

NDA 203858/S-027

SUPPLEMENT APPROVAL

Chiesi Farmaceutici S.p.A
C/O: Chiesi USA, Inc.
Attention: Veronica Backlund
Regulatory Affairs Lead, Americas, Associate Director, Global Rare Disease
175 Regency Woods Place, Suite 600
Cary, NC 27518

Dear Veronica Backlund:

Please refer to your supplemental new drug application (sNDA) dated and received May 30, 2025, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Juxtapid (lomitapide) capsules.

We acknowledge receipt of your risk evaluation and mitigation strategy (REMS) assessment dated May 30, 2025.

This Prior Approval sNDA provides for the following Juxtapid labeling changes and proposed modifications to the approved Juxtapid REMS:

1. Modifications to the Prescribing Information (PI) to add results of trial APH-19, titled, *A Phase 3, Single-arm, Open-label, International, Multi-center Study to Evaluate the Efficacy and Safety of Lomitapide in Pediatric Patients with Homozygous Familial Hypercholesterolemia on Stable Lipid-lowering Therapy*, and expand the currently approved indication to include pediatric patients 2 years and older with homozygous familial hypercholesterolemia
2. Add a 2 mg strength capsule for use in the pediatric population
3. Revised Section 2, *Dosage and Administration*, of the PI to include additional administration options and recommendations
4. Additional edits made throughout the PI to modernize with current labeling guidances, clarify language, and improve readability and organization of information
5. Revisions to the Medication Guide (MG) to reflect corresponding changes in the PI
6. REMS modified to align with proposed labeling changes to add pediatric population

7. New carton and container labeling for the new 2 mg strength capsule.

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 PI and MG), 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 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).

We request that the labeling approved today be available on your website within 10 days of receipt of this letter.

CARTON AND CONTAINER LABELING

Submit final printed carton and container labeling that are identical to the enclosed carton and container labeling and carton and container labeling submitted on February 13, 2026, 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

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>.

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 Carton and Container Labeling for approved NDA 203858/S-027.**” Approval of this submission by FDA is not required before the labeling is used.

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.

RISK EVALUATION AND MITIGATION STRATEGY (REMS) REQUIREMENTS

The REMS for Juxtapid was originally approved on December 21, 2012, and the most recent REMS modification was approved on June 16, 2022. The REMS consists of elements to assure safe use, an implementation system, and a timetable for submission of assessments of the REMS.

Your proposed modifications to the REMS consist of modifications to the REMS Document and REMS materials to reflect expansion of the currently approved indication to include pediatric patients 2 years and older with homozygous familial hypercholesterolemia. In addition, your proposed modifications include addition of new materials: a *Pediatric Patient Guide* and *Pediatric Patient-Prescriber Acknowledgement Form* specifically intended for pediatric patients and a *Healthcare Provider REMS Letter* to inform healthcare providers about Juxtapid use in the pediatric indication.

Additionally, the following changes were made to one or more REMS documents, as appropriate:

1. Add reference to pediatric patients and clarify where reference is to adult patients
2. Add or differentiate the availability of the adult and pediatric *Patient Guides* and adult and pediatric *Patient-Prescriber Acknowledgment Forms*

Your proposed modified REMS, submitted on May 30, 2025, amended and appended to this letter, is approved.

The timetable for submission of assessments of the REMS remains the same as that approved on February 1, 2022.

The revised REMS assessment plan must include, but is not limited to, the following:

Program Implementation and Operations (Per Reporting Period and Cumulatively)

1. REMS Enrollment Statistics

a. Healthcare Providers Certification:

- i. The number of newly certified healthcare providers and the number of active healthcare providers (having prescribed at least once during the reporting period) in the Juxtapid REMS stratified by healthcare provider credentials (e.g., Doctor of Medicine, Doctor of Osteopathic Medicine, Nurse Practitioner, Physician Assistant) and specialty (cardiology, endocrinology, internal medicine, other and include a full breakdown of prescribing specialties contained in the “other” category), and practice type (e.g., individual practice, group practice, hospital, university (academic) center), and geographic region (as defined by (U.S. Census)
- ii. Method of certification (i.e., through fax or email)

b. Pharmacy Enrollment:

- i. The number of pharmacies that were newly certified and the number of pharmacies that were active (dispensed Juxtapid at least once during the reporting period) in the REMS program, stratified by geographic region (as defined by U.S. Census.)
- ii. Method of certification (e.g., through fax or email)

c. Wholesaler/Distributor Authorization:

- i. The number of wholesalers/distributors that were newly authorized in the REMS program and the number that were active (shipped Juxtapid at least once during the reporting period).

