NDA 208647/S-006
NDA 208647/S-007
NDA 208647/S-008
NDA 208647/S-009
NDA 208647/S-010
NDA 208647/S-011

SUPPLEMENT APPROVAL
FULFILLMENT OF POSTMARKETING REQUIREMENT

Sun Pharmaceutical Industries Limited
C/O Sun Pharmaceutical Industries, Inc.
Attention: Juan Grijalva
Senior Manager, US Agent
2 Independence Way
Princeton, NJ 08540

Dear Juan Grijalva:

Please refer to your supplemental new drug applications (sNDAs) and your amendments, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Ezallor Sprinkle (rosuvastatin) capsules.

Supplement 006

This Prior Approval sNDA, dated and received September 28, 2021, provides for the following updates to the Ezallor Sprinkle Prescribing Information as requested in our July 30, 2021, Prior Approval Supplement Request letter:

- Revisions to Section 4 – *Contraindications* to remove contraindications for use during Pregnancy and Lactation;
- Updates to Section 6.2 regarding drug reaction with eosinophilia and systemic symptoms (DRESS), lichenoid drug reaction, and myasthenia gravis;
- Associated revisions to Section 8 – *Use in Special Populations;*
- Revisions to Section 17 – *Patient Counseling Information;*
- Drug-Drug interactions involving rosuvastatin with the concomitant use of enasidenib and tafamidis; and
- Extensive edits made throughout the Prescribing Information to update, modernize with current labeling guidances and to align with the listed drug.

Supplement 007

This Prior Approval sNDA, dated and received January 2, 2023, provides for the addition of the following indication to Section 1 – *Indication and Usage* of the Ezallor

Sprinkle Prescribing Information: *As an adjunct to other LDL-C-lowering therapies, or alone if such treatments are unavailable, to reduce LDL-C in adults and pediatric patients aged 7 years and older with homozygous familial hypercholesterolemia (HoFH)*. This supplement was submitted to address the following Postmarketing Requirement that was established under the Pediatric Research Equity Act in the December 18, 2018, approval letter.

3559-1 Assessment of Ezallor (rosuvastatin) capsules for the treatment of homozygous familial hypercholesterolemia in pediatric patients ages 7 to 17 years of age (inclusive).

Supplement 008

This Prior Approval sNDA, dated and received April 13, 2023, provides for the addition of the following indication to Section 1 – *Indication and Usage* of the Ezallor Sprinkle Prescribing Information: *To reduce the risk of stroke, myocardial infarction, and arterial revascularization procedures in adults without established coronary heart disease who are at increased risk of cardiovascular (CV) disease based on age, hsCRP ≥2 mg/L, and at least one additional CV risk factor*.

Supplement 009

This Prior Approval sNDA, dated and received April 13, 2023, provides for the addition of the following indication to Section 1 – *Indication and Usage* of the Ezallor Sprinkle Prescribing Information: *As an adjunct to diet to reduce LDL-C in adults with primary hyperlipidemia*.

Supplement 010

This Prior Approval sNDA, dated and received April 13, 2023, provides for the addition of the following indication to Section 1 – *Indication and Usage* of the Ezallor Sprinkle Prescribing Information: *As an adjunct to diet to reduce low-density lipoprotein cholesterol (LDL-C) and slow the progression of atherosclerosis in adults*.

Supplement 011

This Prior Approval sNDA, dated and received April 13, 2023, provides for the addition of the following indication to Section 1 – *Indication and Usage* of the Ezallor Sprinkle Prescribing Information: *As an adjunct to diet to reduce LDL-C in adults and pediatric*

patients aged 8 years and older with heterozygous familial hypercholesterolemia (HeFH).

APPROVAL & LABELING

We have completed our review of these applications, as amended. They are approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling with minor editorial revisions listed below and reflected in the enclosed labeling.

- Revision month date updated in the Prescribing Information, Patient Package Insert, and Instructions for Use to reflect supplement approval.

WAIVER OF ½ PAGE LENGTH REQUIREMENT FOR HIGHLIGHTS

Please note that we have previously granted a waiver of the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of Prescribing Information.

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, and Instructions for Use), with the addition of any labeling changes in pending "Changes Being Effected" (CBE) supplements, 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 from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that include labeling changes for this NDA, including CBE supplements for which FDA has not yet issued an

[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.

action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in Microsoft Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes. To facilitate review of your submission(s), provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

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 note that you have fulfilled the pediatric study requirement for ages 7 to less than 18 years for this application.

FULFILLMENT OF POSTMARKETING REQUIREMENT

Supplement 007 addressed the following postmarketing requirement listed in the December 18, 2018, approval letter:

3559-1	Assessment of Ezallor (rosuvastatin) capsules for the treatment of homozygous familial hypercholesterolemia in pediatric patients ages 7 to 17 years of age (inclusive).

We have reviewed your submission and conclude that the above requirement was fulfilled.

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]

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

You must submit final promotional materials and Prescribing Information, accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 314.81(b)(3)(i)]. Form FDA 2253 is available at FDA.gov.[4] Information and Instructions for completing the form can be found at FDA.gov.[5]

PATENT LISTING REQUIREMENTS

Pursuant to 21 CFR 314.53(d)(2) and 314.70(f), certain changes to an approved NDA submitted in a supplement require you to submit patent information for listing in the Orange Book upon approval of the supplement. You must submit the patent information required by 21 CFR 314.53(d)(2)(i)(A) through (C) and 314.53(d)(2)(ii)(A) and (C), as applicable, to FDA on Form FDA 3542 within 30 days after the date of approval of the supplement for the patent information to be timely filed (see 21 CFR 314.53(c)(2)(ii)). You also must ensure that any changes to your approved NDA that require the submission of a request to remove patent information from the Orange Book are submitted to FDA at the time of approval of the supplement pursuant to 21 CFR 314.53(d)(2)(ii)(B) and 314.53(f)(2)(iv).

REPORTING REQUIREMENTS

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

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

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

Sincerely,

{See appended electronic signature page}

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

ENCLOSURES:

- Content of Labeling
  - Prescribing Information
  - Patient Package Insert
  - Instructions for Use

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
08/04/2023 12:25:48 PM