AMGEN®

One Amgen Center Drive
Thousand Oaks, CA 91320-1799
805.447.1000
www.amgen.com

November 2005

Dear Health Care Professional:

Amgen Inc. wishes to inform you that sections of the product prescribing information for Aranesp® (darbepoetin alfa) have been updated regarding the fact that, recently, *pure red cell aplasia (PRCA) and severe anemia, with or without other cytopenias, associated with neutralizing antibodies to erythropoietin have been reported in patients treated with Aranesp®.* This new information is contained in the WARNINGS, ADVERSE REACTIONS, and DOSAGE AND ADMINISTRATION sections. When utilized in accordance with the approved prescribing information, the benefit/risk profile of Aranesp® continues to be favorable.

As the potential for PRCA and anti-erythropoietin antibody-associated severe anemia applies to all marketed erythropoietic proteins, product labeling for all drugs in this class have been updated in a consistent manner to state the following:

(1) If a patient develops a sudden loss of response, accompanied by severe anemia and low reticulocyte count, an evaluation for causative factors should be undertaken. If anti-erythropoietin antibody-associated anemia is suspected, physicians should withhold Aranesp® and other erythropoietic proteins and contact Amgen (1-800-77AMGEN) to perform assays for binding and neutralizing antibodies.

(2) Aranesp® should be permanently discontinued in patients with antibody-mediated anemia.

(3) Patients should not be switched to other erythropoietic proteins, as there is a potential for the antibodies to cross-react.

Specifically, the revised sections of the label are as follows, with new information italicized:

WARNINGS

Pure Red Cell Aplasia

Cases of pure red cell aplasia (PRCA) *and of severe anemia, with or without other cytopenias, associated* with neutralizing antibodies to erythropoietin *have* been *reported* in patients treated with *Aranesp®*. This has been reported predominantly in patients with CRF *receiving Aranesp® by subcutaneous administration*. Any patient *who develops a sudden* loss of response to Aranesp®, *accompanied by severe anemia and low reticulocyte count,* should be evaluated for the etiology of loss of effect, *including the presence of neutralizing antibodies to erythropoietin* (see **PRECAUTIONS: *Lack or Loss of Response to Aranesp®***). *If anti-erythropoietin antibody-associated anemia is suspected, withhold Aranesp® and other erythropoietic proteins. Contact Amgen (1-800-77AMGEN) to perform assays for binding and neutralizing antibodies.* Aranesp® should be *permanently* discontinued in patient*s* with *antibody-mediated anemia. Patients should not be switched to other erythropoietic proteins as antibodies may cross-react (see **ADVERSE REACTIONS: Immunogenicity**).*

ADVERSE REACTIONS

Immunogenicity

*As with all therapeutic proteins, there is a potential for immunogenicity. Neutralizing antibodies to erythropoietin, in association with PRCA or severe anemia (with or without other cytopenias), have been reported in patients receiving Aranesp® (see **WARNINGS: Pure Red Cell Aplasia**) during post-marketing experience.*

In clinical studies, the percentage of patients with antibodies to Aranesp® was examined using the BIAcore assay. Sera from 1501 CRF patients and 1159 cancer patients were tested. At baseline, prior to Aranesp® treatment, binding antibodies were detected in 59 (4%) of CRF patients and 36 (3%) of cancer patients. While receiving Aranesp® therapy (range 22-177 weeks), a follow-up sample was taken. One additional CRF patient and eight additional cancer patients developed antibodies capable of binding Aranesp®. None of the patients had antibodies capable of neutralizing the activity of Aranesp® or endogenous erythropoietin at baseline or at end of study. No clinical sequelae consistent with PRCA were associated with the presence of these antibodies.

The incidence of antibody formation is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody (including neutralizing antibody) positivity in an assay may be influenced by several factors including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies across products within this class (erythropoietic proteins) may be misleading.

DOSAGE AND ADMINISTRATION

Chronic Renal Failure Patients

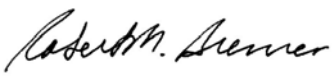
Aranesp® is administered either IV or SC as a single weekly injection. ***In patients on hemodialysis, the IV route is recommended***. The dose should be started and slowly adjusted as described below based on hemoglobin levels. If a patient fails to respond or maintain a response, this should be evaluated (see ***WARNINGS: Pure Red Cell Aplasia***, **PRECAUTIONS:** ***Lack or Loss of Response to Aranesp®*** and ***PRECAUTIONS:*** **Laboratory Tests**). When Aranesp® therapy is initiated or adjusted, the hemoglobin should be followed weekly until stabilized and monitored at least monthly thereafter.

There is no change in the **DOSAGE AND ADMINISTRATION** section of the Aranesp® prescribing information for cancer patients.

You are encouraged to report adverse patient experiences in association with any Amgen product to Amgen's Medical Information Connection™ at 1-800-77-AMGEN or online at http://www.amgenmedinfo.com. Alternatively, this information may be reported to FDA's MedWatch reporting system by phone (1-800-FDA-1088), facsimile (1-800-FDA-0178), the MedWatch website (https://www.accessdata.fda.gov/scripts/medwatch), or mail to MedWatch, 5600 Fishers Lane Rockville, MD 20852-9787. Both health care professionals and consumers should use Form 3500 (available at the MedWatch website) for reporting adverse events.

A copy of the revised prescribing information and patient package insert for Aranesp® is enclosed. Should you have any questions or require further information regarding the use of Aranesp®, please contact Amgen's Medical Information Connection™ at 1-800-77-AMGEN or online at http://www.amgenmedinfo.com.

Sincerely,



Robert Brenner, MD
Sr. Director and Nephrology Therapeutic
Area Head, Medical Affairs
Amgen Inc.

Roy Baynes, MD, PhD
Vice President, Oncology Clinical Development
and Acting Oncology Therapeutic Area Head,
Medical Affairs
Amgen Inc.