DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20852

Our STN: BL 103234/5053

JUN 30 2004

Amgen, Incorporated
Attention: Douglas Hunt
Director, Regulatory Affairs
One Amgen Center Drive
Thousand Oaks, CA 91320-1799

Dear Mr. Hunt:

Your request to supplement your biologics license application for Epoetin alfa to update the Clinical Pharmacology, Indications and Usage, Precautions, Adverse Reactions, and Dosage Administration sections of the package insert to incorporate an alternative weekly dosing regimen for the treatment of anemia due to chemotherapy in patients with non-myeloid malignancies, 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 five to eighteen years until December 31, 2004. We are also deferring submission of your pediatric studies for ages zero to less than five years until June 30, 2005.

Postmarketing Studies subject to reporting requirements of 21 CFR 601.70.

Your deferred pediatric studies required under section 2 of the Pediatric Research Equity Act (PREA) are considered required postmarketing study commitments. The statuses of these postmarketing studies shall be reported annually according to 21 CFR 601.70. These commitments are listed below.

1. To obtain efficacy and safety data to evaluate weekly dosing of Procrit (Epoetin alfa) in children with solid tumors, Hodgkin's disease, ALL, or NHL, in study PR99-11-034/044 a Randomized Double-Blind, Placebo Controlled Study to Evaluate the Effect of Weekly Procrit (Epoetin alfa) on Anemia and Quality of Life in Children with Cancer Undergoing Myelosuppressive Chemotherapy. The study was completed on February 18, 2004, and the final study report will be submitted by December 31, 2004.

2. To evaluate the feasibility of conducting a study, in pediatric cancer patients age 0 to less than 5 years, and if appropriate, submit a pediatric study plan or request a waiver by June 30, 2005.

We request that you submit clinical protocols to your IND, with a cross-reference letter to this biologics license application (BLA), STN BL 103234. Submit nonclinical and chemistry, manufacturing, and controls protocols and all study final reports to your BLA STN BL 103234. 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), and
- an explanation of the status including, for clinical studies, the patient accrual rate (i.e. number enrolled to date and the total planned enrollment).

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 April 2001 Draft 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/cber/gdlns/post040401.htm) for further information.

Please submit all final 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). 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 Division of Drug Marketing, Advertising and Communication (HFD-42), Center for Drug Evaluation and Research, 5600 Fishers Lane/Room 8B45, Rockville, MD 20857. Final printed advertising and promotional labeling should be submitted at the time of initial dissemination, accompanied by an 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.

The regulatory responsibility for review and continuing oversight for this product transferred from the Center for Biologics Evaluation and Research to the Center for Drug Evaluation and Research effective June 30, 2003. For further information about the transfer, please see http://www.fda.gov/cder/biologics/default.htm. Until further notice, however, all correspondence, except as provided elsewhere in this letter, should continue to be addressed to:

CBER Document Control Center
Attn: Office of Therapeutics Research and Review
Suite 200N (HFM-99)
1401 Rockville Pike
Rockville, Maryland 20852-1448

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

Sincerely,

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

Enclosure: Package Insert

CONCURRENCE PAGE

Letter Type: LETTER: Approval (AP)
Summary Text: Clinical Supplmt. Efficacy - New/Dosing Regimen
REVIEW COMPLETION REQUIRED BY: RIS

SS Data Check:

- **Place copy of Approval Ltr. with original signature concurrence page in Archival package behind the "Approval Materials" Tab after LAR (Licensing Action Recommendation).**

RIS Data Check:

- **Verify short summary – Ltr. & Submission screen should match.**
- **Check Letter for PMCs (if PMCs – add "PMCs – Approved With" special characteristic code.)**
- **Check if Major Approval – if so – add code.**
- **Perform Review Completion Process**
- **Milestone: Confirm Approved Status**

cc: Patricia Keegan, HFM-570
Karen Weiss, HFM-500
Earl Dye, HFM-585
Glen Jones, HFM-500
Monica Hughes, HFM-588
Kaushikkumar Shastri, HFM-573
Clare Gnecco, HFD-711
Mark Rothmann, HFD-711
DRMP BLA file, HFM-585
RIMS, HFM-110
Carole Broadnax, HFM-602
TFRB Blue file/Michael Smedley, HFM-670
Debbie Taub, HFD-013
Heidi Brubaker, HFD-013
Marci Keister, HFD-042
Patrick Guinn, HFD-006
Barry Poole, HFD-240
Karen Young, HFD-410

History: HughesM: 6-17-04: T. Pagan-Motta: 6.29.04: K. Townsend: 6.30.2004

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