CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

211302Orig1s000

OTHER ACTION LETTERS

U.S. FOOD & DRUG ADMINISTRATION

NDA 211302

COMPLETE RESPONSE

Recordati Rare Diseases Inc.
c/o Intertek Surveying Services
Attention: Jennifer Tillman
U.S. Agent
16441 Space Center Blvd, Suite D-100
Houston, TX 77058

Dear Ms. Tillman:

Please refer to your new drug application (NDA) dated and received March 28, 2019, and your amendments, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Cystadrops (cysteamine ophthalmic solution) 0.37%.

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. Please note that amendments submitted after November 23, 2019, were not reviewed as they were submitted late in the review cycle.

1. The facilities and controls used for, the manufacture, processing, packing, and holding of the drug product do not comply with the current good manufacturing practice (cGMP) regulations in 21 CFR 210 and 211. Specifically, during a recent inspection of the Baccinex SA, FEI# 3007272813, a manufacturing facility for this application, the Agency's field investigators conveyed deficiencies to the representatives of this facility. Satisfactory resolution of these deficiencies is required if this facility remains in the application. All submitted facilities must be in compliance with cGMP before this application may be approved.

2. The methods to be used in, and the facilities and controls used for the manufacture, processing, packing and holding of the drug product are inadequate to preserve its identity, strength, quality, purity, stability or bioavailability. Specifically,

   a. In your amendment submitted on November 5, 2019, the following deficiencies remain unresolved as adequate data are not available for evaluation. In your resubmission, please:

      i. Submit data to demonstrate that (b) (4) [redacted]. These parameters

should be supported by development data and/or registration batch manufacturing data.

ii. Clarify whether (b) (4)

iii. Revise your master batch record to reflect changes pertaining to (b) (4) .

b. (b) (4)

c. We also acknowledge that you intend to complete a (b) (4) study prior to manufacture of Cystadrops commercial batches for the U.S. and that the study will simulate (b) (4) . Please provide the results of this (b) (4) simulation.

We reserve comment on the proposed labeling until the application is otherwise adequate. We encourage you to review the labeling review resources on the PLR Requirements for Prescribing Information and Pregnancy and Lactation Labeling Final Rule websites, including regulations and related guidance documents and the Selected Requirements for Prescribing Information (SRPI) − a checklist of important format items from labeling regulations and guidances.

If you revise labeling, use the SRPI checklist to ensure that the Prescribing Information conforms with format items in regulations and guidances. Your response must include updated content of labeling [21 CFR 314.50(l)(1)(i)] in structured product labeling (SPL)

format as described at FDA.gov.[1]

Please refer to the correspondence dated, June 21, 2019, which addresses the proposed proprietary name, Cystadrops. This name was found acceptable pending approval of the application in the current review cycle. Please resubmit the proposed proprietary name when you respond to the application deficiencies.

SAFETY UPDATE

When you respond to the above deficiencies, please 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.

ADDITIONAL COMMENTS

We have the following requests that are not approvability issues:

1. We acknowledge your revised drug specifications including a test for particulate matter. Please provide a stability update with the particulate matter testing in the NDA resubmission.

2. Please provide the complete analytical method transfer report from (b) (4) to (b) (4) in the NDA resubmission.

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 in this letter and should be clearly marked with "**RESUBMISSION**" in large font, bolded type at the beginning of the cover letter of the submission. The cover letter should clearly state that you consider this resubmission a complete response to the deficiencies outlined in this letter. A partial response to this letter will not be processed as a resubmission and will not start a new review cycle.

You may request a meeting or teleconference 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 draft guidance for industry *Formal Meetings Between the FDA and Sponsors or Applicants of PDUFA Products*.

[1] http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm

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 Lois Almoza, M.S., Senior Regulatory Health Project Manager, at (301) 796-1600.

Sincerely,

{See appended electronic signature page}

Wiley A. Chambers, M.D.
Deputy Director
Division of Ophthalmology
Office of Specialty Medicine
Office of New Drugs
Center for Drug Evaluation and Research

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

WILEY A CHAMBERS
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