



**INLAND EMPIRE HEALTH PLAN**

This policy has been developed through review of medical literature, consideration of medical necessity, generally accepted medical practice standards, and approved by the IEHP Pharmacy and Therapeutics Subcommittee.

**Drug:** Epogen & Procrit (epoetin), and Aranesp (darbepoetin)

**Class:** Erythropoiesis-stimulating agents (ESAs)

**Formulary medication:** N/A

**Effective Date:** April 2007, August 2008, updated August 2009

**Policy/Criteria:**

In March 2007, FDA issued an alert regarding the safety information for erythropoiesis-stimulating agents (ESAs) Aranesp (darbepoetin alfa), Epogen (epoetin alfa), and Procrit (epoetin alfa). A higher chance of serious and life-threatening side effects and/or death were found in patients with cancer with the use of ESAs. In another study, patients scheduled for orthopedic surgery had a higher rate of deep venous thrombosis when treated with epoetin at the approved dose. In May 2007, FDA panel recommended additional clinical trials to be conducted to investigate the safety of these products. Furthermore, the panel recommended that the use of ESAs should be discontinued after a chemotherapy regimen is completed and the degree of anemia with a subsequent chemo regimen is re-evaluated. The top hemoglobin level of 12g/dl is recommended and reaffirmed by the panel. The panel did not address issues and concerns in end stage renal disease patients, however, it is scheduled to be discussed in the upcoming months.

IEHP covers ESAs for various FDA approved indication. Due to the FDA warning, the top range of hemoglobin level should be kept at 12g/dL. Providers will receive an authorization for the use of ESAs, the administration of ESAs (interval and dosing) is depended on members' condition (hematocrit / hemoglobin level). The final approval of payment is contingent on the appropriateness of the use of ESAs based on members' hematocrit/hemoglobin level.

IEHP Clinical Criteria for the erythropoiesis-stimulating agents (ESAs):

- **Supplemental Erythropoetin is covered for the following indications:**

- Members with anemia associated with end stage renal disease (ESRD) or chronic renal failure (CRF) whether or not they are receiving dialysis
- Members with non-myeloid malignancies developing anemia due to chemotherapy
- Members with HIV/AIDS developing anemia due to the drug Zidovudine (AZT)
- Members with Hepatitis C developing anemia from chemotherapy (e.g. ribavirin)
- Members with anemia scheduled to undergo elective non-cardiac, non-vascular surgery (e.g. total hip or total knee) or those at risk for substantial perioperative blood loss

**A. Members with anemia due to ESRD or chronic renal failure:**

- For initial treatment the Hematocrit (Hct) should be at or less than 33% or Hemoglobin (Hgb) at or less than 11 g/dl.
- Therapy may be initiated at a dosing level determined by the Member's provider for a period of eight weeks
- The Member should have a serum creatinine level greater than or equal to 2 mg/dL or estimated GFR lesser than or equal to 45 ml/min
- For continuing treatment: will cover a Hct up to and including 36% or a Hgb up to and including 12 g/dL
- A repeat Hct or Hgb should be submitted after 3 months of therapy for reevaluation
- Adequate iron stores should be demonstrated by means of bone marrow iron or serum ferritin levels (100ng/mL) or serum iron saturation (>20%) studies. Supplemental iron should be administered as indicated
- For dialysis claim: ESA will be approved if Hgb is less than 12 g/dl. The Hgb and/or Hct level must be submitted along with the claim (should be obtained at least twice a month). Patients whose Hgb level is between 11-12 should be evaluated closely (at least weekly) to determine if the dose needs to be adjusted. Dose given to the patient with a Hgb level of over 12 will be denied.

**B. Members with anemia due to chemotherapy:**

- For initial treatment the Hematocrit (Hct) should be at or less than 30% or Hemoglobin (Hgb) at or less than 10 g/dl
- Therapy may be initiated with Epoetin alfa up to 40,000 Units weekly for four (4) weeks and up to 60,000 Units weekly for four (4) more weeks if no response OR Darbepoetin: 2.25 mcg/KG weekly or 500 mcg every 3 weeks for six (6) weeks and up to 4.5 mcg/kg weekly for six (6) more weeks if no response
- Adequate iron stores should be demonstrated by means of bone marrow iron or serum ferritin levels (100ng/mL) or serum iron saturation (>20%) studies. Supplemental iron should be administered as indicated
- If there is no response on initial therapy (less than 3% rise in Hct or less than 1 g/dl rise in Hgb) after eight (8) weeks of Epoetin alfa or twelve (12) weeks Darbepoetin, further therapy is generally considered not medically necessary

- For continuing treatment: will cover a Hct up to and including 36% or a Hgb up to and including 12 g/dL for 2 months

**C. Members with HIV/AIDS with anemia due to the drug Zidovudine (AZT):**

- Erythropoetin is indicated for Members with an endogenous serum erythropoetin level equal to or less than 500 mUnits/ml and who are receiving a dose of AZT equal to or less than 4200mg/week
- For treatment with Epoetin alfa or Darbepoetin, IEHP will cover a Hematocrit (Hct) up to and including 36% or Hemoglobin (Hgb) up to and including 12 g/dL
- The therapy may be initiated with Epoetin alfa up to 40,000 Units weekly for four (4) weeks and up to 60,000 Units weekly for four (4) more weeks if no response OR Darbepoetin: 2.25 mcg/KG weekly or 500 mcg every 3 weeks for six (6) weeks and up to 4.5 mcg/kg weekly for six (6) more weeks if no response
- If there is no response on initial therapy (less than 3% rise in Hct or less than 1 gram/dl rise in Hgb) after eight (8) weeks of Epoetin alfa or twelve (12) weeks Darbepoetin, further therapy is generally considered not medically necessary
- Adequate iron stores should be demonstrated by means of bone marrow iron or serum ferritin levels (100ng/mL) or serum iron saturation (>20%) studies. Supplemental iron should be administered as indicated

**D. Members with anemia scheduled to undergo elective non-cardiac, non-vascular surgery or those at risk for substantial perioperative blood loss:** Erythropoetin is indicated for reduction of blood transfusions prior to elective hip or knee replacement surgery. The Member should not be a candidate for autologous blood transfusion, is expected to lose more than 2 units of blood and should have a diagnosis of anemia of chronic disease. The treatment regimen should begin 3 weeks prior to surgery

- For treatment with Epoetin alfa or Darbepoetin IEHP will cover a Hemoglobin (Hgb) level greater than or equal to 10 and lesser than or equal to 12.5 grams/dl
- The use of Erythropoetin is not covered when used in conjunction with, prior to, or following phlebotomy for autologous transfusion
- Adequate iron stores should be demonstrated by means of bone marrow iron or serum ferritin levels (100ng/mL) or serum iron saturation (>20%) studies. Supplemental iron should be administered as indicated