DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

BLA 125522/S-013, S-014

SUPPLEMENT APPROVAL
FULFILLMENT OF POSTMARKETING REQUIREMENTS

Amgen, Inc.
Attention: Adam Rupert
Senior Manager, Regulatory Affairs
One Amgen Center Drive, Mail Stop 17-2-B
Thousand Oaks, CA 91320-1799

Dear Mr. Rupert:

Please refer to your Supplemental Biologics License Applications (sBLAs), dated and received June 2, 2017, and your amendments, submitted under section 351(a) of the Public Health Service Act for Repatha (evolocumab) injection.

Supplement -013 proposes to add a new indication to reduce the risk of myocardial infarction, stroke, and coronary revascularization in adults with established cardiovascular disease.

Supplement -014 proposes to broaden the lipid-lowering indication based on previously reviewed clinical studies and the cardiovascular outcomes trial. The supplement also proposes to revise section 12.3 of the package insert to include information on use in patients with severe renal impairment or patients with ESRD receiving hemodialysis.

APPROVAL & LABELING

We have completed our review of this supplemental application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed, agreed-upon labeling text.

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 http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm, that is identical to the enclosed labeling (text for the prescribing information, text for the patient labeling) 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 titled "SPL Standard for Content of Labeling Technical Qs and As" at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

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 MS Word format that includes the changes approved in this supplemental application.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, 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.

For Supplement -013, we are waiving the pediatric study requirement for this application because necessary studies are impossible or highly impracticable.

For Supplement -014, because none of these criteria apply to this application, you are exempt from this requirement.

FULFILLMENT OF POSTMARKETING REQUIREMENTS

Supplement -013 contained the final reports for the following postmarketing requirements listed in the August 27, 2015, approval letter for BLA 125522.

2946-3	Conduct a large, randomized, controlled, long-term trial in which the incidence and severity of new-onset diabetes mellitus, injection site reactions, hypersensitivity, immunogenicity, and adverse events potentially related to demyelination with Repatha (evolocumab) will be evaluated.
2946-4	Conduct a randomized, controlled, long-term trial that prospectively evaluates changes in neurocognitive function with Repatha (evolocumab) treatment. The trial must be adequately powered to exclude a clinically meaningful adverse effect.

We have reviewed your supplemental application, as amended, and conclude that the above requirements were fulfilled.

We remind you that there are postmarketing requirements and postmarketing commitments listed in the August 27, 2015, approval letter for BLA 125522 that are still open. We also remind you that there are postmarketing commitments listed in the July 8, 2016, approval letter for BLA 125522/S-001 that are still open.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit, in triplicate, a cover letter requesting advisory comments, the

proposed materials in draft or mock-up form with annotated references, and the prescribing information to:

OPDP Regulatory Project Manager
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion
5901-B Ammendale Road
Beltsville, MD 20705-1266

Alternatively, you may submit a request for advisory comments electronically in eCTD format. For more information about submitting promotional materials in eCTD format, see the draft Guidance for Industry (available at: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM443702.pdf).

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 http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf. Information and Instructions for completing the form can be found at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf. For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

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).

If you have any questions, call Kati Johnson, Senior Regulatory Project Manager, at (301) 796-1234.

Sincerely,

{See appended electronic signature page}

James P. Smith, MD, MS
Deputy Director
Division of Metabolism and Endocrinology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

ENCLOSURE:
Content of Labeling (Prescribing Information, Patient Labeling)