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RESEARCH**

APPLICATION NUMBER:
201517Orig1s000

OTHER ACTION LETTERS



NDA 201517

COMPLETE RESPONSE

Lannett Holdings, Inc.
13200 Townsend Road
Philadelphia, PA 19154-1014

Attention: Ernest Sabo
Vice President, Regulatory and Corporate Compliance

Dear Mr. Sabo:

Please refer to your New Drug Application (NDA) dated February 26, 2010, received March 1, 2010, pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Morphine Sulfate Oral Solution, 20 mg/mL.

We acknowledge receipt of your amendments dated March 26, April 29, June 23, July 1, 9, 15, 16 and 20, August 18, October 1 and 25(2), and November 12 and 17, 2010.

We also acknowledge receipt of your amendments dated December 7, 2010, 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.

FACILITY INSPECTIONS

During a recent inspection of the Lannett Company, Inc., 9001 Torresdale Avenue, Philadelphia, PA, 19136-1514, our field investigator conveyed deficiencies to the representative of the facility. Satisfactory resolution of these deficiencies is required before this application may be approved.

PRODUCT QUALITY

DMF (b) (4) for morphine sulfate held by (b) (4) was found deficient and the holder notified on December 2, 2010. Satisfactory resolution of this deficiency is required before this application may be approved.

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>.

Add the following bolded statement or appropriate alternative to the carton and container labels per 21 CFR 208.24(d): "**ATTENTION PHARMACIST: Each patient is required to receive the enclosed Medication Guide.**"

RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS

Section 505-1 of the FDCA authorizes FDA to require the submission of a REMS if FDA determines that such a strategy is necessary to ensure that the benefits of the drug outweigh the risks [section 505-1(a)].

We acknowledge receipt of your proposed REMS, included in your submission dated March 1, 2010, and amended on March 26, 2010, and November 17, 2010, which contains a Medication Guide and a timetable for submission of assessments of the REMS. In accordance with section 505-1 of the FDCA, we agree that a REMS will be necessary for Morphine Sulfate Oral Solution, 20 mg/mL, if it is approved, to ensure that the benefits of the drug outweigh the risk of medication errors resulting in life-threatening overdose. The REMS, should it be approved, will create enforceable obligations. We will continue discussion of your proposed REMS after your complete response to this action letter has been submitted.

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.

In addition, while not approvability issues, we have the following comments that should be addressed in your resubmission:

1. Provide the source and qualification procedures for the (b) (4) reference standards.
2. Submit a revision to Section 3.2.P.5.6 to include the revised acceptance criterion for (b) (4)
3. Explain why the (b) (4) for the Oral Doser Barrel is different for the 30 mL package size (b) (4) from the (b) (4) for the 120 mL and 240 mL package sizes (b) (4)
4. Explain why the CFR citations for the Colorant used in the Oral Dosers include sections that are not usually associated with colorants for plastics:
 - 176.170 Components of paper and paperboard in contact with aqueous and fatty foods
 - 175.105 Adhesives
 - 175.300 Resinous and polymeric coatings
 - 175.320 Resinous and polymeric coatings for polyolefin films
5. Based on a statistical analysis of the data provided the expiration period should be (b) (4) (b) (4) This is based on an acceptance criterion of NLT (b) (4) for sodium benzoate (30 mL package size, Batch 09801017. We note that you have proposed to test batches on stability for antimicrobial effective testing if the values of any preservative is between (b) (4)

(b) (4) However this type of testing is not applicable to determining an expiration date.

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>.

The drug product may not be legally marketed until you have been notified in writing that this application is approved.

If you have any questions, call Diana L. Walker, Ph.D., Regulatory Health Project Manager, at (301) 796-4029.

Sincerely,

{See appended electronic signature page}

Sharon H. 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
12/10/2010