DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

BLA 103234/5281

**SUPPLEMENT BLA APPROVAL**

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

Dear Mrs. Yu:

Please refer to your Supplemental Biologics License Application (sBLA) 103234/5281, dated July 19, 2011, received July 20, 2011submitted under section 351 of the Public Health Service Act for Epogen®/Procrit® (epoetin alfa).

We acknowledge receipt of your amendments submitted on August 4, 2011, August 24, 2011, September 28, 2011, February 14, 2012, May 24, 2012, May 30, 2012 and your risk evaluation and mitigation strategy (REMS) assessment dated July 19, 2011.

This Prior Approval labeling supplement provides for the following:

1. To include modifications to the approved ESA REMS as follows:
   - to accurately identify the marketer and distributor of Procrit, Janssen Products, LP;
   - to remove references to the previous marketer and distributor of Procrit, Centocor Ortho Biotech Products, LP;
   - to delete the sentence (b) (4) from REMS materials other than the professional labeling (Prescribing Information) for Epogen, Procrit, or Aranesp, as appropriate; and
   - to correct minor typographical errors.

2. Revisions to the Procrit package insert, instructions for use, carton, and container labeling incorporating the name and logo of current marketer and distributor of Procrit, Janssen Products, LP, and removal of references to the previous marketer and distributor, Centocor Ortho Biotech Products, LP.

3. Revision to the Procrit package insert to include new contact information for reporting suspected adverse reactions and for performance of assays for binding and neutralizing antibodies for Procrit.

4. Revisions to the Epogen and the Procrit package inserts to correct an error in Dosage & Administration Section 2.5

5. Revisions to all of the Procrit carton and immediate container labeling to identify Amgen, Inc. as the manufacturer.

6. Revisions to all of the Epogen carton and immediate container labeling to identify Amgen, Inc. as the manufacturer

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 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 103234/5281**."

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.

## CARTON AND IMMEDIATE CONTAINER LABELS

Submit final printed carton and container labels that are identical to the enclosed carton and immediate container labels submitted on DATE, as soon as they are available, but no more than 30 days after they are printed. Please submit these labels electronically according to the guidance for industry titled "Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (June 2008)." Alternatively, you may submit 12 paper copies, with 6 of the copies individually mounted on heavy-weight paper or similar material. For administrative purposes, designate this submission "**Product Correspondence – Final Printed Carton and Container Labels for approved BLA STN 103234/5281**." 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, 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 Epogen®/Procrit® (epoetin alfa) was originally approved on February 16, 2010, and a REMS modification was approved on June 24, 2011. 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 modifications to the REMS consist of revisions to the REMS document, Medication Guide, and appended REMS materials. These modifications are to revise the REMS document and the ESA APPRISE Oncology Program REMS materials, including the REMS website, to incorporate the name and logo change of the marketer and distributor of Procrit from Centocor Ortho Biotech to Janssen Products, LP.

Your proposed modified REMS, submitted on July 19, 2011 (sBLA 103234/5281) as amended, and appended to this letter, is approved.

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

The REMS assessment plan will remain the same as that approved on February 16, 2010.

We remind you that assessments of an approved REMS under section 505-1(g)(3) include, in section 505-1(g)(3)(A), an assessment of the extent to which the elements to assure safe use are meeting the goal or goals to mitigate a specific serious risk listed in the labeling of the drug, or whether the goal or goals or such elements should be modified.

We also remind you that assessments of an approved REMS must also include, under section 505-1(g)(3)(B) and (C), information on the status of any postapproval study or clinical trial required under section 505(o) 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 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 with the following wording in bold capital letters at the top of the first page of the submission:

**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.

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

## 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 Dr. Mona Patel, Regulatory Project Manager, at (301) 796-4236.

Sincerely,

/Patricia Keegan/
Patricia Keegan, M.D.
Director
Division of Oncology Products 2
Office of Hematology & Oncology Products
Center for Drug Evaluation and Research

ENCLOSURES:
- Content of Labeling
- Instructions For Use
- REMS Concise Template
- Medication Guides
- Dear Healthcare Provider (DHCP) Letter to Healthcare Providers (HCPs) who prescribe or prescribe and dispense ESAs for patients with cancer
- Dear Director of Pharmacy/Administrator Letter to hospitals that dispense ESAs for patients with cancer
- ESA APPRISE Oncology Program Website screenshots
- ESA REMS Flashcard
- ESA APPRISE Oncology Program Enrollment Forms for Healthcare Providers
- ESA APPRISE Oncology Program Training Module for Healthcare Providers
- ESA APPRISE Oncology Program for Healthcare Provider Flashcard
- ESA APPRISE Oncology Program Patient and Healthcare Professional (HCP)Acknowledgement Form
- HCP Program Starter Kit
- ESA APPRISE Oncology Program Enrollment Forms for Hospitals

- ESA APPRISE Oncology Program Training Module for Hospital Designees
- ESA APPRISE Oncology Program Hospital Process Overview Flashcard
- Guidelines for PAF Integration within Healthcare Systems and Clinics
- Carton & Container Labeling

---

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

---

/s/

---

JOSEPH E GOOTENBERG on behalf of PATRICIA KEEGAN
05/31/2012