NATIONAL PBM ALERT

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DEPARTMENT OF VETERANS AFFAIRS - VETERANS HEALTH ADMINISTRATION (VHA)
PHARMACY BENEFITS MANAGEMENT SERVICES (PBM), MEDICAL ADVISORY PANEL (MAP),
CENTER FOR MEDICATION SAFETY PSCI (VA MedSAFE),
AND ONCOLOGY FIELD ADVISORY COMMITTEE

UPDATE ALERT FOR ERYTHROPOIESIS STIMULATING AGENTS (ESAs): FDA LABELING CHANGES FOR CANCER PATIENTS RECEIVING MYELOSUPPRESSIVE CHEMOTHERAPY

I. ISSUE

As part of the ongoing safety review of ESAs (epoetin and darbepoetin), the FDA has notified the manufacturer of a decision to require additional safety language in the label following the recommendations made by the Oncology Drugs Advisory Committee.

II. BACKGROUND

In March 2007, the FDA approved interim revised ESA product labeling based on data from several trials showing higher mortality rates and a shorter time to progression in patients receiving ESAs compared to placebo. Some of the trials employed dosing to a target hemoglobin higher than recommended in the package insert (targets of ≥12 g/dL) while others included cancer patients with anemia who were not receiving chemotherapy or radiotherapy. These data were discussed by the Oncology Drugs Advisory Committee in March of 2008, during which time recommendations were made to the FDA for additional safety-related changes to the label.

III. DISCUSSION

The labeling changes for both epoetin and darbepoetin are as follows:

- An addition to the Box Warning stating: ESAs are not indicated for patients receiving myelosuppressive chemotherapy when the anticipated outcome is cure.
- Therapy should not be initiated at hemoglobin levels ≥ 10g/dL.
- Removal of wording that implied it was safe to treat patients to a maximum hemoglobin level of 12 g/dL. Per the FDA, maintaining the hemoglobin between 10 and 12 g/dL to avoid transfusion did not improve survival or decrease morbidity.

The FDA states that there will be further discussion on when to initiate and discontinue therapy.

IV. VA MEDSAFE RECOMMENDATIONS *reinforce those of the FDA and include*:

- **Warning:** ESAs are not indicated for use in cancer patients receiving myelosuppressive chemotherapy with the intent of cure.
- **Initiation:** ESAs should not be started at hemoglobin levels ≥ 10g/dL and adjusted to maintain the lowest hemoglobin level needed to avoid transfusions.
- **Withholding Therapy:** ESAs should be withheld when the hemoglobin exceeds the level needed to avoid transfusion (there is no longer a safe upper range).

V. REFERENCES

1. Food and Drug Administration Alert 7/31/08. http://www.fda.gov/medwatch/safety/2008/safety08.htm#ESA2.