently presented, the tablet layout is confusing for the following reasons:
 - The tablets to be taken for each week are lined up in vertical columns that are adjacent to one another and there is no line or other demarcation to separate them.

- Under each vertical column there is a boxed statement of strength and it is not immediately clear why they are positioned under the vertical columns.
- It is not immediately clear where a patient should start and in which direction a patient should go as the tablets are taken (i.e., should a patient progress across in a row or down in a column).

We request you provide data to support the proposed configuration. Provide the results of an FMEA and usability testing that demonstrate the current layout is not confusing and patients can follow the dosing schedule as provided. If you do not have data to support your proposed configuration, we recommend you revise the format as follows:

Reconfigure the tablet layout so that one week of therapy is contained on one panel or each week of therapy is separated and distinct from the other (see example below). Ensure that for each day of therapy, the numerical day of the week is stated (i.e., Day 1, Day 2, Day 3, etc.) and placed in close proximity to the respective dose (see example below) rather than the current presentation of “Days X-Y”.

Week 1

Day 1 Day 2 Day 3 Day 4
Day 5 Day 6 Day 7

Week 2

Day 1 Day 2 Day 3 Day 4
Day 5 Day 6 Day 7

2. The letters “A” and “B”, and “A”, “B”, and C” are on the patient starter package and physician sample package, respectively. Each letter is accompanied by a circle that encloses one of the tablet strengths, however, there are no instructions that explain the meaning of these letters. Explain the intended meaning of these letters and whether these letters were tested to ensure they can be understood. If tested, provide the results of the testing.
3. The instructions to the patient about how the package should be used do not appear complete. These are some of the questions that should be answered in the instructions to the patient:
 - a. What is the procedure for removing the tablets from the package?
 - b. Where does the patient start (e.g., show the patient which tablet, week, and day to start with; consider using the statement “start here” along with an arrow pointing to the tablet that should be used first)?

In the instructions under “How to take Viibryd (vilazodone HCl) Tablets”, the tablet strengths have a dash between the number and unit of measure (i.e., 10-mg, 20-mg, 40-mg). This may be confusing. Delete the dash that separates the number and unit of measure (e.g., 10 mg, 20 mg, and 40 mg)

4. The package does not state the number of weeks or days of therapy it contains. Revise to include the number of weeks or days of therapy that the package contains and place this statement on the principal display panel.
5. The starter package and physician sample do not have a net quantity statement. The principal display panel contains only the three strengths without reference to how many tablets of each strength are contained in the pack. Revise to include a net quantity statement on the principal display panel. Revise the statement of strength to reflect the number of tablets of each strength included in the package. For example:

Each starter pack contains:	XX tablets
containing XX mg—Week 1	XX tablets
containing XX mg—Week 2	XX tablets containing
XX mg—Week 3	

6. It is not clear how the tablet strengths will appear on the packages. Each tablet position is represented by a circle and inside the circle the respective tablet strength is specified (i.e., 10, 20, or 40). However, it is unclear whether this information will be printed on the package or how it will appear on the marketed package. Please clarify. We recommend you print the individual tablet strengths on the front card

immediately below each tablet in order to help minimize confusion by ensuring that the information is easily seen. Additionally, ensure the dosage unit is also specified (e.g., revise “10” to read “10 mg” and “20” to read “20 mg”, etc.)

7. The active ingredient statement “vilazodone HCl” is printed in a light grey color that lacks sufficient contrast against the white background and is, thus, difficult to see. Additionally, the dosage form statement “Tablets” appears more prominent than the active ingredient statement because it is presented in a dark green font color. The active ingredient and dosage form statements make up the established name and, thus, ensure they appear in the same color and are commensurate in size, font, etc.

Thanks,

Bill

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/s/

WILLIAM H BENDER
01/10/2011

Bender, William

From: Bender, William
Sent: Tuesday, January 04, 2011 1:09 PM
To: 'Fabrizio, Kimberly'
Subject: Pharm Tox PMR for vilazodone NDA 22567

Hi Kim,

Below is an additional PMR regarding pharmacology/toxicology:

Because the major human metabolite M17 was not demonstrated to be present in plasma of either rats or rabbits, the embryo-fetal reproductive toxicity studies with vilazodone did not adequately assess the toxicity of M17. Consequently, you will need to commit to assessing the reproductive toxicity of metabolite M17 in an embryo-fetal study.

However, because M17 was formed by hepatocytes isolated from rabbits, it is possible that M17 is present in plasma of rabbits treated with vilazodone. If the systemic exposure to M17 at the doses of vilazodone that were used in the original embryo-fetal study is demonstrated to be equal to or greater than the exposure in humans at the MRHD, the original rabbit study would be considered to have adequately assessed the embryo-fetal toxicity for M17.

Otherwise, an embryo-fetal study in either rats or rabbits where M17 is administered by a route that will produce systemic exposure equal to or greater than the exposure in humans at the MRHD will be required.

Final Protocol Submission Date: Not applicable
Study/Trial Completion Date: November 30, 2012
Final Report Submission: January 30, 2013

Please let me know if you concur with this PMR as soon as possible.

Thanks,

Bill

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/s/

WILLIAM H BENDER
01/04/2011

Bender, William

From: Bender, William
Sent: Wednesday, January 05, 2011 11:59 AM
To: 'Fabrizio, Kimberly'
Subject: NDA 22567 MedGuide label

Attachments: Viibryd MG DRISK clean copy_121620.doc

Hi Kim,

As promised, attached is the "MedGuide" label. Please bring any questions/comments that you may have during our teleconference tomorrow. You can then formally submit the revised label officially to your NDA.



Viibryd MG DRISK
clean copy_12...

Thanks,
Bill

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/s/

WILLIAM H BENDER
01/05/2011

Bender, William

From: Bender, William
Sent: Thursday, December 23, 2010 10:39 AM
To: 'Fabrizio, Kimberly'
Subject: NDA 22567 Vilazodone

Attachments: Laughren Edits_122210_Levin_122210b_22567 Vilazodone Label_FDA_122210_PGxHealth_120810.doc

Hi Kim,

Attached is a marked-up word version of the label with our recommended changes (second round). Please accept all the changes and use this label as a base document. Please make any additional changes (deletions, additions, and comments) using track changes to a clean version of what we have sent you. Please return your edited labeling document to me via email with any changes/recommendations that you may have by Wednesday, December 29, 2010. You can then formally submit the revised label officially to your NDA.

Our comments regarding your medication guide will follow shortly.

I am on leave next week but will be checking my email periodically.

Thanks,
Bill



Laughren
ts_122210_Levin_1

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/s/

WILLIAM H BENDER
12/23/2010

Bender, William

From: Bender, William
Sent: Thursday, December 23, 2010 11:21 AM
To: 'Fabrizio, Kimberly'
Subject: RE: NDA 22567 Vilazodone

Attachments: Laughren Edits_122210_Levin_122210b_22567 Vilazodone Label_FDA_122210_PGxHealth_120810.doc

Hi Kim,

Here is the label that incorporates our comments.

Thanks,
Bill



Laughren
ts_122210_Levin_1

Hi Kim,

Attached is a marked-up word version of the label with our recommended changes (second round). Please accept all the changes and use this label as a base document. Please make any additional changes (deletions, additions, and comments) using track changes to a clean version of what we have sent you. Please return your edited labeling document to me via email with any changes/recommendations that you may have by Wednesday, December 29, 2010. You can then formally submit the revised label officially to your NDA.

Our comments regarding your medication guide will follow shortly.

I am on leave next week but will be checking my email periodically.

Thanks,
Bill

<< File: Laughren Edits_122210_Levin_122210b_22567 Vilazodone Label_FDA_122210_PGxHealth_120810.doc >>

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/s/

WILLIAM H BENDER
12/23/2010

Bender, William

From: Bender, William
Sent: Wednesday, December 22, 2010 5:35 PM
To: 'Fabrizio, Kimberly'
Subject: NDA 22567 Vilazodone PMR/PMCs

Hi Kim,

Attached are the PMR/PMCs that we would like agreement with you:

22567 Vilazodone- Requested Postmarketing Requirements and Commitments

Required Pediatric Assessments

We are waiving the pediatric study requirement for ages 0 to 6 years-old in the treatment of major depressive disorder, because studies are highly impractical due to the low prevalence of this disorder in this age range. We are deferring submission of your pediatric studies for ages 7 to 17 years-old in the treatment of major depressive disorder, because this product is ready for approval for use in adults, and the pediatric studies have not been completed.

Your deferred pediatric studies are required postmarketing studies. These required studies are listed below.

1. A deferred pediatric study under PREA for the treatment of major depressive disorder in pediatric patients ages 7 to 17 years-old. A study to obtain pharmacokinetic, safety, and tolerability data and provide information pertinent to dosing of vilazodone in the relevant pediatric population.

(b) (4)

2. Deferred pediatric studies under PREA for the treatment of major depressive disorder in pediatric patients ages 7 to 17 years-old.

(b) (4)

(b) (4)

3. To support the use of vilazodone in children less than 13 years of age, you must conduct a study to assess the safety of vilazodone in juvenile rats. This study must include evaluation of neurological/behavioral development and reproductive development. You should submit the protocol for our comments prior to initiating the study.

