DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

BLA 103234/5323

SUPPLEMENT APPROVAL
REMOVE REMS ELEMENTS

Amgen, Inc.
Attention: Tai H., Yu, MS, RAC
Senior Manager, Regulatory Affairs
One Amgen Center Drive
Mail Stop 17-2-A
Thousand Oaks, CA 91320-1799

Dear Mr. Yu:

Please refer to your Supplemental Biologics License Application (sBLA), dated November 16, 2012, received November 16, 2012, submitted under section 351(a) of the Public Health Service Act for Epoetin alfa (EPOGEN®/PROCRIT®).

We acknowledge receipt of your amendments dated December 11, 2012, January 31, April 24, July 11, September 20, November 19 and December 13, 2013, and your risk evaluation and mitigation strategy (REMS) assessment dated February 15, 2013.

This "Prior Approval" supplemental biologics application provides for modifications to the ESA REMS to revise the REMS goals, remove the Medication Guide from the REMS, re-design the Patient Acknowledgement Form, revise the prescriber certification, revise training modules in the REMS, and include new training elements in support of prescriber and hospital enrollment under ETASU A and B, respectively, and revisions to the prescribing information.

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.

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 Epoetin alfa (EPOGEN®/PROCRIT®) was originally approved on February 16, 2010, and the most recent REMS modification was approved on March 27, 2013. The REMS consists of a Medication Guide, communication plan, elements to assure safe use, implementation system, and a timetable for submission of assessments of the REMS.

Your proposed modification to the REMS consists of eliminating the requirement for the Medication Guide and the communication plan as elements of the REMS.

We have determined that maintaining the Medication Guide as part of the approved labeling is adequate to address the serious and significant public health concern and meets the standard in 21 CFR 208.1. Therefore, it is no longer necessary to include the Medication Guide as an element of the approved REMS to ensure that the benefits of the Epoetin alfa (EPOGEN®/PROCRIT®) outweigh the risks.

Therefore, we agree with your proposal, and a Medication Guide is no longer required as part of the REMS for Epoetin alfa (EPOGEN®/PROCRIT®).

In addition, because revisions to required prescriber training have been incorporated into the elements to assure safe use, we have also determined that it is no longer necessary to include the communication plan as an element of the approved REMS to ensure that the benefits of the drug outweigh the risks.

Therefore, a communication plan is no longer required as part of the REMS for Epoetin alfa (EPOGEN®/PROCRIT®).

Your proposed modified REMS, submitted on November 19, 2013, and appended to this letter, is approved.

The modified REMS consists of, elements to assure safe use, implementation system, and a timetable for submission of assessments of the REMS.

We remind you that the Medication Guide will continue to be part of the approved labeling for Epoetin alfa (EPOGEN®/PROCRIT®) in accordance with 21 CFR 208.

The timetable for submission of assessments of the REMS will remain the same as that approved on February 16, 2010.

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

1. Assess compliance with the erythropoiesis stimulating agents (ESA) APPRISE (Assisting Providers and Cancer Patients with Risk Information for the safe use of ESAs) Oncology Program Certification:

    a. An assessment of prescriber certification statistics including the number and percentage of Healthcare Providers (HCPs) actively prescribing Epoetin alfa (EPOGEN®/PROCRIT®) for cancer, by setting (private practice and hospitals), who are specially certified in the ESA APPRISE Oncology Program during the reporting period and cumulatively.

    b. An assessment of the hospital certification statistics including the number and percentage of institutions who order ESAs that have certified in the ESA APPRISE Oncology Program during the reporting period and cumulatively.

    c. Results of hospital audits including:

        i. The number of ESA prescribers who prescribe ESAs for cancer patients in comparison to the documentation maintained by the hospitals of ESA prescribers that are certified.

        ii. The number of patient-HCP signed Acknowledgement Forms retained by the hospital compared to the number of patients initiating a new course of ESA therapy.

        iii. An evaluation of the reasons for hospital noncompliance with the program requirements.

        iv. A report on corrective actions taken to address noncompliance by site.

    d. Results of audits of private practice clinics including:

        i. The number of ESA prescribers who prescribe ESAs compared to those that are certified.

        ii. The number of patient-HCP signed Acknowledgement Forms retained by the private clinic compared to the number of patients initiating a new course of ESA therapy.

        iii. An evaluation of the reasons for noncompliance with program requirements.

        iv. A report on corrective actions taken to address noncompliance by site.

2. Provide results of baseline and follow-up surveys of prescribers' understanding of the serious risks of Epoetin alfa (EPOGEN®/PROCRIT®), safe use conditions, and requirements of ESA APPRISE Oncology Program.

3. Evaluate Epoetin alfa (EPOGEN®/PROCRIT®) utilization patterns including the following:

    a. Hemoglobin levels in association with ongoing Epoetin alfa (EPOGEN®/PROCRIT®) therapy.

    b. Rates of Epoetin alfa (EPOGEN®/PROCRIT®) cessation following cessation of chemotherapy.

    c. Concomitant prescribing of Epoetin alfa (EPOGEN®/PROCRIT®) and myelosuppressive chemotherapy.

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 1 or more such goals or such elements should be modified.

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.

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/BLA 103234 REMS CORRESPONDENCE**
> **(insert concise description of content in bold capital letters, e.g.,**
> **UPDATE TO REMS SUPPORTING DOCUMENT - ASSESSMENT METHODOLOGY)**

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.

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 103234 REMS ASSESSMENT

NEW SUPPLEMENT FOR BLA 103234
PROPOSED REMS MODIFICATION
REMS ASSESSMENT

NEW SUPPLEMENT (NEW INDICATION FOR USE)
FOR BLA 103234
REMS ASSESSMENT
PROPOSED REMS MODIFICATION (if included)

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

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 Mrs. Diane Leaman, Regulatory Project Manager, at (301) 796-1424.

Sincerely,

{See appended electronic signature page}

Ann T. Farrell, M.D.
Division Director
Division of Hematology Products
Office of Hematology and Oncology Products
Center for Drug Evaluation and Research

ENCLOSURES:

Package Insert
Content of Labeling (Medication Guide)
REMS

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

ANN T FARRELL
12/31/2013