# IMPORTANT DRUG WARNING

**SUBJECT: Strengthened Oncology Safety Information and New Medication Guide and Patient Instructions for Use for EPOGEN®/PROCRIT® and Aranesp®**

August 7, 2008

Dear Health Care Professional:

On August 6, 2008, the EPOGEN®/PROCRIT® (Epoetin alfa) and Aranesp® (darbepoetin alfa) labeling were revised to strengthen the safety information for healthcare professionals and patients. The changes are summarized as follows:

- Safety-related labeling changes for cancer patients receiving chemotherapy. The prescribing information has been revised to clarify the FDA-approved conditions for use of erythropoiesis-stimulating agents (ESAs) in patients with cancer and revised directions for dosing to state the hemoglobin level (≥ 10 g/dL) at which treatment with an ESA should not be initiated. The new label states that ESAs are not indicated for patients receiving myelosuppressive therapy when the anticipated outcome is cure.

- Medication Guide and Patient Instructions for Use for all indications. The new Medication Guide contains information that FDA has determined is necessary for patients' safe and effective use of ESAs, and that could affect patients' decision to take this drug. Federal regulations require that the Medication Guide be distributed to patients.

The specific changes are described below.

## 1. REVISIONS TO BOXED WARNINGS, INDICATIONS AND USAGE, WARNINGS, DOSAGE AND ADMINISTRATION FOR CANCER PATIENTS RECEIVING CHEMOTHERAPY

The **BOXED WARNINGS** section of the EPOGEN®/PROCRIT® and Aranesp® prescribing information has been revised as follows:

***Cancer*:**

- **ESAs shortened overall survival and/or increased the risk of tumor progression or recurrence in some clinical studies in patients with breast, non-small cell lung, head and neck, lymphoid, and cervical cancers (see WARNINGS: Table 1).**
- **To decrease these risks, as well as the risk of serious cardio- and thrombovascular events, use the lowest dose needed to avoid red blood cell transfusion.**
- **Use ESAs only for treatment of anemia due to concomitant myelosuppressive chemotherapy.**
- **ESAs are not indicated for patients receiving myelosuppressive therapy when the anticipated outcome is cure.**
- **Discontinue following the completion of a chemotherapy course.**

The **INDICATIONS AND USAGE** and **WARNINGS: Increased Mortality and/or Increased Risk of Tumor Progression or Recurrence** sections have been revised to be consistent with the changes in the Boxed Warnings.

The **DOSAGE AND ADMINISTRATION:** ***Cancer Patients Receiving Chemotherapy*** section has been revised to include the following sentence:

> "Therapy should not be initiated at hemoglobin levels ≥ 10 g/dL."

Important changes have also been made to this section to ensure use of the lowest dose needed to avoid transfusion and to discontinue treatment with ESAs if after 8 weeks of therapy there is no response as measured by hemoglobin levels or if transfusions are still required.

## 2. MEDICATION GUIDE AND PATIENT INSTRUCTIONS FOR USE FOR ALL INDICATIONS

The EPOGEN®/PROCRIT® and Aranesp® patient package insert has been replaced by two new documents: a Medication Guide and Patient Instructions for Use. The Medication Guide provides patients with important safety information necessary for safe and effective use of EPOGEN®/PROCRIT® and Aranesp®. The Medication Guide must be distributed to all patients who are dispensed/administered these products.

The **PRECAUTIONS: Information for Patients** section of the prescribing information has also been updated with the following sentence:

> "Patients should be instructed to read the EPOGEN®/PROCRIT®/Aranesp® Medication Guide and Patient Instructions for Use and should be informed that the Medication Guide is not a disclosure of all possible side effects."

Amgen and Ortho Biotech are disseminating this important prescribing information to inform healthcare professionals about the important new safety information for prescribing EPOGEN®/PROCRIT® and Aranesp®. Over the coming weeks, our field forces will be calling on healthcare professionals and will communicate this revised safety information. Prescribing healthcare professionals should review the full prescribing information, including the Medication Guide and Patient Instructions for Use with patients, in order to make appropriate treatment decisions based on the benefit-risk profile of these products.

Prescribing healthcare professionals should discuss with their patients before starting or continuing therapy with ESAs, the benefits of treatment with ESAs and the potential and demonstrated risks of ESAs for thrombovascular events, shortened time to tumor progression or recurrence, and shortened survival time of cancer patients.

Copies of the revised prescribing information, Medication Guide, and Patient Instructions for Use for EPOGEN®/PROCRIT® and Aranesp® are enclosed and available on the Amgen Inc. website at www.amgen.com and the Ortho Biotech Products, L.P. website at www.procrit.com.

Should you have any questions, require further information on product safety, or wish to report adverse patient experiences:

> For Aranesp® and EPOGEN®, please contact Amgen's Medical Information Connection™ at 1-800-77-AMGEN.
>
> For PROCRIT®, please contact Ortho Biotech's Medical Information at 1-888-227-5624.

Alternatively, adverse events may be reported to FDA's MedWatch reporting system

- by phone (1-800-FDA-1088), by facsimile (1-800-FDA-0178),
- online (https://www.accessdata.fda.gov/scripts/medwatch/) or
- mailed, using the MedWatch for FDA 3500 postage paid form, to the FDA Medical Products Reporting Program, 5600 Fishers Lane, Rockville, MD 20852-9787.

Sincerely,

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| Sean E. Harper, MD<br>Senior Vice President, Global Development and Chief Medical Officer<br>Amgen | Craig Tendler, MD<br>Vice President, Medical Affairs<br>Ortho Biotech |