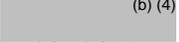
Final Protocol Submission Date: by January 30, 2012

(b) (4)

Postmarketing Commitments

1.  (b) (4)
2. It is not apparent from the trials you have conducted in major depressive disorder that the lowest effective dose of vilazodone has been identified, since only one dose (40 mg/day) was studied. However, there are suggestions that 20 mg/day may be effective at least in some subjects. In the trials, those who did not tolerate 40 mg/day could continue in the study on a dose of 20 mg/day, and some may have had a significant treatment effect. In addition, data from the phase 2 fixed-dose studies suggest that there may have been a signal of efficacy with the 20 mg/day dose, as measured by the secondary efficacy measure (MADRS). Moreover, some important adverse reactions are dose-related. Thus, we ask that you further characterize the efficacy and safety of vilazodone in the treatment of adults with MDD using fixed doses of vilazodone (20 mg and 40 mg), an active control (for assay sensitivity), and placebo in an adequate and well controlled trial.
 (b) (4)
3.  (b) (4)
4. Vilazodone is extensively metabolized; however, the pharmacokinetics of vilazodone in patients with severe hepatic impairment has not been assessed. We request that you conduct a Phase 1 study to evaluate the pharmacokinetics of vilazodone in patients with severe hepatic impairment.

Final Protocol Submission: by  (b) (4)
Trial Completion: by  (b) (4)
Final Report Submission: by February 28, 2013
5. Information on the effect of PgP on the pharmacokinetics of vilazodone and the effect of vilazodone on PgP was not submitted. We request that you conduct an in vitro study to evaluate whether vilazodone is a substrate or inhibitor of PgP.

Final Protocol Submission: by  (b) (4)
Trial Completion: by September 30, 2011
Final Report Submission: by  (b) (4)

Please let me know if you concur with us.

Thanks,
Bill

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/s/

WILLIAM H BENDER
12/22/2010

Bender, William

From: Bender, William
Sent: Monday, December 20, 2010 2:23 PM
To: 'Fabrizio, Kimberly'
Subject: NDA 22567 Vilazodone

Follow Up Flag: Follow up
Flag Status: Red

Hi Kim,

We have the following comments and some further questions for the Sponsor:

We appreciate your (12/20/10) response addressing the presence of M17 as a metabolite in the plasma of vilazodone-treated dogs. We agree that you should submit your response to the NDA and that you should correct Table 3 (Cross Species Comparison) to reflect the presence of M17 in plasma of dogs and humans.

However, qualification of major human metabolites requires studies other than those that assess chronic toxicity, as in the 52-week study in dogs that you cite.

Specifically, the potentials for reproductive (embryo-fetal) toxicity, genotoxicity, and carcinogenicity need to be addressed. We have the following questions:

- Regarding embryo-fetal toxicity, were M10 and M17 detected and quantified in plasma of rats or rabbits and, if so, at what levels? This would determine whether the embryo-toxicity studies for vilazodone in rats and rabbits would also assess the embryo-fetal toxicity of the metabolites.
- Regarding genotoxicity, does either M10 or M17 have structural alerts?
- Regarding carcinogenicity, were M10 and M17 detected and quantified in plasma of rats or mice and, if so, at what levels? This would determine whether the carcinogenicity studies for vilazodone in rats and mice would also assess the carcinogenicity of the metabolites.

Please respond as soon as possible.

Thanks,

Bill

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/s/

WILLIAM H BENDER
12/20/2010

Bender, William

From: Bender, William
Sent: Tuesday, December 14, 2010 2:31 PM
To: 'Fabrizio, Kimberly'
Subject: NDAA 222567

Hi Kim,

We have the following request:

In your initial submission of NDA 22-567, you only identified one metabolite (M10) that was circulating at significant levels in humans; and that metabolite (M10) was also present in plasma of rats and dogs. However, your recent (8/31/10) amendment to the report for the mass-balance study (PGX-08-P1-07) of ¹⁴C-vilazodone in healthy male subjects indicates that there are 2 major metabolites in humans, M10 and M17, which each accounted for greater than 10% of total exposure to drug-related species.

You will need to address the safety of metabolites M10 and M17, as assessed in non-clinical studies. We refer you to the ICH Guidance: M3(R2) Nonclinical Safety Studies for the Conduct of Human Clinical Trials and Marketing Authorization for Pharmaceuticals (2010); and the CDER Guidance: Safety Testing of Drug Metabolites (2008).

You should submit your response regarding this important issue as soon as possible.

Thanks,
Bill

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/s/

WILLIAM H BENDER
12/16/2010

Bender, William

From: Bender, William
Sent: Thursday, December 09, 2010 8:39 AM
To: 'Fabrizio, Kimberly'
Subject: FW: NDA 22567 Vilazodone REMS

Attachments: DRISK REVIEW.pdf

Hi Kim,

We have the following comments and recommendations regarding your proposed REMS, letter date of November 12, 2010. Please provide us with your response by December 16, 2010.



DRISK
VIEW.pdf (90 K)

Thanks,
Bill

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/s/

WILLIAM H BENDER
12/10/2010

REQUEST FOR DDMAC LABELING REVIEW CONSULTATION

****Please send immediately following the Filing/Planning meeting****

TO: **CDER-DDMAC-RPM**
Attention: Amy Toscano
Jessica Cleck Derenick

FROM: (Name/Title, Office/Division/Phone number of requestor)
Bill Bender, RPM, Division of Psychiatry Products

REQUEST DATE December 8, 2010	IND NO.	NDA/BLA NO. 22567	TYPE OF DOCUMENTS (PLEASE CHECK OFF BELOW) Labeling
----------------------------------	---------	----------------------	---

NAME OF DRUG Viibryd (Vilazodone HCL)	PRIORITY CONSIDERATION Standard	CLASSIFICATION OF DRUG Antidepressant	DESIRED COMPLETION DATE (Generally 1 week before the wrap-up meeting) December 13, 2010
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NAME OF FIRM: PGxHealth, LLC	PDUFA Date: January 22, 2010
---------------------------------	------------------------------

TYPE OF LABEL TO REVIEW

TYPE OF LABELING: (Check all that apply) <input checked="" type="checkbox"/> PACKAGE INSERT (PI) <input type="checkbox"/> PATIENT PACKAGE INSERT (PPI) <input checked="" type="checkbox"/> CARTON/CONTAINER LABELING <input type="checkbox"/> MEDICATION GUIDE <input type="checkbox"/> INSTRUCTIONS FOR USE(IFU)	TYPE OF APPLICATION/SUBMISSION <input checked="" type="checkbox"/> ORIGINAL NDA/BLA <input type="checkbox"/> IND <input type="checkbox"/> EFFICACY SUPPLEMENT <input type="checkbox"/> SAFETY SUPPLEMENT <input type="checkbox"/> LABELING SUPPLEMENT <input type="checkbox"/> PLR CONVERSION	REASON FOR LABELING CONSULT <input checked="" type="checkbox"/> INITIAL PROPOSED LABELING <input type="checkbox"/> LABELING REVISION
--	--	---

EDR link to submission:
<\\CDSESUB1\EVSPROD\NDA022567\022567.ENX>
Jessica Cleck Derenick has been reviewing the label since September 2010. Revised labeling has been provided to her as there have been negotiations with the sponsor. This formal consult has been placed into DARRTS per the request of DDMAC.

Please Note: There is no need to send labeling at this time. DDMAC reviews substantially complete labeling, which has already been marked up by the CDER Review Team. The DDMAC reviewer will contact you at a later date to obtain the substantially complete labeling for review.

COMMENTS/SPECIAL INSTRUCTIONS:

Mid-Cycle Meeting: 08/22/2010

Labeling Meetings: 09/29/2010; 10/25/2010, 11/30/2010

Wrap-Up Meeting: 12/14/2010

SIGNATURE OF REQUESTER
Bill Bender, RPM, DPP

SIGNATURE OF RECEIVER **Reference ID: 2874742**

METHOD OF DELIVERY (Check one)

	<input checked="" type="checkbox"/> eMAIL	<input type="checkbox"/> HAND

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/s/

WILLIAM H BENDER
12/09/2010

THOMAS P LAUGHREN
12/09/2010

Bender, William

From: Bender, William
Sent: Friday, December 03, 2010 7:04 AM
To: 'Fabrizio, Kimberly'
Subject: FW: NDA 22-567 Vilazodone

Attachments: Laughren Edits_Levin_120110_22567 FDA Label_12-1-10.doc; Laughren Edits_Levin_120110_22567 FDA Label_12-1-10.doc

Good Morning Kim,

Some minor changes in the clinical studies section are attached. Please use this label.

Thanks,
Bill



Laughren
_Levin_120110_

From: Bender, William
Sent: Thursday, December 02, 2010 3:09 PM
To: 'Fabrizio, Kimberly'
Subject: NDA 22-567 Vilazodone

Hi Kim,

Regarding your label that you submitted with your application for NDA 22-567, Vilazodone, we have the following comments:

-  (b) (4)

- Provide NDC numbers of all packaging configurations for each tablet strength in the "How Supplied" section (16).

-  (b) (4)

- Please add the phone number under the "Adverse Reaction" section in the Highlights portion of the label.

Also attached is a marked-up word version of the label with our recommended changes. Please accept all the changes and use this label as a base document. Please make any additional changes (deletions, additions, and comments) using track changes to a clean version of what we have sent you. Please return your edited labeling document to me via email with any changes/recommendations that you may have by Wednesday, December 8, 2010. You can then formally submit the revised label officially to your NDA.

Our comments on your medication guide will follow shortly.

Thank you,
Bill



Laughren
_Levin_120110_

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/s/

WILLIAM H BENDER
12/03/2010

Bender, William

From: Bender, William
Sent: Wednesday, November 24, 2010 1:19 PM
To: 'Fabrizio, Kimberly'
Subject: FW: 22567 Request for information - weight changes

Hi Kim,

The clinical team has the following request:

Please provide a new outlier analysis for weight changes, using the following criteria:

Subjects with a weight increase or decrease $\geq 7\%$ of body weight.