2. REMS Compliance

a. Provide a summary of non-compliance identified, including but not limited to:

- i. Provide a copy of the non-compliance plan used during that reporting period, including the criteria for non-compliance for each stakeholder,

actions taken to address non-compliance for each case, and which events lead to de-certification from the REMS

- ii. Detailed description of root cause of noncompliance with REMS-required dispensing and any corrective and/or preventive actions taken to address noncompliance during the reporting period and cumulatively
- iii. Provide a copy of the audit plan for each stakeholder (i.e., REMS Call Center, certified pharmacies, wholesalers/distributors, or other entities) including any auditing surveys or protocols used
- iv. Report of audit finding for each stakeholder
 1. The number of audits expected and the number of audits conducted
 2. The number and types of deficiencies noted for each group of audited stakeholders
 3. For those with deficiencies noted, report the number that successfully completed a corrective and preventive action (CAPA) within one month of audit
 4. Include a unique ID for each stakeholder that had deviations to track deviations by stakeholder over time

b. Healthcare Providers

- i. Number of healthcare providers that had their certification revoked during the reporting period and cumulatively and the reason for the revocation
- ii. Information on the number of prescribers who have submitted an altered Prescription Authorization Form (and what alterations were made)

c. Pharmacies

- i. Number of pharmacies that had their certification revoked during the reporting period and cumulatively and the reason for the revocation
- ii. The number of instances certified pharmacies dispensed Juxtapid using a prescription that was not accompanied by a Patient-Prescriber Acknowledgement Form

- iii. Number of instances certified pharmacies dispensed Juxtapid in response to a prescription received on an altered Prescription Authorization Form
 - iv. The number of new prescriptions received, and the number that were not accompanied by the Prescription Authorization Form
- d. Wholesaler/Distributors
- i. Number of wholesalers/distributors that had their authorization revoked during the reporting period and cumulatively and the reason for the revocation
 - ii. Number of Juxtapid orders shipped to non-certified pharmacies
3. REMS Call Center
- a. Summary of issues and complaints received by REMS Call Center; summary of resolution of the issues and complaints
 - b. Summary of the reasons (and numbers per reason) for calls into the REMS Call Center
4. Juxtapid Utilization Data
- a. The number of prescriptions dispensed for Juxtapid, including quantity of capsules (mean, minimum, maximum) and dosage strength overall and subset by compliance with the REMS requirements (e.g., received from Juxtapid certified vs. non-certified healthcare providers, number of initial prescriptions dispensed without a signed agreement on the Prescription Authorization Form). Dispensing details are to be obtained from the pharmacies.
 - b. Volume of prescriptions for each prescriber stratified by specialty, including a full breakdown of prescribing specialties contained in the “other” category.
 - c. Specialties of the “high volume” prescribers, i.e., those who write more than 4 prescriptions in an assessment period and cumulatively, including a full breakdown of prescribing specialties contained in the “other” category.
 - d. The number of Juxtapid orders shipped to pharmacies, including number of bottles, bottle size, and dosage strength.
 - e. The number and demographics (e.g., including gender, age, geographic location) of unique patients who received Juxtapid during the reporting period

- and annually. The number is to be calculated by reconciling orders dispensed to unique patients.
- f. Number of unique patients (e.g., including age, gender, and geographic location) who received their first/initial prescription during the period. The number is to be calculated by reconciling orders dispensed to unique patients.
 - g. Duration of therapy for patients (mean, median, range).
 - h. Number of unique patients (e.g., including age, gender, and geographic location) who discontinued Juxtapid therapy during the period, i.e., received no prescription dispenses for greater than 90 days. The number is to be calculated by reconciling orders dispensed to unique patients.
 - i. The number of prescriptions pending and canceled, as well as the reason for prescriptions pending and canceled.
 - j. Specific criterion used to classify a prescription as canceled.
 - k. Report of number, length, and reasons for shipment delays to patients and whether or not these reasons were related to the REMS, and any additional information from insurance payers as to what they are stating as the reason for delay/non-payment.
 - l. Percentage of fill delays that involve new prescriptions versus refills.

