DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20852

Our STN: BL 103951/5097

Amgen, Incorporated
Attention: Randy Steiner, DPA
Associate Director, Regulatory Affairs
One Amgen Center Drive
Thousand Oaks, CA 91320-1799

MAR 2 3 2006

Dear Dr. Steiner:

Your request to supplement your biologics license application for Darbepoetin alfa to include the new dosing regimen of 500 μg once every 3 weeks (Q3W) for the treatment of anemia in adults with non-myeloid malignancies, where anemia is due to the effect of concomitantly administered chemotherapy, has been approved.

All applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred. We are deferring submission of your pediatric studies for ages 1 to less than 17 years until May 31, 2006.

Postmarketing Studies subject to reporting requirements of 21 CFR 601.70.

We acknowledge your written commitments to provide additional information on ongoing studies and to conduct postmarketing studies as described in your letters of February 27, 2006, February 28, 2006, and March 16, 2006, as outlined below:

1. Deferred pediatric studies, which are required under section 2 of the Pediatric Research Equity Act (PREA), are also considered required postmarketing study commitments. The status of this postmarketing study shall be reported annually according to 21 CFR 601.70. This commitment is listed below.

    a. A deferred, randomized, dose-ranging, placebo-controlled pediatric study, required under PREA, that will assess the safety and effectiveness of Darbepoetin alfa administered every three weeks for the treatment of anemia in approximately 200 pediatric patients, ages 1 to less than 17 years, with non-myeloid malignancies receiving multi-cycle chemotherapy. A clinical protocol will be submitted by May 31, 2006, the study will be completed by February 28, 2009, and the final study report will be submitted by May 31, 2009.

b. Final Report Submission: May 31, 2009

Submit final study reports to this BLA. For administrative purposes, all submissions related to this pediatric postmarketing study commitment must be clearly designated "Required Pediatric Study Commitment."

2. To complete and submit the final study report, including the primary data and analyses, of the ongoing, randomized, placebo-controlled study, Protocol 20010145, being conducted in 600 patients with small-cell lung cancer assessing the relative safety of Darbepoetin alfa administered at 300 μg QW weeks 1-4 followed by 300 μg Q3W, as compared to placebo, for the treatment of chemotherapy-induced anemia (CIA). Patient accrual will be completed by June 28, 2006, the study will be completed by June 1, 2007, and the final study report will be submitted to the FDA by October 31, 2007.

3. To obtain and submit a final study report, including the primary data and analyses, of the ongoing, randomized, observational-control, investigator-sponsored study, Protocol DE-2001-0033, being conducted in 720 patients with breast cancer receiving neoadjuvant (PREPARE) chemotherapy assessing the safety of Darbepoetin alfa administered at 4.5 μg/kg Q2W, as compared to transfusion support, for the treatment of chemotherapy-induced anemia (CIA). Patient accrual was completed as of March 31, 2005, the study will be completed by April 30, 2007, and the final study report will be submitted to the FDA by November 30, 2007.

4. To obtain and submit a final study report, including the primary data and analyses, of the ongoing, randomized, observational-control, investigator-sponsored study, Protocol DE-2002-0015, being conducted in 1000 patients with breast cancer receiving adjuvant (ARA-03) chemotherapy assessing the safety of Darbepoetin alfa administered at 300 μg QW followed by 300 μg Q3W as compared to transfusion support, for the treatment of chemotherapy-induced anemia (CIA). Patient accrual will be completed by May 31, 2008, the study will be completed by November 31, 2010, and the final study report will be submitted to the FDA by May 31, 2011.

5. To obtain and submit a final study report, including the primary data and analyses, of the ongoing, randomized, observational-control, investigator-sponsored study, Protocol SE-2002-9001, being conducted in 600 patients with head-and-neck cancer (DAHANCA-10) assessing the safety of Darbepoetin alfa administered at 150 μg QW as compared to transfusion support, for the treatment of chemotherapy-induced anemia (CIA). Patient accrual will be completed by June 30, 2007, the study will be completed by March 31, 2008, and the final study report will be submitted to the FDA by September 30, 2008.

6. To obtain and submit a final study report, including the primary data and analyses, of the ongoing, randomized, observational-control, investigator-sponsored study, Protocol FR-2003-3005, being conducted in 600 patients with diffuse large B-Cell lymphoma (GELA LNH03-6B) assessing the safety of Darbepoetin alfa administered at 2.25 μg/kg QW as compared to transfusion support, for the treatment of chemotherapy-induced anemia (CIA). Patient accrual will be completed by February 28, 2009, the study will be completed by February 28, 2010, and the final study report will be submitted to the FDA by August 31, 2010.

7. To conduct and provide the data and results of a meta-analysis of adverse outcomes, utilizing the data from studies 20010145, DE-2001-0033, DE-2002-0015, DE-2002-9001, and FR-2003-3005. The meta-analysis will be provided to the FDA by December 31, 2011.

We request that you submit clinical protocols to your IND, with a cross-reference letter to this biologics license application (BLA), STN BL 103951. Submit nonclinical and chemistry, manufacturing, and controls protocols and all study final reports to your 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 Studies – 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.

Pursuant to 21 CFR 201.57(f)(2), patient labeling must be reprinted at the end of the package insert.

Please submit all final printed labeling at the time of use and include implementation information on FDA Form 356h. Please provide SPL and PDF-format electronic copy as well as original paper copies (ten for circulars and five for other labels). In addition, you may wish to submit draft copies of the proposed introductory advertising and promotional labeling with a cover letter requesting advisory comments to the Food and Drug Administration, Center for Drug Evaluation and Research, Division of Drug Marketing, Advertising and Communication, 5901-B Ammendale Road, Beltsville, MD 20705-1266. Final printed advertising and promotional labeling should be submitted at the time of initial dissemination, accompanied by a FDA Form 2253.

All promotional claims must be consistent with and not contrary to approved labeling. You should not make a comparative promotional claim or claim of superiority over other products unless you have substantial evidence to support that claim.

Please refer to http://www.fda.gov/cder/biologics/default.htm for important information regarding therapeutic biological products, including the addresses for submissions. Effective August 29, 2005, the new address for all submissions to this application is:

Food and Drug Administration
Center for Drug Evaluation and Research
Therapeutic Biological Products Document Room
5901-B Ammendale Road
Beltsville, Maryland 20705-1266

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

Sincerely,

Patricia Keegan

Patricia Keegan, M.D.
Director
Division of Biological Oncology Products
Office of Oncology Drug Products
Center for Drug Evaluation and Research

Enclosure: Package Insert