[Have a Great Thanksgiving!](#)

Thanks.

Bill

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/s/

WILLIAM H BENDER
12/07/2010



NDA 022567

**PROPRIETARY NAME REQUEST
CONDITIONALLY ACCEPTABLE**

PGx Health, LLC
Five Science Park
New Haven, Connecticut 06511

ATTENTION: Kimberly Fabrizio
Vice President, Regulatory Affairs

Dear Ms. Fabrizio:

Please refer to your New Drug Application (NDA) dated March 22, 2010, received March 22, 2010, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Vilazodone Hydrochloride Tablets, 10 mg, 20 mg and 40 mg.

We also refer to your August 23, 2010, correspondence, received August 23, 2010, requesting review of your proposed proprietary name, Viibryd. We have completed our review of the proposed proprietary name, Viibryd, and have concluded that it is acceptable.

If **any** of the proposed product characteristics as stated in your August 23, 2010 submission are altered prior to approval of the marketing application, the proprietary name should be resubmitted for review.

If you have any questions regarding the contents of this letter or any other aspects of the proprietary name review process, contact Sandra Griffith, Safety Regulatory Project Manager in the Office of Surveillance and Epidemiology, at (301) 796-2445. For any other information regarding this application contact the Office of New Drugs (OND) Regulatory Project Manager, William Bender at (301) 796-2145.

Sincerely,

{See appended electronic signature page}

Carol Holquist, RPh.
Director
Division of Medication Error Prevention and Analysis
Office of Surveillance and Epidemiology
Center for Drug Evaluation and Research

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/s/

CAROL A HOLQUIST
11/17/2010

Bender, William

From: Bender, William
Sent: Wednesday, November 10, 2010 5:39 PM
To: 'Fabrizio, Kimberly'
Subject: NDA 22567 Vilazodone

Follow Up Flag: Follow up
Flag Status: Purple

Hi Kim,

We were informed by our Peds team that you need to submit a pediatric plan for your NDA application. Attached is basically what you need to submit. You can email it to me and then submit it formally as you usually do. I can call you this Friday if you have any questions (please let me know what a good phone number is for you).

22567 Vilazodone – Requirements for a pediatric plan

We request that you provide a general outline of the pediatric studies that you plan to conduct. You may use this outline of the required studies to draft your pediatric plan. The required studies would include:

- 1) Pharmacokinetic, safety, and tolerability study(ies) in the relevant pediatric population to fully explore the range of tolerated doses and to characterize the pharmacokinetics of vilazodone.
- 2) Two safety and efficacy studies: randomized, double-blind, placebo-controlled and active-controlled (fluoxetine or escitalopram), 6-8-week studies of vilazodone in the relevant pediatric population. We recommend that the studies use a fixed-dose design, in order to assess for dose-response relationships.

Thanks,
Bill

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/s/

WILLIAM H BENDER
11/18/2010



NDA 022567

PRE-APPROVAL REMS NOTIFICATION

PgxHealth, LLC
Attention: Kimberly Fabrizio
Vice President, Regulatory Affairs
Five Science Park
New Haven, CT 06511

Dear Ms. Fabrizio:

Please refer to your March 22, 2010 New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for vilazodone hydrochloride (HCL) 10 mg, 20 mg, and 40 mg Tablets.

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, we have determined that a REMS is necessary for vilazodone HCL 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.

Your proposed REMS must include the following:

Medication Guide: As one element of a REMS, FDA may require the development of a Medication Guide as provided for under 21 CFR 208. Pursuant to 21 CFR 208, FDA has determined that vilazodone HCL poses a serious and significant public health concern requiring the distribution of a Medication Guide. The Medication Guide is necessary for patients' safe and effective use of vilazodone HCL. FDA has determined that vilazodone HCL is a product for which patient labeling could help prevent serious adverse effects and that the Medication Guide is important to health and patient adherence to directions for use is crucial to the drug's effectiveness.

Under 21 CFR 208, you are responsible for ensuring that the Medication Guide is available for distribution to patients who are dispensed vilazodone HCL tablets.

Timetable for Submission of Assessments: The proposed REMS must include a timetable for submission of assessments that shall be no less frequent than 18 months, three years, and seven years after the REMS is initially approved. You should specify the reporting interval (dates) that each assessment will cover and the planned date of

submission to the FDA of the assessment. To facilitate inclusion of as much information as possible while allowing reasonable time to prepare the submission, the reporting interval covered by each assessment should conclude no earlier than 60 days before the submission date for that assessment. For example, the reporting interval covered by an assessment that is to be submitted by July 31st should conclude no earlier than June 1st.

Your proposed REMS submission should include two parts: a “proposed REMS” and a “REMS supporting document.” Attached is a template for the proposed REMS that you should complete with concise, specific information pertinent to vilazodone HCL tablets (see Appendix A). Once FDA finds the content acceptable and determines that the application can be approved, we will include these documents as an attachment to the approval letter that includes the REMS. The REMS, once approved, will create enforceable obligations.

The REMS supporting document should be a document explaining the rationale for each of the elements included in the proposed REMS (see Appendix B).

Before we can continue our evaluation of this NDA, you will need to submit the proposed REMS.

Under 21 CFR 208.24(d), you are responsible for ensuring that the label of each container or package includes a prominent and conspicuous instruction to authorized dispensers to provide a Medication Guide to each patient to whom the drug is dispensed, and states how the Medication Guide is provided. You should submit marked up carton and container labels of all strengths and formulations with the required statement alerting the dispenser to provide the Medication Guide. 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.”

For administrative purposes, designate the proposed REMS submission “**PROPOSED REMS for NDA 022567**” and all subsequent submissions related to the proposed REMS “**PROPOSED REMS-AMENDMENT for NDA 022567.**” If you do not submit electronically, please send 5 copies of your REMS-related submissions.

If you have any questions, call CDR Bill Bender, Regulatory Project Manager, at (301) 796-2145.

Sincerely,

{See appended electronic signature page}

Victor Crentsil, M.D., M.H.S
Deputy Director for Safety
Division of Psychiatry Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

ENCLOSURES:

REMS Appendices A and B

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/s/

VICTOR D CRENTSIL
11/01/2010



NDA 22-567

INFORMATION REQUEST

PGxHealth, LLC
Attention: Kimberly Fabrizio
Vice President, Regulatory Affairs
5 Science Park
New Haven, CT 06516

Dear Ms. Fabrizio:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Vilazodone Hydrochloride Tablets.

We are reviewing the Chemistry, Manufacturing, and Controls section of your submission and have the following comments and information requests. We request a prompt written response in order to continue our evaluation of your NDA.

1. Provide representative (b) (4) of starting materials (b) (4). Provide justifications of your purity specification for the starting materials. Discuss how impurities in the starting material may affect the quality of the API and include a limit for individual impurities in the specifications for (b) (4).
2. Provide additional information on (b) (4).
3. The current drug substance particle size specification is (b) (4). Discuss how this specification was set. Provide graphical depiction of the particle size distribution curve including (b) (4).
4. Provide a description and appropriate validation data of the analytical methods used for key intermediates (b) (4).
5. Provide (b) (4) data to demonstrate the limit of quantitation of this method to detect other polymorphs in the presence of polymorph form IV.
6. In addition to 6 potential genotoxic (b) (4) impurities (b) (4), we consider (b) (4) to be genotoxic,

based on the positive in vitro findings for mutagenicity (Ames test) and clastogenicity (chromosomal aberration test in V79 Chinese hamster cells). Consequently, your proposed limit for (b) (4) of not more than (b) (4), as an unspecified impurity, is not acceptable. Therefore, update your proposed in-process and/or drug substance specifications to control this impurity at a level of not more than (b) (4) ug/day clinical exposure, as you have done for each of the other 6 impurities. You need to provide an updated analytical method and validation data for (b) (4) with an appropriate lower detection limit to meet the total daily exposure requirement, as well as updated batch results to show that the exposure to this impurity is not more than (b) (4) ug/day.

Additionally, we have some concern because these 7 impurities share a common structural alert for genotoxicity (they are all (b) (4)). Therefore, we recommend that you further evaluate whether these 7 impurities can be controlled at levels lower than the currently proposed levels to reduce the overall patient exposure to this class of potentially genotoxic impurities. We also recommend that you provide any information that is available on the levels of each of these 7 impurities in the batches of drug substance used for the carcinogenicity studies in rats and mice, as well as any other information that might be relevant regarding the carcinogenic potential of these impurities.

7. Develop an analytical method to monitor the polymorphic form of the drug substance in the drug product release and stability testing. Provide drug polymorph data in the drug product to support the claim that testing for the polymorphic form in the tablets at release and during stability monitoring is not necessary.
8. Provide data to demonstrate how the (b) (4) time was determined and optimized. Discuss how (b) (4) will affect the quality of the drug product.
9. The current manufacturing batch record suggests that the tablets are (b) (4). Discuss if the manufacturing process is robust to produce tablets with acceptable physical chemical properties including assay, weight variation, thickness, hardness, and disintegration time (b) (4) is needed.
10. Discuss how the particle size specification for (b) (4) is determined. Provide additional data to demonstrate that adequate specifications (b) (4) are selected so that a robust manufacturing process and adequate performance of the drug product are validated within the range of specification limits for the excipients.
11. Provide additional data to show that the drug substance is stable in the dissolution medium using a compound specific method (i.e. HPLC).