Knowledge (per reporting period and cumulatively)

- 5. Knowledge Surveys of Prescribers to assess understanding of:
 - a. The approved indication of Juxtapid
 - b. The risk of hepatotoxicity associated with Juxtapid use
 - c. The need to monitor patients during treatment with Juxtapid as per product labeling
- 6. Knowledge Surveys of patients to assess understanding of:
 - a. The risk of hepatotoxicity
 - b. The need for baseline and periodic monitoring

7. Specification of measures that would be taken to increase awareness if prescriber surveys indicate that prescriber awareness of the risks associated to Juxtapid is not adequate

Safe Use Conditions (per reporting period and cumulatively)

8. Prescription Authorization Form (PAF)
 - a. Number of patients with completed PAFs who have not received a dispensed prescription for Juxtapid
 - b. Time between receipt of PAF and prescription dispensing and analysis and summary of reasons for delays
 - c. Proportion of dispensed prescriptions associated with updated Adult and Pediatric PPAFs after modification of May 2025 (PAS-027, amended January 2026)

Health Outcomes and/or Surrogates of Health Outcomes (per reporting period and cumulatively)

9. With regard to the risk of hepatotoxicity associated with Juxtapid, provide an analysis of the post-marketing cases of specific hepatic adverse events reported in association with Juxtapid to Chiesi, including outcome.

Overall Assessment of REMS Effectiveness

10. The requirements for assessments of an approved REMS under section 505-1(g)(3) include with respect to each goal included in the strategy, an assessment of the extent to which the approved strategy, including each element of the strategy, is meeting the goal or whether one or more such goals or such elements should be modified.

We remind you that in addition to the REMS assessments submitted according to the timetable in the approved REMS, you must include an adequate rationale to support a proposed REMS modification for the addition, modification, or removal of any goal or element of the REMS, as described in section 505-1(g)(4) of the FDCA.

We also remind you that you must submit a REMS assessment when you submit a supplemental application for a new indication for use, as described in section 505-1(g)(2)(A) of the FDCA. This assessment should include:

- a) An evaluation of how the benefit-risk profile will or will not change with the new indication;

- b) A determination of the implications of a change in the benefit-risk profile for the current REMS;
- c) *If the new indication for use introduces unexpected risks:* A description of those risks and an evaluation of whether those risks can be appropriately managed with the currently approved REMS.
- d) *If a REMS assessment was submitted in the 18 months prior to submission of the supplemental application for a new indication for use:* A statement about whether the REMS was meeting its goals at the time of that last assessment and if any modifications of the REMS have been proposed since that assessment.
- e) *If a REMS assessment has not been submitted in the 18 months prior to submission of the supplemental application for a new indication for use:* Provision of as many of the currently listed assessment plan items as is feasible.
- f) *If you propose a REMS modification based on a change in the benefit-risk profile or because of the new indication of use, submit an adequate rationale to support the modification, including:* Provision of the reason(s) why the proposed REMS modification is necessary, the potential effect on the serious risk(s) for which the REMS was required, on patient access to the drug, and/or on the burden on the health care delivery system; and other appropriate evidence or data to support the proposed change. Additionally, include any changes to the assessment plan necessary to assess the proposed modified REMS. *If you are not proposing REMS modifications,* provide a rationale for why the REMS does not need to be modified.

If the assessment instruments and methodology for your REMS assessments are not included in the REMS supporting document, or if you propose changes to the submitted assessment instruments or methodology, you should update the REMS supporting document to include specific assessment instrument and methodology information at least 90 days before the assessments will be conducted. Updates to the REMS supporting document may be included in a new document that references previous REMS supporting document submission(s) for unchanged portions. Alternatively, updates may be made by modifying the complete previous REMS supporting document, with all changes marked and highlighted.

