DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration
Rockville, MD 20857

Our STN: BL 103234/5122

MAR 0 9 2007

Amgen, Incorporated
Attention: Randy Steiner, DPA
Regulatory Affairs General Medicine Therapeutic Head AC
One Amgen Center Drive
Thousand Oaks, CA 91320-1799

Dear Dr. Steiner:

Your request to supplement your biologics license application for Epoetin alfa (Epogen; Procrit) to add a Boxed Warning for increased risks of death, of serious cardiovascular and thromboembolic events, of more rapid tumor progression and to clarify dosing strategies; to update Warnings subsections to incorporate new clinical study results; to update Indications and Usage: Reduction of Allogeneic Blood Transfusion in Surgery Patients section based on new studies; to remove claims and statements for implied symptomatic improvement from the Clinical Studies and Precautions sections; to include information strengthening the description of risks in subsections for patients with chronic renal failure and with HIV, to remove the subsections on Tumor Growth Potential and on Surgery Patients: Thrombotic/Vascular Events and include this information in Warnings, and to modify the Information for Patients subsection to advise communication of the new safety information in the Precautions section; to remove statements minimizing risks in the Adverse Reactions section; to modify the Overdosage section with information on increased risks for cardiovascular events; and to modify the Dosage and Administration sections of the package insert has been approved. Your request to update the Patient Package Insert regarding the increased risks of deaths, increased thromboembolic events, and decreased time to tumor progression in patients receiving erythropoietin stimulating agents (ESAs) and removal of irrelevant information regarding anemia has also been approved.

We acknowledge your written commitment as described in your letter of March 8, 2007, as outlined below:

Postmarketing Study Commitment subject to reporting requirements of 21 CFR 601.70.

To examine the "quality of life" (QOL) claims in the Clinical Experience section of the Epogen product labeling and to:

a. perform an assessment of physician-measured functional status data (by the Karnofsky Performance Scale) used to support this aspect of the claim. This analysis will include a comprehensive assessment of the published literature

supporting and refuting evidence for retention of the functional status and activity level claims in the Epogen label;

b. perform an assessment of the patient-reported outcome (PRO) data used to support the PRO claims. This analysis of the PRO data will determine the extent to which the PRO data met the criteria described in the FDA guidance document entitled, "Guidance for Industry Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims;"

c. perform a comprehensive assessment of the published literature to identify supporting and refuting evidence for retention of the PRO claims in the Epogen label. This review will also assess the extent to which the literature-based evidence complies with the FDA PRO guidance cited above; and,

d. submit results of the functional status and PRO data assessments along with recommendations for possible retention of the QOL claims in the Epogen label. Each recommendation will be annotated to identify the availability of the source data and its compliance with the PRO expectations described in the FDA guidance cited above.

You agreed to provide the results of these assessments and provide recommendations by June 15, 2007.

We request that you submit clinical protocols to your IND, with a cross-reference letter to this biologics license application (BLA), STN BL 103951. Please use the following designators to label prominently all submissions, including supplements, relating to these postmarketing study commitments as appropriate:

- Postmarketing Study Protocol
- Postmarketing Study Final Report
- Postmarketing Study Correspondence
- Annual Report on Postmarketing Studies

For each postmarketing study subject to the reporting requirements of 21 CFR 601.70, you must describe the status in an annual report on postmarketing studies for this product. The status report for each study should include:

- information to identify and describe the postmarketing commitment,
- the original schedule for the commitment,
- the status of the commitment (i.e. pending, ongoing, delayed, terminated, or submitted),
- an explanation of the status including, for clinical studies, the patient accrual rate (i.e. number enrolled to date and the total planned enrollment), and
- a revised schedule if the study schedule has changed and an explanation of the basis for the revision.

As described in 21 CFR 601.70(e), we may publicly disclose information regarding these postmarketing studies on our Web site (http://www.fda.gov/cder/pmc/default.htm). Please refer to the February 2006 Guidance for Industry: Reports on the Status of Postmarketing Study Commitments - Implementation of Section 130 of the Food and Drug Administration Modernization Act of 1997 (see http://www.fda.gov/cder/guidance/5569fnl.htm) for further information.

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert, and the text for the patient package insert) submitted March 8, 2007. Marketing product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

Pursuant to 21 CFR 201.57(c)(18) and 201.80(f)(2), patient labeling must be reprinted immediately following the last section of labeling or, alternatively, accompany the prescription drug labeling.

Please submit all final (Epogen; Procrit) printed labeling at the time of use and include implementation information on FDA Form 356h. Please provide a PDF-format electronic copy as well as original paper copies (ten for circulars and five for other labels). Please also submit ten copies of the final, signed DHCP letter, envelope, and labeling.

Please submit within 30 days content of labeling [21 CFR 601.14(b)] in structured product labeling (SPL) format, as described at http://www.fda.gov/oc/datacouncil/spl.html, that is identical in content to the enclosed labeling text dated March 8, 2007. Upon receipt and verification, we will transmit that version to the National Library of Medicine for posting on the DailyMed website.

This information will be included in your biologics license application file.

Sincerely,

Rafel Dwaine Rieves, M.D.
Acting Director
Division of Medical Imaging and Hematology Products
Office of Oncology Drug Products
Center for Drug Evaluation and Research

Enclosure: Patient Package Inserts
Package Inserts