- 12 [REDACTED] (b) (4)
Provide a chromatogram of the blank sample solution of the drug product injected into the HPLC system for identification of peaks generated from the blank solution.
13. Provide all available stability information for the 20mg tablets to demonstrate that the tablet color does not change on stability.
14. You only provided dissolution data at one time point (at 30 min) on month 12 for the primary stability batches and on month 6 for the second stability batches (Module 2.3.P, p.12-15). Please submit the individual and mean (n=12 tablets/lot) dissolution data and profiles of the three proposed strengths of the to-be-marketed G10, G20, and G40 formulations (clinically tested and/or commercial lots). The above needed dissolution data/profiles could not be located in the submission. To avoid delay in Agency's review of the NDA, please provide the above needed data/information ASAP.

If you have any questions, contact Teshara G. Bouie, Regulatory Project Manager, at (301) 796-1649.

Sincerely,

{See appended electronic signature page}

Ramesh Sood, Ph.D.
Branch Chief
Division of New Drug Quality Assessment I
Office of New Drug Quality Assessment
Center for Drug Evaluation and Research

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/s/

RAMESH K SOOD
10/15/2010

Executive CAC

Date of Meeting: October 5, 2010

Committee: David Jacobson-Kram, Ph.D., OND IO, Chair
Abby Jacobs, Ph.D., OND IO, Member
Paul Brown, Ph.D., OND IO, Member
Sushanta Chakder, Ph.D., DGP, Alternate Member
Linda Fossom, Ph.D., DPP, Team Leader
Violetta Klimek, Ph.D., DPP, Presenting Reviewer

Author of Draft: Violetta Klimek

The following information reflects a brief summary of the Committee discussion and its recommendations.

NDA # 22-567

Drug Name: Vilazodone

Sponsor: PGx Health, LLC

Background: Vilazodone is an inhibitor of the serotonin reuptake transporter and a partial agonist at the serotonin 5-HT_{1A} receptor. This NDA is for the use of vilazodone for treatment of major depressive disorder.

Vilazodone was clastogenic at cytotoxic concentrations in two *in vitro* assays for chromosome aberrations; 1) using V79 CHO cells in the presence and in absence of S9 metabolic activation and 2) using human lymphocytes in the presence of S9 activation. Vilazodone was negative for mutagenicity in the Ames test and in the HPRT assay using V79 CHO cell line. It was also negative in several *in vivo* studies that include: 1) chromosomal aberration in the rat bone marrow cells; 2) micronucleus test in rats; 3) unscheduled DNA synthesis (UDS) test.

Protocols for the mouse and rat carcinogenicity study were presented to the Executive – CAC in two rounds: 1) in the original meeting on July 14, 1998, at which no concurrence on dose selection was given and the Committee recommended that the Sponsor perform dose range finding studies (in mice and rat) at higher doses; and 2) in the second meeting on April 11, 2000, at which revised dosing proposed by the Sponsor was considered (after dosing in both 2-year studies had been initiated), based on data from 13-week studies conducted in mice and rats at much higher doses. Based on results of these 13-week studies, the Committee had agreed with the higher doses proposed (and already being administered) for carcinogenicity studies in mice (0, 15, 45 and 135 mg/kg/day) and rats (0, 7.5, 25, and 75 mg/kg/day and a higher dose of 150 mg/kg/day added 9 months later with a concurrent control group).

Rat Carcinogenicity Study

Wistar HsdCpB:WU rats were administered oral gavage doses of vilazodone at 0, 7.5, 25, 75, and 150 mg/kg/d in 0.25 % aqueous hydroxypropyl methyl cellulose for 2 years. The exposure to vilazodone during the study period was verified in TK groups of rats; the exposure (AUC₀₋₂₄) at the high dose was 15x (males) and 40x (females) of the human exposure at therapeutic dose of 40 mg/day. The organs and tissues from all rats of all study groups were histologically examined.

No biologically relevant, drug-related increases in neoplasm incidence were observed in rats administered vilazodone. The only significant observations included increases in non-neoplastic lesions; minimal to severe fibrohistiocytic granulomas in the mesenteric lymph nodes (up to 82% incidence) and in the mediastinal lymph nodes (up to 100% incidence) in male and female rats at the high dose.

Mouse Carcinogenicity Study

B6C3F1 mice were treated with vilazodone by oral gavage in 0.25 % aqueous hydroxypropyl methyl cellulose at 15, 45, and 135 mg/kg/day. The exposure (AUC₀₋₂₄) at the high dose was 30x (males) and 28x (females) of the human exposure at therapeutic dose of 40 mg/day. The organs and tissues from all mice of all study groups were histologically examined. Survival was sufficient for an adequate assessment of tumorigenic potential.

Increased incidences of mammary gland adenocarcinomas and adenoacanthomas combined in females (high dose) and increased incidences of hepatocellular adenomas, carcinomas, (separately and combined) in males at the high dose were statistically significant by trend and pairwise tests in mice treated with vilazodone as indicated in the following table:

Organ name	Tumor name	Control n = 120	15 mg/kg N = 60	45 mg/kg N = 60	135 mg/kg N = 60	Trend test P-value	Pairwise test (C vs H) P-value
Mammary gland – (females)	Adenocarcinoma + adenoacanthoma	3	1	6	8*	< 0.0017*	< 0.0069*
	Adenocarcinoma	3	1	6	7	< 0.0050*	(< 0.0166)
Liver – (males)	Adenoma + carcinoma	36	32	20	40*	< 0.001*	< 0.001*
	Adenoma	22	23	14	27*	< 0.001*	< 0.001*
	Carcinoma	15	11	10	19*	< 0.0012*	< 0.0016*

Executive CAC Recommendations and Conclusions:

Rat:

The Committee concurred that the study was acceptable, noting that selection of the high doses had received prior concurrence.

The Committee concurred that there were no drug-related neoplasms.

Mouse:

The Committee concurred that the study was acceptable.

The Committee concurred that the increased incidences of mammary adenocarcinomas and adenoacanthomas (combined) in females at the high dose and hepatocellular neoplasms (adenomas, carcinomas, and adenomas or carcinomas, combined), in male mice at the high dose were drug related.

David Jacobson-Kram, Ph.D.
Chair, Executive CAC

cc:\n
/Division File, DPP
/Linda Fossom, DPP
/Barry Rosloff, DPP
/Violetta Klimek, DPP
/William Bender, DPP
/Adele Seifried, OND IO

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/s/

ADELE S SEIFRIED
10/08/2010

DAVID JACOBSON KRAM
10/08/2010



NDA 22-567

INFORMATION REQUEST

PgxHealth, LLC
Attention: Kimberly Fabrizio
Vice President, Regulatory Affairs
Five Science Park
New Haven, CT 06511

Dear Ms. Fabrizio:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Vilazodone 10 mg, 20 mg, and 40 mg tablets.

We request you to compile and tabulate abuse-related information (adverse events) regarding NDA 22-567, Vilazodone .

According to 21 CFR 314.50(d)(5)(vii), you must submit in the NDA an assessment of studies and other information related to the potential abuse of a drug and include a proposal for scheduling if the drug affects the central nervous system (CNS), is chemically or pharmacologically similar to other drugs with known abuse potential, or produces psychoactive effects such as sedation, euphoria, and mood changes.

You did not perform a clinical abuse potential assessment, provide a recommendation for scheduling, and did not include a dedicated abuse potential section in the NDA. To evaluate the abuse potential of Vilazodone, you must submit a formal analysis of abuse-related adverse events (AEs). This analysis should include all clinical studies (e.g. Phase 1, 2 and 3 studies). For each clinical study, AEs should be categorized by dose and presented in tabular format.

You must also provide a pooled analysis of abuse-related AEs. The pooled analysis should contain all AEs, collapsed across studies, and categorized by dose.

The specific AEs of interest appear below:

Abuse-Related AE Terms for Use in Clinical Efficacy Studies

All clinical studies should be evaluated for indicators of abuse potential. The list below is a compilation of abuse-related adverse events terms, based on our experience to date. The list includes specific terms that are in the MedDRA 12.0 dictionary as well as frequently used verbatim terms, words or phrases. Most terms are listed under General, Neurological, and Psychiatric Disorders High Level Groupings.

The presence of euphoria or other positive mood changes is a key observation that may influence a recommendation for scheduling. However, the overall behavioral profile and pharmacologic similarity to a scheduled drug is critical in determining whether scheduling will be recommended, and if so, into which schedule the drug will be recommended for placement.

Euphoria-related terms:

Euphoric mood: euphoria, euphoric, exaggerated well-being, excitement excessive, feeling high, felt high, high*, high* feeling, laughter. (* Exclude terms that clearly are not related or relevant such as “high blood pressure,” etc.)

Elevated mood: mood elevated, elation.

Feeling abnormal: cotton wool in head, feeling dazed, feeling floating, feeling strange, feeling weightless, felt like a zombie, floating feeling, foggy feeling in head, funny episode, fuzzy, fuzzy head, muzzy head, spaced out, unstable feeling, weird feeling, spacey.

Feeling drunk: drunkenness feeling of, drunk-like effect, intoxicated, stoned, drugged.

Feeling of relaxation: feeling of relaxation, feeling relaxed, relaxation, relaxed, increased well-being, excessive happiness.

Dizziness: dizziness and giddiness, felt giddy, giddiness, light headedness, light-headed, light-headed feeling, lightheadedness, swaying feeling, wooziness, woozy.

Thinking abnormal: abnormal thinking, thinking irrational, wandering thoughts.

Hallucination: (auditory, visual, and all hallucination types), illusions, flashbacks, floating, rush, and feeling addicted.

Inappropriate affect: elation inappropriate, exhilaration inappropriate, feeling happy inappropriately, inappropriate affect, inappropriate elation, inappropriate laughter, inappropriate mood elevation.

