BLA 125559/S-039

SUPPLEMENT APPROVAL

Regeneron Pharmaceuticals, Inc
Attention: Kaileen Musum, PharmD, MHS
Manager, Regulatory Affairs
777 Old Saw Mill River Road, 3rd Floor
Tarrytown, NY 10591-6707

Dear Dr. Musum:

Please refer to your supplemental biologics license application (sBLA), dated and received May 10, 2023, and your amendments, submitted under section 351(a) of the Public Health Service Act for Praluent (alirocumab) injection.

This Prior Approval sBLA provides for addition of the following indication to the Prescribing Information (PI) and changes to the Patient Package Insert (PPI) and Instructions for Use (IFU).

- As an adjunct to diet and other LDL-C-lowering therapies in pediatric patients aged 8 years and older with HeFH to reduce LDL-C

These changes are based on the results of trials DFI14223, titled, *An 8-Week Open-Label, Sequential, Repeated Dose-Finding Study to Evaluate the Efficacy and Safety of Alirocumab in Children and Adolescents with Heterozygous Familial Hypercholesterolemia Followed by an Extension Phase* and EFC14643, titled, *A randomized, double-blind, placebo-controlled study followed by an open label treatment period to evaluate the efficacy and safety of alirocumab in children and adolescents with heterozygous familial hypercholesterolemia,* which were conducted to address the following postmarketing requirement (PMR) listed in the July 24, 2015, approval letter:

2927-1 Conduct a dose-finding study (Phase 2) and an efficacy and safety study (Phase 3) evaluating alirocumab in patients with heterozygous familial hypercholesterolemia (HeFH) ages 10 years to less than 18 years. If children younger than age 10 are included, the eligibility criteria should ensure that other available interventions to lower LDL -C have been insufficient. Phase 2 will be a randomized, open-label, 8-week, ascending repeated dose finding study of alirocumab with an optional open-label extension study in patients 10 years to less than 18 years of age with HeFH on stable lipid modifying therapy with LDL-C > or equal to 130 mg/dL. Phase 3 will be a randomized, 6-month, double-blind, placebo-controlled, parallel-group, multicenter efficacy and safety study followed by an 18-month open-label extension in patients 10 years to less than 18

years with HeFH on stable lipid-modifying therapy with LDL-C > or equal to 130 mg/dL. Patients treated in Phase 2, the dose-finding study, will be offered enrollment in Phase 3, the efficacy and safety study.

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 HIGHLIGHTS 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, via the FDA automated drug registration and listing system (eLIST), the content of labeling [21 CFR 601.14(b)] in structured product labeling (SPL) format, as described at FDA.gov,[1] that is identical to the enclosed labeling (text for the PI, PPI, and IFU) and include the labeling changes proposed in any pending "Changes Being Effected" (CBE) supplements.

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.

Also within 14 days, amend all pending supplemental applications that include labeling changes for this BLA, including pending "Changes Being Effected" (CBE) supplements, for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 601.12(f)] 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).

[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.

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(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

With this supplement approval, we note that you have fulfilled the pediatric study requirement for ages 10 years to less than 18 years for this application.

FULFILLMENT OF POSTMARKETING REQUIREMENT

This sNDA contained the final report for PMR 2927-1, cited above. We have reviewed the submission and conclude that the above requirement has been fulfilled.

We remind you that there is a postmarketing requirement listed in the September 3, 2020, postapproval postmarketing requirement letter and postmarketing commitments that are still open.

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 601.12(f)(4), 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 BLA (in 21 CFR 600.80 and in 21 CFR 600.81).

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

[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

product (21 CFR 4, Subpart B). Additional information on combination product postmarketing safety reporting is available at FDA.gov.

If you have any questions, call Ron Picking, Regulatory Project Manager, at 240-402-3211.

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
03/08/2024 05:16:02 PM