



NDA 022567

NDA APPROVAL

Trovis Pharmaceuticals 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 (FDCA) for Viibryd (vilazodone hydrochloride) 10 mg, 20 mg, and 40 mg tablets.

We acknowledge receipt of your amendments dated May 4, 2010, May 7, 2010, May 18, 2010, May 19, 2010, May 25, 2010, June 3, 2010, June 8, 2010, June 30, 2010, August 4, 2010, August 19, 2010, August 23, 2010, August 31, 2010, September 27, 2010, November 4, 2010, November 18, 2010, November 30, 2010, December 3, 2010, December 13, 2010, December 15, 2010, December 23, 2010, December 29, 2010, January 4, 2011, January 6, 2011, January 7, 2011, January 11, 2011, and January 13, 2011.

This new drug application provides for the use of Viibryd (vilazodone hydrochloride) for the treatment of Major Depressive Disorder.

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling text.

We request that the labeling approved today be available on your website within 10 days of receipt of this letter.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit, via the FDA automated drug registration and listing system (eLIST), the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format, as described at <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>, that is identical to the enclosed labeling. Information on submitting SPL files using eLIST may be found in the guidance for industry titled "SPL Standard for Content of Labeling Technical Qs and As" at

<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf>.

The SPL will be accessible via publicly available labeling repositories.

CARTON AND IMMEDIATE CONTAINER LABELS

Submit final printed carton and container labels that are identical to the carton and immediate container labels as agreed upon in our January 14, 2011 communication as soon as they are available, but no more than 30 days after they are printed. Please submit these labels electronically according to the guidance for industry titled “Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (June 2008).” Alternatively, you may submit 12 paper copies, with 6 of the copies individually mounted on heavy-weight paper or similar material. For administrative purposes, designate this submission “**Final Printed Carton and Container Labels for approved NDA 22567.**” Approval of this submission by FDA is not required before the labeling is used.

Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

ADVISORY COMMITTEE

Your application for vilazodone was not referred to an FDA advisory committee because this drug is not the first in its class, and the safety profile is similar to that of other drugs approved for this indication.

PROPRIETARY NAME

The Division of Medication Error and Prevention and Analysis (DMEPA) and the Division of Psychiatry Products do not object to the use of the proprietary name, Viibryd, for this product.

REQUIRED PEDIATRIC ASSESSMENTS

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(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

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 required under section 505B(a) of the Federal Food, Drug, and Cosmetic Act are required postmarketing studies. The status of these postmarketing studies must be reported annually according to 21 CFR 314.81 and section 505B(a)(3)(B) of the FDCA. These required studies are listed below.

1723-1 Deferred pediatric study under PREA for the treatment of major depressive disorder in pediatric patients aged 7 to 17. Conduct a study to obtain pharmacokinetic, safety, and tolerability data and provide information pertinent to dosing of vilazodone in the relevant pediatric population.

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

1723-2 Deferred pediatric study under PREA for the treatment of major depressive disorder in pediatric patients aged 7 to 17. Conduct 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

1723-3 Deferred pediatric study under PREA for the treatment of major depressive disorder in pediatric patients aged 7 to 17. Conduct 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

1723-4 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

Submit final reports to this NDA. For administrative purposes, all submissions related to this required pediatric postmarketing study must be clearly designated “**Required Pediatric Assessment(s).**”

POSTMARKETING REQUIREMENTS UNDER 505(o)

Section 505(o)(3) of the FDCA authorizes FDA to require holders of approved drug and biological product applications to conduct postmarketing studies and clinical trials for certain purposes, if FDA makes certain findings required by the statute.

The major human metabolite of vilazodone, M17, was not demonstrated to be present in plasma of either rats or rabbits. Therefore the embryo-fetal reproductive toxicity studies with vilazodone did not adequately assess the potential reproductive toxicity of M17.

We have determined that an analysis of spontaneous postmarketing adverse events reported under subsection 505(k)(1) of the FDCA will not be sufficient to assess the reproductive toxicity of the major human metabolite M17.

Furthermore, the new pharmacovigilance system that FDA is required to establish under section 505(k)(3) of the FDCA is not yet sufficient to assess this serious risk.

Therefore, based on appropriate scientific data, FDA has determined that you are required to conduct the following:

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 maximum recommended human dose (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 are able to address postmarketing study 1723-6 adequately through analyses of existing data, FDA may release you from postmarketing study 1723-5.

Submit the protocol to your IND 54613, with a cross-reference letter to this NDA. Submit all final report(s) to your NDA. Prominently identify the submission with the following wording in bold capital letters at the top of the first page of the submission, as appropriate: **“Required Postmarketing Protocol Under 505(o),” “Required Postmarketing Final Report Under 505(o),” “Required Postmarketing Correspondence Under 505(o).”**

Section 505(o)(3)(E)(ii) of the FDCA requires you to report periodically on the status of any study or clinical trial required under this section. This section also requires you to periodically report to FDA on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Section 506B of the FDCA, as well as 21 CFR 314.81(b)(2)(vii), requires you to report annually on the status of any postmarketing commitments or required studies or clinical trials.

FDA will consider the submission of your annual report under section 506B and 21 CFR 314.81(b)(2)(vii) to satisfy the periodic reporting requirement under section 505(o)(3)(E)(ii) provided that you include the elements listed in 505(o) and 21 CFR 314.81(b)(2)(vii). We remind you that to comply with 505(o), your annual report must also include a report on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Failure to submit an annual report for studies or clinical trials required under 505(o) on the date required will be considered a violation of FDCA section 505(o)(3)(E)(ii) and could result in enforcement action.

POSTMARKETING COMMITMENTS SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitments agreed upon in your communications dated January 19, 2011:

1723-7	A controlled 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.
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Final Protocol Submission:	September 30, 2011
Trial Completion Date:	January 31, 2015
Final Report Submission:	January 31, 2016

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