Terms indicative of impaired attention, cognition, mood, and psychomotor events:

Somnolence: groggy, groggy and sluggish, groggy on awakening, stupor.

Mood disorders and disturbances: mental disturbance, depersonalization, psychomotor stimulation, mood disorders, emotional and mood disturbances, deliria, delirious, mood altered, mood alterations, mood instability, mood swings, emotional liability, emotional disorder, emotional distress, personality disorder, impatience, abnormal behavior, delusional disorder, irritability.

Mental impairment disorders: memory loss (exclude dementia), amnesia, memory impairment, decreased memory, cognition and attention disorders and disturbances, decreased concentration, cognitive disorder, disturbance in attention, mental impairment, mental slowing, mental disorders.

Drug tolerance, Habituation, Drug withdrawal syndrome, Substance-related disorders

Dissociative/psychotic terms:

Psychosis: psychotic episode or disorder.

Aggressive: hostility, anger, paranoia.

Confusion and disorientation: confusional state, disoriented, disorientation, confusion, disconnected, derealization, dissociation, detached, fear symptoms, depersonalization, perceptual disturbances, thinking disturbances, thought blocking, sensation of distance from one's environment, blank stare, muscle rigidity, non-communicative, sensory distortions, slow slurred speech, agitation, excitement, increased pain threshold, loss of a sense of personal identity.

If you have any questions, call CDR Bill Bender, Regulatory Project Manager, at (301) 796-2145 or email at William.bender@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Thomas Laughren, M.D.
Director
Division of Psychiatry Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22567	ORIG-1	PGXHEALTH LLC	VILAZODONE HCL

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/s/

THOMAS P LAUGHREN
08/20/2010

Bender, William

From: Bender, William
Sent: Tuesday, August 03, 2010 7:29 AM
To: 'Fabrizio, Kimberly'
Subject: NDA 22-567 Vilazodone

Good Morning Kim,

We have the following question regarding NDA 22-567, Vilazodone application:

In your rat carcinogenicity study (2-year bioassay; study no. T 14059) in the Tables (Table 2 and 3) of microscopic findings as well as in SAS data sets, there is Pancreas and Pancreas Sample 1. Please explain what Pancreas Sample 1 stands for.

Thanks,
Bill

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22567	ORIG-1	PGXHEALTH LLC	VILAZODONE HCL

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/s/

WILLIAM H BENDER
08/06/2010



NDA 022567

**PROPRIETARY NAME REQUEST
UNACCEPTABLE**

PGxHealth, LLC
Five Science Park
New Haven, Connecticut 06511

ATTENTION: Kimberly Fabrizio,
Vice President, Regulatory Affairs

Dear Ms. Fabrizio:

Please refer to your New Drug Application (NDA) dated March 22, 2010, received March 22, 2010, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Vilazodone Tablets, 10 mg, 20 mg, and 40 mg.

We also refer to your May 4, 2010, correspondence, received May 4, 2010, requesting review of your proposed proprietary name, (b) (4). We have completed our review of this proposed proprietary name, (b) (4) and have concluded that this name is unacceptable for the following reasons.

1.

(b) (4)

2.



(b) (4)

3.



(b) (4)

4.



(b) (4)

We recognize this conclusion differs from that of the external study conducted by (b) (4) (b) (4) did not identify (b) (4) as having orthographic similarity with (b) (4). Additionally, although (b) (4) indicated six of the 158 respondents in their study thought there was a high probability of confusion between (b) (4) they did not provide an explanation as to why the name was acceptable in light of the study findings. Our analysis indicates that these products are (b) (4) that increase the potential for name confusion.

We note that you have not proposed an alternate proprietary name for review. If you intend to have a proprietary name for this product, we recommend that you submit a new request for a proposed proprietary name review. (See the draft Guidance for Industry, *Complete Submission for the Evaluation of Proprietary Names*, <http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm121568.htm> and “PDUFA Reauthorization Performance Goals and Procedures Fiscal Years 2008 through 2012”.)

If you have any questions regarding the contents of this letter or any other aspects of the proprietary name review process, contact Sandra Griffith, Safety Regulatory Project Manager in the Office of Surveillance and Epidemiology, at (301) 796-2445. For any other information regarding this application contact the Office of New Drugs (OND) Regulatory Project Manager, William Bender at (301) 796-2145.

Sincerely,

{See appended electronic signature page}

Denise P. Toyer, Pharm.D.
Deputy Director
Division of Medication Error Prevention and Analysis
Office of Surveillance and Epidemiology
Center for Drug Evaluation and Research

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
----- NDA-22567	----- ORIG-1	----- PGXHEALTH LLC	----- VILAZODONE HCL

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/s/

DENISE P TOYER
08/02/2010

DEPARTMENT OF HEALTH AND
HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

REQUEST FOR CONSULTATION

TO (Division/Office):
OND/OAP/DAIOP
Attn: Wiley Chambers
WO22 RM6336

FROM:
HFD-130/PSYCHIATRIC PRODUCTS

Date	IND No.	NDA No.	TYPE OF DOCUMENT	DATE OF DOCUMENT
07/07/2010		22-567	Original Application	03/22/2010

NAME OF DRUG: Vilazodone HCl

NAME OF DRUG COMPANY: PGxHealth, LLC

INDICATION OF DRUG: Major Depressive Disorder

DESIRED COMPLETION DATE: 08/20/2010

REASON FOR REQUEST

The sponsor has submitted an original NDA (22567) for vilazodone in the treatment of depression. Vilazodone has two serotonergic mechanisms of action: it is an SSRI as well as an agonist at the 5-HT1A receptor. We would appreciate your assessment of the ophthalmologic findings and conclusions submitted by the sponsor.

Due to the finding of corneal opacities in dogs, the sponsor conducted ophthalmologic safety assessments in the clinical program. In two controlled, 8-week clinical study (reviewed by Dr. Chambers in May 2001), Dr. Chambers concluded that the rate of reporting for cataract formation was very high for an 8-week study, and cataract formation appeared to be occurring at an unacceptable rate. There were abnormalities of the retina as well. Reduction in tear production was dose-dependent. In a second consult (December 2005), Dr. Chambers provided responses to the sponsor's questions about the need to conduct additional ophthalmologic assessments in the clinical program. Dr. Chambers responded as follows:

Conclusions: Ocular testing has detected abnormalities in tear production, cataract formation and retinal abnormalities, but there have been methodological problems in the monitoring. The ocular dryness and corneal opacities appear to be a related problem, i.e., ocular dryness, if left untreated can lead to corneal opacities particularly in dogs. Vilazodone appears to cause ocular dryness within the first two weeks of treatment. This is similar to many other drug products and could be labeled and treated with Over-the-Counter demulcents. It is unlikely that significant additional information will be learned from ocular monitoring for dry eye in the proposed eight week study."

Lens opacities and the development of retinal lesions can only be evaluated in studies extending for 18-24 months in the case of lens opacities and 12-24 months in the case of retinal lesions. The likelihood of detecting significant changes in the lens or retina in 8 week studies is very low.

Recommended Regulatory Action: Ocular testing is not necessary in the currently proposed study [8-week study]. Ocular testing should be conducted in longer term (18-24 month) studies during the development of this drug product. Monitoring should occur at 6 month intervals in the longer term studies.

The sponsor has provided data from five 8-week clinical studies and one 52-week open-label study of vilazodone. In addition, the sponsor has provided an independent expert's review of the ophthalmologic data. In the sponsor's opinion, the results of the ophthalmologic assessments did not demonstrate clinically significant changes in 'eye health' or ocular function in subjects treated with vilazodone. The report indicates that the presence of treatment-emergent cataracts was identified by slit-lamp biomicroscopy in 22 subject-eyes among 12 subjects. For cortical, nuclear sclerotic, and posterior subcapsular cataract types, the number of subject-eyes that shifted from negative at baseline to positive at the end of treatment was 'small'. Of 110 subjects with cataract at baseline, the overall cataract severity was

determined to have worsened for 14 (12.7%) subjects and to have remained stable (change in summed score <0) for 96 (87.3%) subjects at end of treatment.

In a zip file, we have included: two previous ophthalmology consults, two safety summaries containing relevant ophthalmologic data, and the study report for the 52-week clinical study. **Please let us know who the reviewer is so that we can email them the zip file.**

We have the following questions:

- 1) What is your assessment of the ophthalmologic findings?
- 2) Has the sponsor adequately assessed the ophthalmologic safety profile of vilazodone?
- 3) Could the ophthalmologic risks be managed through labeling? Would you recommend any specific labeling?
- 4) Would you recommend that we request any additional information from the sponsor?

The Clinical reviewer is Cheri Lindberg, M.D., and the TL is Robert Levin, M.D.; the Pharmacology/Toxicology (non-clinical) reviewer is Violetta Klimek, Ph.D., and the TL is Linda Fossom, Ph.D. Let me know if you have any questions to send to the sponsor.

The link to the NDA original application can be found at:

<\\CDSESUB1\EVSPROD\NDA022567\022567.ENX>

We will also send a zip file that contains relevant summaries and data.

