

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

201194Orig1s000

OTHER ACTION LETTERS



NDA 201194

COMPLETE RESPONSE

VistaPharm Inc.
7265 Ulmerton Road
Largo, FL 33771

Attention: John G. Lay
Director, Regulatory Affairs and Quality Assurance

Dear Mr. Lay:

Please refer to your new drug application (NDA) dated May 4, 2010, received May 5, 2010, submitted under section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act, for Oxycodone Hydrochloride Oral Solution USP, 5 mg/5 mL.

We acknowledge receipt of your amendments dated May 21 and 27 (2), July 9, September 7, October 11, and December 28, 2010, and January 7 and 12, 2011.

We also acknowledge receipt of your amendments dated February 4 (2) and 7, 2011, which were not reviewed for this action. You may incorporate applicable sections of these amendments by specific reference as part of your response to the deficiencies cited in this letter.

We have completed our review of this application, as amended, and have determined that we cannot approve this application in its present form. We have described our reasons for this action below and, where possible, our recommendations to address these issues.

CLINICAL

An audit performed by the Agency of the bioequivalence study, R09-0988, identified deficiencies in the methods used at the analytical site. Because of these deficiencies, the bioequivalence study cannot be relied upon to establish bioequivalence of your proposed drug product to the reference product.

This deficiency may be addressed by doing one of the following:

1. Provided adequate samples are available, reanalyze blood samples collected in Study R09-0988 and submit data establishing the bioequivalence of Oxycodone Hydrochloride Oral Solution 5 mg/5 mL with Roxycodone tablets. Ensure that the inspectional findings identified in the Agency's audit of Study R09-0988 are properly addressed in the reanalysis of blood samples.

OR

2. Conduct another pharmacokinetic study and establish the bioequivalence of Oxycodone Hydrochloride Oral Solution with Roxycodone tablets under fasting conditions using an adequately validated analytical methodology.

OR

3. Conduct a clinical development program with clinical efficacy and safety studies to support your product.

LABELING

We reserve comment on the proposed labeling until the application is otherwise adequate. If you revise labeling, your response must include updated 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>.

RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS

We acknowledge receipt of your voluntary submission dated May 4, 2010, of a proposed Risk Evaluation and Mitigation Strategy (REMS) and your amendment dated January 12, 2011, containing a revised proposed REMS. We have determined that, at this time, a REMS is not necessary for Oxycodone Hydrochloride Oral Solution to ensure that its benefits outweigh its risks. We will notify you if we become aware of new safety information and make a determination that a REMS is necessary.

SAFETY UPDATE

When you respond to the above deficiencies, include a safety update as described at 21 CFR 314.50(d)(5)(vi)(b). The safety update should include data from all nonclinical and clinical studies/trials of the drug under consideration regardless of indication, dosage form, or dose level.

1. Describe in detail any significant changes or findings in the safety profile.
2. When assembling the sections describing discontinuations due to adverse events, serious adverse events, and common adverse events, incorporate new safety data as follows:
 - Present new safety data from the studies/clinical trials for the proposed indication using the same format as the original NDA submission.
 - Present tabulations of the new safety data combined with the original NDA data.

- Include tables that compare frequencies of adverse events in the original NDA with the retabulated frequencies described in the bullet above.
 - For indications other than the proposed indication, provide separate tables for the frequencies of adverse events occurring in clinical trials.
3. Present a retabulation of the reasons for premature trial discontinuation by incorporating the drop-outs from the newly completed trials. Describe any new trends or patterns identified.
 4. Provide case report forms and narrative summaries for each patient who died during a clinical trial or who did not complete a trial because of an adverse event. In addition, provide narrative summaries for serious adverse events.
 5. Describe any information that suggests a substantial change in the incidence of common, but less serious, adverse events between the new data and the original NDA data.
 6. Provide updated exposure information for the clinical studies/trials (e.g., number of subjects, person time).
 7. Provide a summary of worldwide experience on the safety of this drug. Include an updated estimate of use for drug marketed in other countries.
 8. Provide English translations of current approved foreign labeling not previously submitted.

OTHER

Within one year after the date of this letter, you are required to resubmit or take other actions available under 21 CFR 314.110. If you do not take one of these actions, we may consider your lack of response a request to withdraw the application under 21 CFR 314.65. You may also request an extension of time in which to resubmit the application. A resubmission must fully address all the deficiencies listed. A partial response to this letter will not be processed as a resubmission and will not start a new review cycle.

Under 21 CFR 314.102(d), you may request a meeting or telephone conference with us to discuss what steps you need to take before the application may be approved. If you wish to have such a meeting, submit your meeting request as described in the FDA's "Guidance for Industry - Formal Meetings Between the FDA and Sponsors or Applicants," May 2009 at <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM153222.pdf>.

If you have any questions, call Dominic Chiapperino, Regulatory Project Manager, at (301) 796-1183.

Sincerely,

{See appended electronic signature page}

Sharon Hertz, M.D.
Deputy Director
Division of Anesthesia and Analgesia Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

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

/s/

SHARON H HERTZ
03/03/2011