DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

BLA 125268/S-077

SUPPLEMENT BLA APPROVAL
REMOVE REMS ELEMENTS
REMS MODIFICATION
December 6, 2011

Amgen, Inc.
Attention: Augustus Kamassah, M.S., RAC
Manager, Regulatory Affairs
One Amgen Center Drive
Mail Stop 17-2-B
Thousand Oaks, CA 91320-1799

Dear Mr. Kamassah:

Please refer to your Supplemental Biologics License Application (sBLA), dated March 31, 2011, received April 1, 2011, submitted under section 351 of the Public Health Service Act for Nplate® (romiplostim) for Subcutaneous Injection.

We acknowledge receipt of your amendments dated April 22, 2011, August 17, 2011, September 13, 2011, October 31, 2011, November 4, 11, and 17, 2011 and December 2, 2011 and your risk evaluation and mitigation strategy (REMS) assessment dated March 31, 2011.

We also refer to our REMS modification notification letter dated November 30, 2010; the February 24, 2011, teleconference between the Division of Hematology Products and Amgen, Inc. when we discussed the REMS for Nplate; and our REMS advice letter dated July 25, 2011.

This "Prior Approval" supplement to your biologics license application provides for revisions to the labeling (package insert and Medication Guide) for Nplate® (romiplostim); modifications to the Nplate® (romiplostim) REMS to eliminate the elements to assure safe use (ETASU), the Medication Guide, and the implementation system from the REMS; revisions to the communication plan to provide for the dissemination of information about the REMS modification eliminating the requirement for the ETASU, about how to obtain Nplate® (romiplostim), and reminding prescribers about the serious risks associated with Nplate® (romiplostim) and appropriate patient selection.

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 package insert, Medication Guide) 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. For administrative purposes, please designate this submission "**Product Correspondence – Final SPL for approved BLA STN 125268/S-077**."

Also within 14 days, amend all pending supplemental applications 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.

The SPL will be accessible via publicly available labeling repositories.

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

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.

Because none of these criteria apply to your application, you are exempt from this requirement.

RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS

The REMS for Nplate® (romiplostim) was originally approved on August 22, 2008, and the most recent REMS modification was approved on July 21, 2011. The REMS consists of a Medication Guide, a communication plan, ETASU, an implementation system, and a timetable for submission of assessments of the REMS.

Your proposed modifications to the REMS consist of eliminating the requirement for the Medication Guide, the ETASU, and the implementation system as elements of the REMS; and revising the communication plan and timetable for submission of assessments of the REMS.

We have determined that maintaining the Medication Guide as part of approved labeling is adequate to address the serious and significant public health concern and meets the standard in 21 CFR 208.1. We have also determined that revised product labeling and communication plan are adequate to address the serious risks associated with the use of Nplate (romiplostim). Therefore, it is no longer necessary to include the Medication Guide, the ETASU, and the implementation system as elements of the approved REMS to ensure that the benefits of Nplate® (romiplostim) outweigh the risks. We remind you that the Medication Guide will continue to be part of the approved labeling for Nplate® (romiplostim) in accordance with 21 CFR part 208.

Your proposed modified REMS, submitted on December 2, 2011, and appended to this letter, is approved.

The modified REMS consists of a revised communication plan and a revised timetable for submission of assessments of the REMS. We remind you that the timetable for submission of assessments was revised to June 30, 2012, June 30, 2015, and June 30, 2019.

At least 90 days before the assessments will be conducted, you should update the REMS supporting document to include revised assessment instrument and methodology information. 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:

> **BLA 125268 REMS CORRESPONDENCE**
> **(insert concise description of content in bold capital letters, e.g.,**
> **UPDATE TO REMS SUPPORTING DOCUMENT - ASSESSMENT METHODOLOGY)**

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

1. An evaluation of healthcare providers' understanding of the serious risks associated with the use of Nplate® (romiplostim).

2. Only for the REMS assessment due by June 30, 2012, provide the following information about the revised communication plan:

    - The date of the launch of the revised communication plan
    - Number of recipients of the Dear Health Care Provider (DHCP) letter
    - Number of DHCP letters returned
    - Number of electronic DHCP letters opened
    - Source of recipient lists
    - Number of Dear Professional Society letters sent
    - Number of Dear Professional Society letters returned

3. Information on the status of any postapproval study or clinical trial required under section 505(o)(3) or otherwise undertaken to investigate a safety issue. With respect to any such

postapproval study, you must include the status of such study, including whether any difficulties completing the study have been encountered. With respect to any such postapproval clinical trial, you must include the status of such clinical trial, including whether enrollment has begun, the number of participants enrolled, the expected completion date, whether any difficulties completing the clinical trial have been encountered, and registration information with respect to requirements under subsections (i) and (j) of section 402 of the Public Health Service Act. You can satisfy these requirements in your REMS assessments by referring to relevant information included in the most recent annual report required under section 506B and 21 CFR 601.70 and including any material or significant updates to the status information since the annual report was prepared. Failure to comply with the REMS assessments provisions in section 505-1(g) could result in enforcement action.

In addition to the assessments submitted according to the timetable included in the approved REMS, you must submit a REMS assessment and may propose a modification to the approved REMS when you submit a supplemental application for a new indication for use as described in section 505-1(g)(2)(A) of FDCA.

Prominently identify the 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:

BLA 125268 REMS ASSESSMENT

NEW SUPPLEMENT FOR BLA 125268
PROPOSED REMS MODIFICATION
REMS ASSESSMENT

NEW SUPPLEMENT (NEW INDICATION FOR USE)
FOR BLA125268
REMS ASSESSMENT
PROPOSED REMS MODIFICATION (if included)

If you do not submit electronically, please send 5 copies of REMS-related submissions.

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 package insert(s) to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications
5901-B Ammendale Road
Beltsville, MD 20705-1266

As required under 21 CFR 601.12(f)(4), you must submit final promotional materials, and the package insert(s), at the time of initial dissemination or publication, accompanied by a Form FDA 2253. For instruction on completing the Form FDA 2253, see page 2 of the Form. For more information about submission of promotional materials to the Division of Drug Marketing, Advertising, and Communications (DDMAC), 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 Mara Miller, Regulatory Project Manager, at (301) 796-0683.

Sincerely,

/Robert Kane/
Robert Kane, M.D.
Acting Deputy Director for Safety
Division of Hematology Products
Office of Hematology and Oncology Products
Center for Drug Evaluation and Research

ENCLOSURE(S):
Content of Labeling
REMS