Meetings scheduled include:

July 7, 2010

August 25, 2010 (Mid-Cycle meeting)

September 29, 2010

October 25, 2010

November 30, 2010

Submission dates:

Receipt date: 03-22-2010

Day 45: 05-06-2010

Day 60: 05-21-2010

Day 74: 06-04-2010

Month 5: 08-22-2010

Month 8: 11-27-2010

Month 10 (PDUFA Goal Date): 01-22-2011

SIGNATURE OF REQUESTER

CDR William H. Bender

Senior Regulatory Project Manager

301-796-2145

William.bender@fda.hhs.gov

METHOD OF DELIVERY (CHECK ONE)

MAIL

HAND

SIGNATURE OF RECEIVER

SIGNATURE OF DELIVERER

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22567	ORIG-1	PGXHEALTH LLC	VILAZODONE HCL

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/s/

WILLIAM H BENDER
07/07/2010

THOMAS P LAUGHREN
07/07/2010

DEPARTMENT OF HEALTH AND
HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

REQUEST FOR CONSULTATION

TO (Division/Office): Controlled Substance Staff
HFD: -009
5515 Security Lane
Attention: Corinne Moody

FROM:
HFD-130/PSYCHIATRIC PRODUCTS

Date	IND No.	NDA No.	TYPE OF DOCUMENT	DATE OF DOCUMENT
06/25/2010		22-567	Original Application	03/22/2010

NAME OF DRUG: Vilazodone HCl

NAME OF DRUG COMPANY: PGxHealth, LLC

INDICATION OF DRUG: Major Depressive Disorder

DESIRED COMPLETION DATE: 09/22/2010

REASON FOR REQUEST

At the suggestion of your group that vilazodone has pharmacological properties sometimes associated with abuse liability, we are requesting consultation from you to evaluate the abuse and dependence potential of this compound and to recommend studies, if needed, to define its abuse liability and addictive potential.

PGxHealth has submitted NDA 22567 for the use of vilazodone to treat Major Depressive Disorder. Vilazodone is a novel dual-acting serotonergic antidepressant candidate which demonstrates partial agonism of 5-HT_{1a} receptors, in addition to the 5-HT reuptake inhibition seen with conventional SSRIs. The applicant reports that vilazodone has been systematically studied in animal behavior models of physical dependence and did not demonstrate dependence or abuse potential. The individual study reports are provided in Module 4, while summaries are provided in Module 2.6.2, Section 5.2.9.

The Clinical reviewer is Cheri Lindberg, M.D., and the TL is Robert Levin, M.D.; the Pharmacology/Toxicology (non-clinical) reviewer is Violetta Klimek, Ph.D., and the TL is Linda Fossom, Ph.D. Let me know if you have any questions to send to the sponsor.

The link to the NDA original application can be found at:

<\\CDSESUB1\EVSPROD\NDA022567\022567.ENX>

Meetings scheduled include:

July 7, 2010

August 25, 2010 (Mid-Cycle meeting)

September 29, 2010

October 25, 2010

November 30, 2010

Submission dates:

Receipt date: 03-22-2010

Day 45: 05-06-2010

Day 60: 05-21-2010

Day 74: 06-04-2010

Month 5: 08-22-2010

Month 8: 11-27-2010

Month 10 (PDUFA Goal Date): 01-22-2011

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22567	ORIG-1	PGXHEALTH LLC	VILAZODONE HCL

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/s/

WILLIAM H BENDER
06/28/2010

THOMAS P LAUGHREN
06/28/2010



NDA 22-567

FILING COMMUNICATION

PGxHealth, LLC
Attention: Kimberly Fabrizio
Vice President, Regulatory Affairs
Five Science Park
New Haven, CT 06511

Dear Ms. Fabrizio:

Please refer to your new drug application (NDA) dated March 22, 2010, received March 22, 2010, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act, for Vilazodone 10 mg, 20 mg, and 40 mg tablets.

We have completed our filing review and have determined that your application is sufficiently complete to permit a substantive review. Therefore, in accordance with 21 CFR 314.101(a), this application is considered filed 60 days after the date we received your application. The review classification for this application is **Standard**. Therefore, the user fee goal date is January 22, 2011.

We are reviewing your application according to the processes described in the Guidance for Review Staff and Industry: Good Review Management Principles and Practices for PDUFA Products. Therefore, we have established internal review timelines as described in the guidance, which includes the timeframes for FDA internal milestone meetings (e.g., filing, planning, mid-cycle, team and wrap-up meetings). Please be aware that the timelines described in the guidance are flexible and subject to change based on workload and other potential review issues (e.g., submission of amendments). We will inform you of any necessary information requests or status updates following the milestone meetings or at other times, as needed, during the process. If major deficiencies are not identified during the review, we plan to communicate proposed labeling and, if necessary, any postmarketing requirement/commitment requests by December 4, 2010.

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication in pediatric patients unless this requirement is waived, deferred, or inapplicable. We acknowledge receipt of your request for a (b) (4)

the (b) (4) (b) (4) Once we have reviewed your request, we will notify you if the (b) (4) is denied. We also acknowledge receipt of your request for a (b) (4)

the (b) (4) (b) (4) Once we have reviewed your request, we will notify you if the (b) (4) is denied.

If you have any questions, call CDR William Bender, Senior Regulatory Project Manager, at (301) 796-2145

Sincerely,

{See appended electronic signature page}

Thomas Laughren, M.D.
Director
Division of Psychiatry Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22567	ORIG-1	PGXHEALTH LLC	VILAZODONE HCL

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/s/

THOMAS P LAUGHREN
05/28/2010

Bender, William

From: Bender, William
Sent: Wednesday, May 26, 2010 12:43 PM
To: 'Fabrizio, Kimberly'
Subject: NDA 22567

Follow Up Flag: Follow up
Flag Status: Red

For the study report TGX-08-PI-06, entitled:

“A Double-Blind Randomized Parallel Study to Define the ECG Effects of Vilazodone Using a Clinical and a Supratherapeutic Dose Compared to Placebo and Moxifloxacin in Healthy Volunteers: A Thorough ECG Study.”

, please update datasets Hm-1 to hm-10 with QTcl and subject specific slope for QTcl.

Thank you,

Bill

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22567	ORIG-1	PGXHEALTH LLC	VILAZODONE HCL

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/s/

WILLIAM H BENDER
06/02/2010

Bender, William

From: Bender, William
Sent: Thursday, May 20, 2010 3:23 PM
To: 'Fabrizio, Kimberly'
Subject: NDA 22-567

Attachments: Data format table.pdf

Hi Kim,

This is not a filing issue, but our Biometric reviewer is requesting that you reformat your SAS datasets to replicate the attached format table which is also in our guidance document. It makes it easier for them to review the data.

Please let me know if you have any questions. I am on leave tomorrow but will be back in the office on Monday.

Thanks,
Bill



Data format
table.pdf (16 KB)

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22567	ORIG-1	PGXHEALTH LLC	VILAZODONE HCL

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/s/

WILLIAM H BENDER
05/24/2010

Bender, William

From: Bender, William
Sent: Wednesday, May 19, 2010 2:28 PM
To: 'Fabrizio, Kimberly'
Subject: NDA 22-567, Vilazodone

Follow Up Flag: Follow up
Flag Status: Red

Hi Kim,

We have another request regarding Vilazodone:

1) For study CLDA-07-DP-02, you submitted (b) (4) marker status designations (positive/negative) for pharmacogenetic analyses. Please submit (b) (4) genotype data for the two (b) (4) that make up this marker for subjects who provided a DNA sample in this study. SAS data sets would be fine; a formal report is not needed.

2) For study GNSC-04-DP-02, please submit genotype data (minimally for (b) (4)) for subjects who provided a DNA sample. SAS data sets would be fine; a formal report is not needed. You may also submit genotype data for candidates other than (b) (4)

3) Please submit genotype data for any exploratory safety pharmacogenetic analyses performed, as well as for any analyses involving CYP3A5, CYP2C19, and/or CYP2D6 variants.

Thanks,
Bill

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22567	ORIG-1	PGXHEALTH LLC	VILAZODONE HCL

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/s/

WILLIAM H BENDER
05/20/2010

REQUEST FOR CONSULTATION

TO (Office/Division): QT IRT Team/Devi Kozeli

FROM (Name, Office/Division, and Phone Number of Requestor): HFD-130
(Psychiatry Products); Thomas Laughren, M.D.

DATE
05/17/2010

IND NO.
54613

NDA NO.
22567

TYPE OF DOCUMENT
TQT Study PGX-08-P1-06: final clinical report

DATE OF DOCUMENT
July 27, 2009

NAME OF DRUG
Vilazodone

PRIORITY CONSIDERATION
NDA- Standard

CLASSIFICATION OF DRUG
Antidepressant

DESIRED COMPLETION DATE
9/1/2010

NAME OF FIRM: PGxHealth, LLC

REASON FOR REQUEST

I. GENERAL

- | | | |
|--|--|--|
| <input type="checkbox"/> NEW PROTOCOL | <input type="checkbox"/> PRE-NDA MEETING | <input type="checkbox"/> RESPONSE TO DEFICIENCY LETTER |
| <input type="checkbox"/> PROGRESS REPORT | <input type="checkbox"/> END-OF-PHASE 2a MEETING | <input type="checkbox"/> FINAL PRINTED LABELING |
| <input type="checkbox"/> NEW CORRESPONDENCE | <input type="checkbox"/> END-OF-PHASE 2 MEETING | <input type="checkbox"/> LABELING REVISION |
| <input type="checkbox"/> DRUG ADVERTISING | <input type="checkbox"/> RESUBMISSION | <input type="checkbox"/> ORIGINAL NEW CORRESPONDENCE |
| <input type="checkbox"/> ADVERSE REACTION REPORT | <input type="checkbox"/> SAFETY / EFFICACY | <input type="checkbox"/> FORMULATIVE REVIEW |
| <input type="checkbox"/> MANUFACTURING CHANGE / ADDITION | <input type="checkbox"/> PAPER NDA | <input checked="" type="checkbox"/> OTHER (SPECIFY BELOW): |
| <input type="checkbox"/> MEETING PLANNED BY | <input type="checkbox"/> CONTROL SUPPLEMENT | |

