RATIONALE FOR INCLUSION IN PA PROGRAM

Background
Epogen, Procrit and Retacrit are erythropoiesis-stimulating agents (ESAs) that bind to progenitor stem cells and stimulates the production and differentiation of red blood cells (RBC). Epogen, Procrit and Retacrit stimulate erythropoiesis by the same mechanism as endogenous erythropoietin. Epogen, Procrit and Retacrit increase the reticulocyte count within 10 days of initiation, followed by increases in the RBC count, hemoglobin, and hematocrit, usually within 2 to 6 weeks. The rate of hemoglobin increase varies among patients and is dependent upon the dose of Epogen, Procrit, or Retacrit being administered. Retacrit is a biosimilar to Epogen. (1-3).

Regulatory Status
FDA-approved indication: Epogen, Procrit and Retacrit are erythropoiesis-stimulating agents (ESA) indicated for: (1-3)

1. Treatment of anemia due to
   a. Chronic Kidney Disease (CKD) in patients on dialysis and not on dialysis.
   b. Zidovudine in HIV-infected patients.
   c. The effects of concomitant myelosuppressive chemotherapy, and upon initiation, there is a minimum of two additional months of planned chemotherapy.

1. Reduction of allogeneic RBC transfusions in patients undergoing elective, non-cardiac, nonvascular surgery

Limitations of Use: (1-3)
Epogen, Procrit and Retacrit have not been shown to improve quality of life, fatigue, or patient wellbeing.

Epogen, Procrit and Retacrit are not indicated for use:

1. In patients with cancer receiving hormonal agents, biologic products, or radiotherapy, unless also receiving concomitant myelosuppressive chemotherapy.

2. In patients with cancer receiving myelosuppressive chemotherapy when the anticipated outcome is cure.

3. In patients with cancer receiving myelosuppressive chemotherapy in whom the anemia can be managed by transfusion
4. In patients scheduled for surgery who are willing to donate autologous blood.
5. In patients undergoing cardiac or vascular surgery.
6. As a substitute for RBC transfusions in patients who require immediate correction of anemia.

**Off-Label Uses:** (4-8)
1. Symptomatic anemia in patients with myelodysplastic syndromes (MDS)
2. Anemia in rheumatoid arthritis
3. Anemia due to hepatitis C treatment with ribavirin in combination with either interferon alfa or peginterferon alfa
4. Allogenic bone marrow transplantation

The FDA defines biosimilar as a biological product that is highly similar to and has no clinically meaningful differences from an existing FDA-approved reference product. A manufacturer developing a proposed biosimilar demonstrates that its product is highly similar to the reference product by extensively analyzing the structure and function of both the reference product and the proposed biosimilar. Minor differences between the reference product and the proposed biosimilar in clinically inactive components are acceptable. Manufacturers must also demonstrate that its proposed biosimilar has no clinically meaningful differences from the reference product in terms of safety, purity, and potency (safety and effectiveness) (9).

Epogen, Procrit and Retacrit carry warnings citing the increased risk of myocardial infarction, stroke, venous thromboembolism, thrombosis of vascular access, and tumor progression or recurrence (1-3).

Myelodysplastic syndromes (MDS) encompass a series of hematological conditions characterized by chronic cytopenias, including anemia, accompanied by abnormal cellular maturation. As a result, patients with MDS are at risk for symptomatic anemia. At least 80 percent of patients are anemic at the time of diagnosis, while about 50 percent have a hemoglobin level less than 10 g/dL. The use of epoetin alfa for the treatment of symptomatic anemia in patients with MDS is an unlabeled or investigational use according to the FDA. However, their use in MDS is supported by the American Society of Hematology (ASH), the American Society of Clinical Oncology (ASCO), and the National Comprehensive Cancer Network (NCCN) (4-5).

Epoetin alfa FEP Clinical Rationale
EPOGEN / PROCRIT (epoetin alfa)
RETACRIT (epoetin alfa-epbx)

Anemia associated with Hepatitis C therapy is a frequent cause of dose reduction or discontinuation of therapy. Clinical recommendation is to reduce the dosage if anemia developed. This reduction increases the likelihood of treatment failure. Addition of an ESA agent allows the optimal probability of treatment success (6).

The National Kidney Foundation Kidney Disease Outcomes Quality Initiative (NKF KDOQI) provides evidence based clinical guidelines for improving treatment and outcomes in patients with kidney disease. Their recommendations for transferrin saturation, serum ferritin and hemoglobin levels establish a standard of care and are incorporated into this criterion (7). Treatment of anemia associated with rheumatoid arthritis has been shown to reduce disease activity (8).

Summary
Epogen, Procrit, and Retacrit are erythropoiesis-stimulating agents (ESAs) that bind to progenitor stem cells and stimulates the production and differentiation of red blood cells (RBC). Epogen, Procrit, and Retacrit stimulate erythropoiesis by the same mechanism as endogenous erythropoietin (1-3).

Prior approval is required to ensure the safe, clinically appropriate and cost effective use of Epogen, Procrit, and Retacrit while maintaining optimal therapeutic outcomes.

References
