

CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

216472Orig1s000

Trade Name: IYUZEH

Generic or Proper Name: (latanoprost ophthalmic solution) 0.005%

Sponsor: Thea Pharma Inc.

Approval Date: December 13, 2022

Indication: For the reduction of elevated intraocular pressure in patients with open-angle glaucoma or ocular hypertension.

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APPROVAL LETTER

NDA 216472

NDA APPROVAL

Thea Pharma Inc.
c/o The Brace Consulting Group
Attention: Jeremy Brace
President
420 Bedford St., Suite 150
Lexington, MA 02420

Dear Mr. Brace:

Please refer to your new drug application (NDA) dated and received February 18, 2022, and your amendments, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for IYUZEH (latanoprost ophthalmic solution) 0.005%. This NDA provides for the use of IYUZEH (latanoprost ophthalmic solution) 0.005% for the reduction of elevated intraocular pressure in patients with open-angle glaucoma or ocular hypertension.

APPROVAL & LABELING

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.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at FDA.gov.¹ Content of labeling must be identical to the enclosed labeling (text for the Prescribing Information, Patient Package Insert, Instructions for Use, and Medication Guide) as well as annual reportable changes not included in the enclosed labeling. Information on submitting SPL files using eLIST may be found in the guidance for industry *SPL Standard for Content of Labeling Technical Qs and As*.² The SPL will be accessible via publicly available labeling repositories.

CARTON AND CONTAINER LABELING

Submit final printed carton and container labeling that are identical to the enclosed carton and container labeling submitted on December 13, 2022, as soon as they are

¹ <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>

² We update guidances periodically. For the most recent version of a guidance, check the FDA Guidance Documents Database <https://www.fda.gov/RegulatoryInformation/Guidances/default.htm>.

available, but no more than 30 days after they are printed. Please submit these labeling electronically according to the guidance for industry *SPL Standard for Content of Labeling Technical Qs & As*. For administrative purposes, designate this submission “**Final Printed Carton and Container Labeling for approved NDA 216472.**” Approval of this submission by FDA is not required before the labeling is used.

DATING PERIOD

Based on the stability data submitted to date, the expiry dating period for IYUZEH (latanoprost ophthalmic solution) 0.005% shall be 24 months from the date of manufacture when stored at 15°C to 25°C (59°F to 77°F).

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients (which includes new salts and new fixed combinations), 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 in pediatric patients unless this requirement is waived, deferred, or inapplicable. Because none of these criteria apply to your application, this requirement is not applicable.

POSTMARKETING COMMITMENTS NOT SUBJECT TO THE REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitment:

- 4366-1 Conduct compatibility and extractables studies to characterize potential process impurities in the bulk solution that are derived from manufacturing equipment (b) (4). The compatibility study should present physicochemical test results derived from equipment exposure to the bulk solution under actual or simulated process conditions at equal or longer processing time. The extractables study should expose the manufacturing equipment under the worst-case scenario of manufacturing conditions (temperature, time of exposure, etc.), using appropriate simulated solvents to establish qualitative or semi-quantitative extractable profiles (volatiles, semi-volatiles, and non-volatiles) with screening analytical methods for which limit of detection (DL) and limit of quantitation (QL) are determined on internal standards based on the risk level evaluated for each compound in the risk assessment as recommended in USP <665>. Evaluate the potential extractables with the (b) (4) ppm qualification threshold (QT) based on concentration (ppm) for the ophthalmic product. For extractables above the QT, conduct toxicological assessment to demonstrate that the observed extractables are not present above safety concern levels in the bulk solution or final drug product. A plan for quantitative leachable studies to be provided based on the outcome of the extractable studies and any toxicological assessments.

The timetable you submitted on 11/15/2022, states that you will conduct this study according to the following schedule:

Final Report Submission: 08/23

Submit nonclinical and chemistry, manufacturing, and controls protocols and all postmarketing final reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii) you should include a status summary of each commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report. All submissions, including supplements, relating to these postmarketing commitments should be prominently labeled “**Postmarketing Commitment Protocol**,” “**Postmarketing Commitment Final Report**,” or “**Postmarketing Commitment Correspondence**.”

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. For information about submitting promotional materials, see the final guidance for industry *Providing Regulatory Submissions in Electronic and Non-Electronic Format—Promotional Labeling and Advertising Materials for Human Prescription Drugs*.³ As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the Prescribing Information, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. Form FDA 2253 is available at FDA.gov.⁴ Information and Instructions for completing the form can be found at FDA.gov.⁵

METHODS VALIDATION

We have not completed validation of the regulatory methods. However, we expect your continued cooperation to resolve any problems that may be identified.

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

Your product is a Part 3 combination product (21 CFR 3.2(e)); therefore, you must also comply with postmarketing safety reporting requirements for an approved combination product (21 CFR 4, Subpart B). Additional information on combination product postmarketing safety reporting is available at FDA.gov.⁶

³ For the most recent version of a guidance, check the FDA guidance web page at <https://www.fda.gov/media/128163/download>.

⁴ <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf>

⁵ <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf>

⁶ <https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products>

If you have any questions, call Lois Almoza, MS, Senior Regulatory Health Project Manager, at (240) 402-5146.

Sincerely,

{See appended electronic signature page}

Wiley A. Chambers, MD
Director
Division of Ophthalmology
Office of Specialty Medicine
Center for Drug Evaluation and Research

ENCLOSURES:

- Content of Labeling
 - o Prescribing Information
 - o Patient Package Insert
 - o Instructions for Use
- Carton and Container Labeling

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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