II. BIOMETRICS

- | | |
|---|---|
| <input type="checkbox"/> PRIORITY P NDA REVIEW | <input type="checkbox"/> CHEMISTRY REVIEW |
| <input type="checkbox"/> END-OF-PHASE 2 MEETING | <input type="checkbox"/> PHARMACOLOGY |
| <input type="checkbox"/> CONTROLLED STUDIES | <input type="checkbox"/> BIOPHARMACEUTICS |
| <input type="checkbox"/> PROTOCOL REVIEW | <input type="checkbox"/> OTHER (SPECIFY BELOW): |
| <input type="checkbox"/> OTHER (SPECIFY BELOW): | |

III. BIOPHARMACEUTICS

- | | |
|--|--|
| <input type="checkbox"/> DISSOLUTION | <input type="checkbox"/> DEFICIENCY LETTER RESPONSE |
| <input type="checkbox"/> BIOAVAILABILITY STUDIES | <input type="checkbox"/> PROTOCOL - BIOPHARMACEUTICS |
| <input type="checkbox"/> PHASE 4 STUDIES | <input type="checkbox"/> IN-VIVO WAIVER REQUEST |

IV. DRUG SAFETY

- | | |
|--|--|
| <input type="checkbox"/> PHASE 4 SURVEILLANCE/EPIDEMIOLOGY PROTOCOL | <input type="checkbox"/> REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY |
| <input type="checkbox"/> DRUG USE, e.g., POPULATION EXPOSURE, ASSOCIATED DIAGNOSES | <input type="checkbox"/> SUMMARY OF ADVERSE EXPERIENCE |
| <input type="checkbox"/> CASE REPORTS OF SPECIFIC REACTIONS (List below) | <input type="checkbox"/> POISON RISK ANALYSIS |
| <input type="checkbox"/> COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP | |

V. SCIENTIFIC INVESTIGATIONS

- | | |
|-----------------------------------|--------------------------------------|
| <input type="checkbox"/> CLINICAL | <input type="checkbox"/> NONCLINICAL |
|-----------------------------------|--------------------------------------|

COMMENTS / SPECIAL INSTRUCTIONS:

Vilazodone HCl is a unique drug that has selective serotonin reuptake inhibitor (SSRI) properties as well as HT1A receptor antagonist properties. The sponsor has submitted an original NDA for vilazodone in the treatment of adults with a diagnosis of Major Depressive Disorder. The sponsor has completed a dedicated QT study (Study PGX-08-P1-06). This was a randomized, double-blind (except for moxifloxacin), moxifloxacin-controlled, placebo-controlled QT study using supratherapeutic doses of vilazodone (up to 80 mg) in healthy male and female subjects. The sponsor reports that there was no significant effect on the QT interval with vilazodone treatment and that assay sensitivity was achieved.

We would appreciate the QT IRT's assessment of the sponsor's QT study conduct, QT analysis, and proposed labeling (Section 6- Adverse Reactions - ECG). Please see the attached draft labeling. The full clinical report of the QT study (PGX-08-P1-06) can be found at: \\CDSESUB1\EVSPROD\NDA022567\022567.ENX under Section 5. Clinical Study Reports; Section 5.3.3.1 PGX-08-P1-06. The ECGs can be found in the ECG Warehouse. Upload ID: 20100511135536. The original NDA submission (5/4/10) is located at: \\CDSESUB1\EVSPROD\NDA022567\ If you have any questions, please feel free to contact me at extension (6-2145) or Robert Levin, M.D. (6-1110).

SIGNATURE OF REQUESTOR	METHOD OF DELIVERY (Check one) <input checked="" type="checkbox"/> DFS <input type="checkbox"/> EMAIL <input type="checkbox"/> MAIL <input type="checkbox"/> HAND
PRINTED NAME AND SIGNATURE OF RECEIVER	PRINTED NAME AND SIGNATURE OF DELIVERER

9 Page(s) of Draft Labeling have been Withheld in Full as b4 (CCI/TS) immediately following this page

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22567	ORIG-1	PGXHEALTH LLC	VILAZODONE HCL

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/s/

WILLIAM H BENDER
05/20/2010

THOMAS P LAUGHREN
05/21/2010

Bender, William

From: Bender, William
Sent: Friday, May 14, 2010 8:54 AM
To: 'Fabrizio, Kimberly'
Subject: NDA 22-567 Vilazodone

Good Morning Kimberly,

Regarding NDA 22-567, Vilazodone, we have the following requests:

1. For Study CLDA-07-DP-02, please provide or if already provided, please let me know where individual patient data listings stratified by dose group, for each clinical investigator site to include: (a) efficacy endpoints (Montgomery-Ashberg Depression Rating Scale subscore and scores, and HAM-D scale scores, by visit number and date), (b) adverse events/serious adverse events/deaths, (c) protocol deviations, (d) subject discontinuations, and (e) concomitant medications. Also, provide current updated principal site investigator phone, e-mail/FAX listed in CLDA-07-DP-02.
2. Please provide current updated principal investigator phone, e-mail/FAX listed in Study GNSC-04-DP-02.
3. Submit requested information by COB May 21, 2010.

Thanks,
Bill

P.S. Have you heard anything from Merck regarding the SAS files?

Thanks again...

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22567	ORIG-1	PGXHEALTH LLC	VILAZODONE HCL

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/s/

WILLIAM H BENDER
05/14/2010

Bender, William

From: Bender, William
Sent: Friday, May 14, 2010 12:00 PM
To: 'Fabrizio, Kimberly'
Subject: RE: NDA 22-567 Vilazodone

Regarding the formatting of data sets for carcinogenicity studies as SAS XPORT transport files, we refer you to <http://www.fda.gov/downloads/ForIndustry/DataStandards/StudyDataStandards/UCM189445.pdf>, particularly Appendix 1.

Thanks,
Bill

From: Fabrizio, Kimberly [mailto:KFabrizio@pgxhealth.com]
Sent: Friday, May 14, 2010 9:20 AM
To: Bender, William
Subject: RE: NDA 22-567 Vilazodone

Good Morning to you to Bill,

We will submit the requested information for the Phase 3 study listed below, no problem. In regards to the SAS files we have been able to retrieve from Merck the raw data from the rat study in regards to tumors and we have converted this successfully to SAS, which is undergoing a QC within our statistical and toxicology groups. We should be able to submit this to the NDA early next week with the clinical data request. In regards to the mouse data, Merck will be able to let us know the status on Monday due to a holiday in Germany this weekend. Have you heard back from the SAS reviewer as to what we will need to do if we cannot locate this data? Thank you and have a great weekend.

Kimberly Fabrizio

Vice President Regulatory Affairs

PGxHealth™, a Division of Clinical Data®

5 Science Park

New Haven, CT 06511 (USA)

Phone: +1 (203) 786-3502 x2502

Email: kfabrizio@pgxhealth.com

Web: <http://www.pgxhealth.com>

This communication and any file transmitted with it may contain information that is confidential, privileged and exempt from disclosure under applicable law. It is intended solely for the use of the individual or entity to which it is addressed. If you are not the intended recipient, you are hereby notified that any use, dissemination or copying of this communication is strictly prohibited. If you have received this communication in error, please notify the sender. Thank you for your cooperation.

From: Bender, William [mailto:William.Bender2@fda.hhs.gov]
Sent: Friday, May 14, 2010 8:54 AM
To: Fabrizio, Kimberly
Subject: NDA 22-567 Vilazodone

5/14/2010

Good Morning Kimberly,

Regarding NDA 22-567, Vilazodone, we have the following requests:

1. For Study CLDA-07-DP-02, please provide or if already provided, please let me know where individual patient data listings stratified by dose group, for each clinical investigator site to include: (a) efficacy endpoints (Montgomery-Ashberg Depression Rating Scale subscore and scores, and HAM-D scale scores, by visit number and date), (b) adverse events/serious adverse events/deaths, (c) protocol deviations, (d) subject discontinuations, and (e) concomitant medications. Also, provide current updated principal site investigator phone, e-mail/FAX listed in CLDA-07-DP-02.
2. Please provide current updated principal investigator phone, e-mail/FAX listed in Study GNSC-04-DP-02.
3. Submit requested information by COB May 21, 2010.

Thanks,
Bill

P.S. Have you heard anything from Merck regarding the SAS files?

Thanks again...

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22567	ORIG-1	PGXHEALTH LLC	VILAZODONE HCL

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/s/

WILLIAM H BENDER
05/14/2010

REQUEST FOR CONSULTATION

TO (Division/Office):

CDER OSE CONSULTS

FROM: HFD-130/Division of Psychiatry Products

DATE
04/15/2010

IND NO.

