CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

206185Orig1s000

OTHER ACTION LETTERS

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 206185

COMPLETE RESPONSE

Sun Pharma Advanced Research Company Limited
c/o Ora, Inc.
Attention: Mr. Aron Shapiro
Vice President
300 Brickstone Square
Andover, MA 01810

Dear Mr. Shapiro:

Please refer to your New Drug Application (NDA) dated and received January 31, 2014, pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Xelpros (latanoprost ophthalmic emulsion), 0.005%.

We acknowledge receipt of your amendment dated July 28, 2016, which constituted a complete response to our July 30, 2015, action 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.

PRODUCT QUALITY/FACILITIES INSPECTION

During a recent inspection of the Sun Pharmaceutical Industries, Ltd., FEI# 3002809586 manufacturing facility for this application, our field investigators conveyed deficiencies to the representative of the facility. Satisfactory resolution of these deficiencies is required before this application may be approved.

LABELS AND LABELING

We acknowledge the submission of proposed carton and container labels as well as proposed labeling (prescribing information) on July 28, 2016. We reserve comment on the proposed labeling until the application is otherwise adequate.

PROPRIETARY NAME

Please refer to correspondence dated October 3, 2016, which addresses the proposed proprietary name, Xelpros. 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, 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 in the original 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 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 FDA Guidance for Industry, "Formal Meetings Between the FDA and Sponsors or Applicants of PDUFA Products," March 2015 at http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm437431.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 Judit Milstein, Chief, Project Management Staff at 301-796-0763.

Sincerely,

{See appended electronic signature page}

Renata Albrecht, MD
Director
Division of Transplant and Ophthalmology Products
Office of Antimicrobial Products
Office of New Drugs
Center for Drug Evaluation and Research

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/s/

RENATA ALBRECHT
12/19/2016

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 206185

COMPLETE RESPONSE

Sun Pharma Advanced Research Company Limited
c/o Ora, Inc.
Attention: Mr. Aron Shapiro
Vice President, Ora, Inc.
300 Brickstone Square
Andover, MA 01810

Dear Mr. Shapiro:

Please refer to your New Drug Application (NDA) dated January 31, 2014, received January 31, 2014, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act, for Xelpros (latanoprost ophthalmic emulsion) 0.005%.

We acknowledge receipt of your amendments dated:

November 26, 2014
April 9, 2015
May 12, 2015

The April 9, 2015, submission constituted a complete response to our November 24, 2014, action 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.

PRESCRIBING INFORMATION

1. Please submit the labeling attached to this correspondence, which contains minor revisions based on the labeling submitted April 9, 2015. Please also re-submit the carton and container labels in the April 9, 2015, submission, as these labels are acceptable.

FACILITY INSPECTIONS

2. During a recent inspection of the Sun Pharmaceutical Industries, Ltd, Halol, India manufacturing facility for this application, our field investigators conveyed deficiencies to the representative of the facility. Satisfactory resolution of these deficiencies is required before this application may be approved.

PROPRIETARY NAME

3. Please refer to correspondence dated July 16, 2015, which addresses the proposed proprietary name, Xelpros. 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, 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.

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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 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 Ms. Diana Willard, Chief, Project Management Staff, at (301) 796-1600.

Sincerely,

{See appended electronic signature page}

Renata Albrecht, M.D.
Director
Division of Transplant and Ophthalmology Products
Office of Antimicrobial products
Center for Drug Evaluation and Research

ENCLOSURES:
Labeling

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/s/

RENATA ALBRECHT
07/30/2015

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 206185

COMPLETE RESPONSE

Sun Pharma Advanced Research Company Limited
c/o Ora, Inc.
Attention: Mr. Aron Shapiro
Vice President, Ora, Inc.
300 Brickstone Square
Andover, MA 01810

Dear Mr. Shapiro:

Please refer to your New Drug Application (NDA) dated January 31, 2014, received January 31, 2014, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act, for Xelpros (latanoprost ophthalmic emulsion) 0.005%.

We acknowledge receipt of your amendments dated:

February 7, 2014	April 11, 2014	July 9, 2014
February 21, 2014	April 30, 2014	July 25, 2014
March 5, 2014	May 23, 2014	September 30, 2014
March 14, 2014	June 6, 2014	October 21, 2014
March 27, 2014	June 27, 2014	October 30, 2014

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.

PRODUCT QUALITY

1. Please update the NDA submission in all appropriate sections to indicate the correct dosage form of ophthalmic emulsion. This can be accomplished by submission of an "Erratum" page with a statement that throughout the NDA the product name was corrected from "latanoprost ophthalmic (b) (4)" to "latanoprost ophthalmic emulsion."

2. The release and stability data indicate that the proposed acceptance limits for (b) (4) (specified identified impurity) and highest unspecified impurity can be tightened. Please revise the limits to the above referenced impurities to NMT (b) (4)% for release and stability.

PRESCRIBING INFORMATION

3. Your proposed prescribing information (PI) must conform to the content and format regulations found at 21 CFR 201.56(a) and (d) and 201.57. We encourage you to review the labeling review resources on the *PLR Requirements for Prescribing Information* website including:

   - The Final Rule (Physician Labeling Rule) on the content and format of the PI for human drug and biological products
   - Regulations and related guidance documents
   - A sample tool illustrating the format for Highlights and Contents, and
   - The Selected Requirements for Prescribing Information (SRPI) − a checklist of 42 important format items from labeling regulations and guidances.

   Submit draft labeling that addresses our proposed revisions in the attached labeling.

   Prior to resubmitting the labeling, use the SRPI checklist to correct any formatting errors to ensure conformance with the format items in regulations and guidances. In addition, submit 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.

   To facilitate review of your submission, provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should include annotations that support any proposed changes.

CARTON AND CONTAINER LABELING

4. On July 9, 2014, you submitted draft carton and container labels for all three presentations containing the words "(b) (4)." Please submit revised labels for all presentations where these words are replaced with "For Topical Use in the Eye."

FACILITY INSPECTIONS

5. During a recent inspection of the Sun Pharmaceutical Industries, Ltd, Halol, India manufacturing facility for this application, our field investigators conveyed deficiencies to the representative of the facility. Satisfactory resolution of these deficiencies is required before this application may be approved.

PROPRIETARY NAME

Please refer to correspondence dated May 19, 2014, which addresses the proposed proprietary name, Xelpros. 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

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Sincerely,

{See appended electronic signature page}

Renata Albrecht, M.D.
Director
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Office of Antimicrobial products
Center for Drug Evaluation and Research

ENCLOSURES:
Labeling

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/s/

RENATA ALBRECHT
11/24/2014