

CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

213072Orig1s000

Trade Name: ROSZET, tablets, for oral use

Generic or Proper Name: rosuvastatin and ezetimibe

Sponsor: Althera Life Sciences, LLC

Approval Date: March 23, 2021

Indication:

- As an adjunct to diet in patients with primary non-familial hyperlipidemia to reduce low-density lipoprotein cholesterol (LDL-C).
- Alone or as an adjunct to other LDL-C-lowering therapies in patients with homozygous familial hypercholesterolemia (HoFH) to reduce LDL-C.

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APPROVAL LETTER



NDA 213072

NDA APPROVAL

Althera Life Sciences, LLC.
Attention: James Medley
Senior Advisor, Regulatory Affairs
89 Headquarters Plaza, Ste 1448
Morristown, NJ 07960

Dear Mr. Medley:

Please refer to your new drug application (NDA) dated and received July 29, 2019, and your amendments, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Roszet (rosuvastatin and ezetimibe) tablets.

We acknowledge receipt of your amendment dated September 23, 2020, which constituted a complete response to our May 26, 2020, action letter.

This new drug application provides for the use of Roszet (rosuvastatin and ezetimibe) tablets for adults:

- As an adjunct to diet in patients with primary non-familial hyperlipidemia to reduce low-density lipoprotein cholesterol (LDL-C).
- Alone or as an adjunct to other LDL-C-lowering therapies in patients with homozygous familial hypercholesterolemia (HoFH) to reduce LDL-C.

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 Patient Package Insert) 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.

CONTAINER LABELING

Submit final printed container labeling that are identical to the enclosed container labeling as soon as they are available, but no more than 30 days after they are printed. Please submit these 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 213072.**” 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 Roszet (rosuvastatin and ezetimibe) tablets shall be 24 months from the date of manufacture when stored at 20 °C to 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.

We are waiving the pediatric study requirement for primary non-familial hyperlipidemia for this application because necessary studies are impossible or highly impracticable. This is because extreme cholesterol elevations requiring pharmacologic intervention are uncommon in children, except among patients with familial hypercholesterolemia (HeFH or HoFH). First-line treatment (diet modification) sufficiently reduces LDL-C in most pediatric patients with non-familial hyperlipidemia.

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>.

We are waiving the pediatric study requirement for HoFH for ages 0 to 2 years because necessary studies are impossible or highly impracticable. This is because HoFH is an extremely rare genetic disease (1 in 1,000,000 individuals), and there is no consensus in clinical practice guidelines regarding the initiation of pharmacologic intervention in children under 2 years of age. The number of pediatric patients under 2 years of age who would require pharmacologic treatment is exceedingly small.

We are deferring submission of your pediatric study for ages 2 to 17 years for this application because this product is ready for approval for use in adults and the pediatric study has not been completed.

Your deferred pediatric study required by section 505B(a) of the FDCA is a required postmarketing study. The status of this postmarketing study must be reported annually according to 21 CFR 314.81 and section 505B(a)(4)(C) of the FDCA. This required study is listed below.

- 4041-1 Conduct a study to collect efficacy and safety data pertaining to the use of ezetimibe with rosuvastatin in pediatric patients with homozygous familial hypercholesterolemia aged 2 to 17 years. Collect pharmacokinetic data as part of this study in pediatric patients younger than 8 years of age.

Draft Protocol Submission:	December 2021
Final Protocol Submission:	June 2022
Study Completion:	March 2023
Final Report Submission:	June 2023

FDA considers the term *final* to mean that the applicant has submitted a protocol, the FDA review team has sent comments to the applicant, and the protocol has been revised as needed to meet the goal of the study or clinical trial.³

Submit the protocols to your IND 136378, with a cross-reference letter to this NDA. Reports of this required pediatric postmarketing study must be submitted as a NDA or as a supplement to your approved NDA with the proposed labeling changes you believe are warranted based on the data derived from this study. When submitting the reports, please clearly mark your submission "**SUBMISSION OF REQUIRED PEDIATRIC ASSESSMENTS**" in large font, bolded type at the beginning of the cover letter of the submission.

³ See the guidance for Industry *Postmarketing Studies and Clinical Trials—Implementation of Section 505(o)(3) of the Federal Food, Drug, and Cosmetic Act (October 2019)*.
<https://www.fda.gov/RegulatoryInformation/Guidances/default.htm>.

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*.⁴

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.⁵ Information and Instructions for completing the form can be found at FDA.gov.⁶

REPORTING REQUIREMENTS

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

If you have any questions, call Martin White, Regulatory Project Manager, at 240-402-6018.

Sincerely,

{See appended electronic signature page}

John Sharretts, M.D.
Deputy Director
Division of Diabetes, Lipid Disorders, and Obesity
Office of Cardiology, Hematology, Endocrinology,
and Nephrology
Center for Drug Evaluation and Research

ENCLOSURES:

- Content of Labeling
 - Prescribing Information
 - Patient Package Insert
- Container Labeling

⁴ For the most recent version of a guidance, check the FDA guidance web page at <https://www.fda.gov/media/128163/download>.

⁵ <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf>

⁶ <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf>

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/

JOHN M SHARRETTS
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