NDA NO.
22-567

TYPE OF DOCUMENT
NDA submission

DATE OF DOCUMENT
03/22/2010

NAME OF DRUG
Vilazodone HCL tablets

PRIORITY CONSIDERATION

CLASSIFICATION OF DRUG
Major Depressive
Disorder

DESIRED COMPLETION DATE
PDUFA due date of
01/22/2011

NAME OF FIRM: PGxHealth, LLC

REASON FOR REQUEST

I. GENERAL

- | | | |
|--|--|--|
| <input type="checkbox"/> NEW PROTOCOL | <input type="checkbox"/> PRE--NDA MEETING | <input type="checkbox"/> RESPONSE TO DEFICIENCY LETTER |
| <input type="checkbox"/> PROGRESS REPORT | <input type="checkbox"/> END OF PHASE II MEETING | <input type="checkbox"/> FINAL PRINTED LABELING |
| <input type="checkbox"/> NEW CORRESPONDENCE | <input type="checkbox"/> RESUBMISSION | <input type="checkbox"/> LABELING REVISION |
| <input type="checkbox"/> DRUG ADVERTISING | <input type="checkbox"/> SAFETY/EFFICACY | <input type="checkbox"/> ORIGINAL NEW CORRESPONDENCE |
| <input type="checkbox"/> ADVERSE REACTION REPORT | <input type="checkbox"/> PAPER NDA | <input type="checkbox"/> FORMULATIVE REVIEW |
| <input type="checkbox"/> MANUFACTURING CHANGE/ADDITION | <input type="checkbox"/> CONTROL SUPPLEMENT | <input type="checkbox"/> OTHER (SPECIFY BELOW): Trade name review |
| <input type="checkbox"/> MEETING PLANNED BY | | |

II. BIOMETRICS

STATISTICAL EVALUATION BRANCH

STATISTICAL APPLICATION BRANCH

- TYPE A OR B NDA REVIEW
 END OF PHASE II MEETING
 CONTROLLED STUDIES
 PROTOCOL REVIEW
 OTHER (SPECIFY BELOW):

- CHEMISTRY REVIEW
 PHARMACOLOGY
 BIOPHARMACEUTICS
 OTHER (SPECIFY BELOW):

III. BIOPHARMACEUTICS

- DISSOLUTION
 BIOAVAILABILITY STUDIES
 PHASE IV STUDIES

- DEFICIENCY LETTER RESPONSE
 PROTOCOL-BIOPHARMACEUTICS
 IN-VIVO WAIVER REQUEST

IV. DRUG EXPERIENCE

- PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL
 DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES
 CASE REPORTS OF SPECIFIC REACTIONS (List below)
 COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP

- REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY
 SUMMARY OF ADVERSE EXPERIENCE
 POISON RISK ANALYSIS

V. SCIENTIFIC INVESTIGATIONS

CLINICAL

PRECLINICAL

COMMENTS/SPECIAL INSTRUCTIONS: The proposed container label and carton labeling for this product can be found at the following link: \\CDSesub1\EVSPROD\NDA022567\022567.ENX

PDUFA DATE: 01/22/2011

ATTACHMENTS: Draft Package Insert, Container and Carton Labels

CC: Archival IND/NDA IND 54,613

HFD-130/Division File

HFD-130/RPM

HFD-130/Reviewers and Team Leaders

NAME AND PHONE NUMBER OF REQUESTER

CDR Bill Bender, RPh., Regulatory Project Manager

301-796-2145

METHOD OF DELIVERY (Check one)

DFS ONLY

MAIL

HAND

SIGNATURE OF RECEIVER	SIGNATURE OF DELIVERER

5/28/05

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22567	ORIG-1	PGX HEALTH LLC	VILAZODONE HCL

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/s/

WILLIAM H BENDER
04/15/2010

THOMAS P LAUGHREN
04/15/2010

DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION		REQUEST FOR CONSULTATION			
TO (Division/Office): OSE/DRISK Attn: Mary Dempsey			FROM: OND/ODE1/DPP HFD-130		
DATE 04/12/2010	IND NO.	NDA NO. 22-567	TYPE OF DOCUMENT Risk MAPP	DATE OF DOCUMENT 03/22/2010	
NAME OF DRUG Vilazodone HCL tablets		PRIORITY CONSIDERATION PDUFA Goal Date: 01/22/2011	CLASSIFICATION OF DRUG Major Depressive Disorder	DESIRED COMPLETION DATE	
NAME OF FIRM: PGxHealth, LLC					
REASON FOR REQUEST I. GENERAL					
<input type="checkbox"/> NEW PROTOCOL <input type="checkbox"/> PROGRESS REPORT <input type="checkbox"/> NEW CORRESPONDENCE <input type="checkbox"/> DRUG ADVERTISING <input type="checkbox"/> ADVERSE REACTION REPORT <input type="checkbox"/> MANUFACTURING CHANGE/ADDITION <input type="checkbox"/> MEETING PLANNED BY <input type="checkbox"/> PRE--NDA MEETING <input type="checkbox"/> END OF PHASE II MEETING <input type="checkbox"/> RESUBMISSION <input checked="" type="checkbox"/> SAFETY/EFFICACY <input type="checkbox"/> PAPER NDA <input type="checkbox"/> CONTROL SUPPLEMENT <input type="checkbox"/> RESPONSE TO DEFICIENCY LETTER <input type="checkbox"/> FINAL PRINTED LABELING <input type="checkbox"/> LABELING REVISION <input type="checkbox"/> ORIGINAL NEW CORRESPONDENCE <input type="checkbox"/> FORMULATIVE REVIEW <input type="checkbox"/> OTHER (SPECIFY BELOW):					
II. BIOMETRICS					
STATISTICAL EVALUATION BRANCH			STATISTICAL APPLICATION BRANCH		
<input type="checkbox"/> TYPE A OR B NDA REVIEW <input type="checkbox"/> END OF PHASE II MEETING <input type="checkbox"/> CONTROLLED STUDIES <input type="checkbox"/> PROTOCOL REVIEW <input type="checkbox"/> OTHER (SPECIFY BELOW):			<input type="checkbox"/> CHEMISTRY REVIEW <input type="checkbox"/> PHARMACOLOGY <input type="checkbox"/> BIOPHARMACEUTICS <input type="checkbox"/> OTHER (SPECIFY BELOW):		
IV. DRUG EXPERIENCE					
<input type="checkbox"/> PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL <input type="checkbox"/> DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES <input type="checkbox"/> CASE REPORTS OF SPECIFIC REACTIONS (List below) <input type="checkbox"/> COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP			<input type="checkbox"/> REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY <input type="checkbox"/> SUMMARY OF ADVERSE EXPERIENCE <input type="checkbox"/> POISON RISK ANALYSIS		
V. SCIENTIFIC INVESTIGATIONS					
<input type="checkbox"/> CLINICAL			<input type="checkbox"/> PRECLINICAL		
COMMENTS/SPECIAL INSTRUCTIONS: Hi Mary, Attached is a RiskMapp that the sponsor sent with their original application regarding NDA 22-567, vilazodone HCL (New Molecular Entity). The PDUFA date is January 22, 2011. Please review the attached RiskMapp and let me know if you have any comments. I have also attached the labeling provided by the sponsor that includes the MedGuide. The EDR link for the entire original submission can be found at: \\CDSESUB1\EVSPROD\NDA022567\022567.ENX I can be reached at either william.bender@fda.hhs.gov or 301-796-2145. Thanks, Bill					
SIGNATURE OF REQUESTER CDR Bill Bender, RPh. Regulatory Project Manager 301-796-2145 william.bender@fda.hhs.gov			METHOD OF DELIVERY (Check one) <input type="checkbox"/> MAIL <input type="checkbox"/> HAND		
SIGNATURE OF RECEIVER			SIGNATURE OF DELIVERER		

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22567	ORIG-1	PGX HEALTH LLC	VILAZODONE HCL

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/s/

WILLIAM H BENDER
04/12/2010

THOMAS P LAUGHREN
04/12/2010

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22567	ORIG-1	PGX HEALTH LLC	VILAZODONE HCL

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/s/

WILLIAM H BENDER
04/13/2010

THOMAS P LAUGHREN
04/13/2010



NDA 22-567

NDA ACKNOWLEDGMENT

PgxHealth, LLC
Attention: Kimberly Fabrizio
Vice President, Regulatory Affairs
Five Science Park
New Haven, CT 06511

Dear Ms. Fabrizio:

We have received your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for the following:

Name of Drug Product: Vilazodone HCL tablets, 10 mg, 20 mg, and 40 mg

Date of Application: March 22, 2010

Date of Receipt: March 22, 2010

Our Reference Number: NDA 22-567

Unless we notify you within 60 days of the receipt date that the application is not sufficiently complete to permit a substantive review, we will file the application on May 21, 2010 in accordance with 21 CFR 314.101(a).

If you have not already done so, promptly submit the content of labeling [21 CFR 314.50(l)(1)(i)] in structured product labeling (SPL) format as described at <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>. Failure to submit the content of labeling in SPL format may result in a refusal-to-file action under 21 CFR 314.101(d)(3). The content of labeling must conform to the content and format requirements of revised 21 CFR 201.56-57.

The NDA number provided above should be cited at the top of the first page of all submissions to this application. Send all submissions, electronic or paper, including those sent by overnight mail or courier, to the following address:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Psychiatry Products
5901-B Ammendale Road
Beltsville, MD 20705-1266

All regulatory documents submitted in paper should be three-hole punched on the left side of the page and bound. The left margin should be at least three-fourths of an inch to assure text is not obscured in the fastened area. Standard paper size (8-1/2 by 11 inches) should be used; however, it may occasionally be necessary to use individual pages larger than standard paper size. Non-standard, large pages should be folded and mounted to allow the page to be opened for review without disassembling the jacket and refolded without damage when the volume is shelved. Shipping unbound documents may result in the loss of portions of the submission or an unnecessary delay in processing which could have an adverse impact on the review of the submission. For additional information, please see <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/DrugMasterFilesDMFs/ucm073080.htm>

If you have any questions, call me at (301) 796-2145.

Sincerely,

{See appended electronic signature page}

CDR Bill Bender, R.Ph., MS HCA
Regulatory Project Manager
Division of Psychiatry Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22567	ORIG-1	PGX HEALTH LLC	VILAZODONE HCL

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/s/

WILLIAM H BENDER
03/24/2010