CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

214133Orig1s000

Trade Name:	Recorlev tablets
Generic or Proper Name:	levoketoconazole
Sponsor:	Strongbridge Biopharma plc
Approval Date:	December 30, 2021
Indication:	For the treatment of endogenous hypercortisolemia in adult patients with Cushing's syndrome for whom surgery is not an option or has not been curative.

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APPLICATION NUMBER:

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APPROVAL LETTER

NDA 214133

NDA APPROVAL

Strongbridge Biopharma plc
US Agent for Strongbridge Dublin Limited
Attention: Susan Thornton
Vice President Global Regulatory Affairs and Quality
900 Northbrook Drive, Suite 200
Trevose, PA 19053 USA

Dear Ms. Thornton:

Please refer to your new drug application (NDA) dated and received March 1, 2021, and your amendments, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Recorlev (levoketoconazole) tablets.

This NDA provides for the use of Recorlev (levoketoconazole) tablets for the treatment of endogenous hypercortisolemia in adult patients with Cushing's syndrome for whom surgery is not an option or has not been curative.

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.

WAIVER OF ½ PAGE LENGTH REQUIREMENT FOR HIGHLIGHTS

We are waiving the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of Prescribing Information. This waiver applies to all future supplements containing revised labeling unless we notify you otherwise.

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 and Medication Guide) as well as annual reportable changes not included in the enclosed labeling. Information on submitting SPL files using eLIST

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

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.

CONTAINER LABELING

Submit final printed container labeling that is identical to the enclosed container labeling as soon as it is available, but no more than 30 days after it is printed. Please submit this labeling electronically according to the guidance for industry *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications*. For administrative purposes, designate this submission "**Final Printed Container Labeling for approved NDA 214133**." 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 Recorlev (levoketoconazole) tablets shall be 60 months from the date of manufacture when stored at 20°C -25°C.

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 this drug product for this indication has an orphan drug designation, you are exempt from this requirement.

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]

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

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]

REPORTING REQUIREMENTS

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

We also remind you of your agreement to conduct enhanced pharmacovigilance for all cases of hepatotoxicity reported with Recorlev (levoketoconazole) tablets, for a period of 5 years from the date of this letter. Submit all cases of hepatotoxicity as 15-day Alert reports (as described under 21 CFR 314.80(c)(1)), and provide detailed analyses of events of hepatotoxicity reported from clinical studies and post-marketing reports in your periodic safety report (i.e., the Periodic Adverse Drug Experience Report [PADER] required under 21 CFR 314.80(c)(2) or the ICH E2C Periodic Benefit-Risk Evaluation Report [PBRER] format). These analyses should show cumulative data relative to the date of approval of Recorlev (levoketoconazole) tablets as well as relative to prior periodic safety reports. Medical literature reviews for case reports/case series of hepatotoxicity reported with Recorlev (levoketoconazole) tablets should also be provided in the periodic safety report.

If you have any questions, call Dana Smith, Regulatory Project Manager, at 240-402-9906.

Sincerely,

{See appended electronic signature page}

Naomi Lowy, MD
Deputy Director
Division of General Endocrinology
Office of Cardiology, Hematology, Endocrinology, and Nephrology
Office of New Drugs
Center for Drug Evaluation and Research

[4] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf
[5] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf

ENCLOSURES:

- Content of Labeling
    - Prescribing Information
    - Medication Guide
- Container Labeling

U.S. Food and Drug Administration
Silver Spring, MD 20993
www.fda.gov

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/

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