Prominently identify the submission containing the assessment instruments and methodology with the following wording in bold capital letters at the top of the first page of the submission:

NDA 203858 REMS ASSESSMENT METHODOLOGY

(insert concise description of content in bold capital letters, e.g.,

ASSESSMENT METHODOLOGY, PROTOCOL, SURVEY METHODOLOGIES, AUDIT PLAN, DRUG USE STUDY)

An authorized generic drug under this NDA must have an approved REMS prior to marketing. Should you decide to market, sell, or distribute an authorized generic drug under this NDA, contact us to discuss what will be required in the authorized generic drug REMS submission.

We remind you that section 505-1(f)(8) of FDCA prohibits holders of an approved covered application with elements to assure safe use from using any element to block or delay approval of an application under section 505(b)(2) or (j). A violation of this provision in 505-1(f) could result in enforcement action.

Prominently identify any submission containing the REMS assessments or proposed modifications of the REMS with the following wording in bold capital letters at the top of the first page of the submission as appropriate:

NDA 203858 REMS ASSESSMENT

or

**NEW SUPPLEMENT FOR NDA 203858/S-000
CHANGES BEING EFFECTED IN 30 DAYS
PROPOSED MINOR REMS MODIFICATION**

or

**NEW SUPPLEMENT FOR NDA 203858/S-000
PRIOR APPROVAL SUPPLEMENT
PROPOSED MAJOR REMS MODIFICATION**

or

**NEW SUPPLEMENT FOR NDA 203858/S-000
PRIOR APPROVAL SUPPLEMENT
PROPOSED REMS MODIFICATIONS DUE TO SAFETY LABELING
CHANGES SUBMITTED IN SUPPLEMENT XXX**

or

**NEW SUPPLEMENT (NEW INDICATION FOR USE)
FOR NDA 203858/S-000
REMS ASSESSMENT
PROPOSED REMS MODIFICATION (if included)**

Should you choose to submit a REMS revision, prominently identify the submission containing the REMS revisions with the following wording in bold capital letters at the top of the first page of the submission:

REMS REVISIONS FOR NDA 203858

To facilitate review of your submission, we request that you submit your proposed modified REMS and other REMS-related materials in Microsoft Word and PDF format. If certain documents, such as enrollment forms, or website screenshots are only in PDF format, they may be submitted as such, but Word and PDF format are preferred.

SUBMISSION OF REMS DOCUMENT IN SPL FORMAT

As soon as possible, but no later than 14 days from the date of this letter, submit the REMS document in Structured Product Labeling (SPL) format using the FDA automated drug registration and listing system (eLIST). Content of the REMS document must be identical to the approved REMS document. The SPL will be publicly available.

Information on submitting REMS in SPL format may be found in the guidance for industry *Providing Regulatory Submission in Electronic Format – Content of the Risk Evaluation and Mitigation Strategies Document Using Structured Product Labeling*.

For more information on submitting REMS in SPL format, please email FDAREMSwebsite@fda.hhs.gov.

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

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

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>

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).

If you have any questions, contact Christine Wright, Regulatory Project Manager, at Anne.Wright@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

John Sharretts, MD
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
 - Juxtapid Prescribing Information
 - Juxtapid Medication Guide
- Juxtapid Carton and Container Labeling
- Juxtapid REMS Document
- Juxtapid REMS Materials:
 - Prescriber Enrollment Form
 - Pediatric Patient Guide
 - Pediatric Patient-Prescriber Acknowledgement Form
 - Adult Patient Guide
 - Adult Patient-Prescriber Acknowledgement Form
 - Pharmacy Enrollment Form
 - Prescriber Training Module and Knowledge Assessment
 - Fact Sheet
 - Pharmacy Training Module and Knowledge Assessment
 - Prescription Authorization Form
 - Healthcare Provider REMS Letter
 - Website Screenshots

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
02/25/2026 03:21:34 PM