Epoetin alfa

Description

Epogen, Procrit (epoetin alfa), Retacrit (epoetin alfa – epbx)

Bolded medications are the preferred products
Epogen is neither preferred nor non-preferred

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.
2. 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

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).

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).

Several sources, such as the Renal Association, recommend therapy with erythropoietin stimulating agents when the hemoglobin level is less than 11 g/dL in patients not on dialysis (9-11).

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) (12).

Related policies
Aranesp

Policy
This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Epogen, Procrit, and Retacrit may be considered medically necessary for the treatment of anemia associated with chronic renal failure, for the treatment of anemia secondary to chemotherapy, for the treatment of anemia in patients who are scheduled to undergo elective, non-cardiac, for the treatment of myelodysplastic syndrome, allogenic bone marrow transplantation, anemia secondary to zidovudine therapy-treated human immunodeficiency virus (HIV) patients, anemia associated with hepatitis C (HCV) treatment, or anemia associated with rheumatoid arthritis/rheumatic disease; and if the conditions indicated below are met.

Epogen, Procrit, and Retacrit may be considered investigational for all other indications.
Prior-Approval Requirements

Diagnoses

Patient must have ONE of the following:

1. Anemia associated with chronic renal failure
   a. Serum ferritin $\geq 100$ ng/ml (labs must have been taken within the last 3 months)

   AND ONE of the following:
   
   If patient is NOT on dialysis
   a. Initial treatment: Hemoglobin < 11 g/dl* (labs must have been taken within the last 3 months)
   b. Continuing treatment: Hemoglobin $\leq 11$ g/dl* (labs must have been taken within the last 3 months)

   If patient is ON dialysis
   a. Initial treatment: Hemoglobin < 10 g/dl* (labs must have been taken within the last 3 months)
   b. Continuing treatment: Hemoglobin $\leq 11$ g/dl* (labs must have been taken within the last 3 months)

   * if the hemoglobin level exceeds this level then the prescribing physician must confirm that the dose will be held or reduced until the hemoglobin level returns to the required level.

2. Anemia secondary to chemotherapy
   a. Concomitant myelosuppressive therapy
   b. There is a minimum of two additional months of planned chemotherapy
   c. Prescriber agrees to discontinue use of Epogen/Procrit upon completion of the chemotherapy
   d. Prescriber agrees that transfusions are NOT an option for treatment (i.e. end organ failure, CKD, high risk bacterial infections)
3. Anemia secondary to zidovudine-treated Human Immunodeficiency Virus (HIV) patients
   a. Endogenous serum erythropoietin levels ≤ 500 mUnits/mL

4. Anemia in patients scheduled to undergo elective, non-cardiac, nonvascular surgery
   a. Hemoglobin >10 and ≤ 13 g/dl

5. Myelodysplastic syndrome

6. Allogenic bone marrow transplantation

7. Anemia associated with Hepatitis C (HCV) treatment

8. Anemia associated with rheumatoid arthritis (RA)/ rheumatic disease

AND the following for ALL diagnoses:
   a. NOT used in combination with another erythropoiesis stimulating agent
   b. **Procrit only:** Patient **MUST** have tried the preferred product (Retacrit) unless the patient has a valid medical exception (e.g. inadequate treatment response, intolerance, contraindication)

**Prior – Approval Renewal Requirements**
Same as above

**Policy Guidelines**

**Pre - PA Allowance**
None

**Prior - Approval Limits**
Duration 6 months

**Prior – Approval Renewal Limits**
Same as above

**Rationale**

**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
### Policy History

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>September 2008</td>
<td>FDA labeling revisions with new indications:</td>
</tr>
<tr>
<td>Epogen / Procrit / Aranesp</td>
<td>- Treatment of Anemia of Chronic Renal Failure Patients</td>
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<tr>
<td></td>
<td>- Treatment of Anemia in Zidovudine-treated HIV-infected Patients (Epogen and Procrit only)</td>
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<tr>
<td></td>
<td>- Treatment of Anemia due to concomitant myelosuppressive chemotherapy- no longer indicated when the anticipated outcome is cure.</td>
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<td></td>
<td>- Reduction of Allogenic Blood Transfusion in Surgery patients (Epogen and Procrit only)</td>
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<td>The August 2008 FDA package insert revisions were two-fold. The first revision was to limit use of any ESA products to patients whom hemoglobin levels are less than 10g/dl. The second revision was to remove the indication for ESA therapy for patients receiving myelosuppressive therapy when the anticipated outcome is cure. Prior to initiation of therapy, the patient’s iron stores should be evaluated. Transferrin saturation should be at least 20% and ferritin at least 100 ng/mL. Individual titration in patients with chronic renal failure should be done to achieve and maintain hemoglobin levels between 10 to 12 g/dL. Procrit and Epogen are indicated for the treatment of anemic patients with hemoglobin levels &gt; 10 to ≤ 13 g/dl who are at risk for perioperative blood loss from elective, noncardiac, nonvascular surgery to reduce the need for allogenic blood transfusions (1).</td>
<td></td>
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<tr>
<td>October 2008</td>
<td>Allowing PA approval for hemoglobin levels outside the recommended levels if the AP confirms that the dose will be held until hemoglobin levels fall within acceptable range will allow for safe use of the medication while making it available for the patient as soon as clinically appropriate.</td>
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<tr>
<td>September 2011</td>
<td>Separation of Aranesp from the other ESAs’ criteria due to differing U.S. Food and Drug administration (FDA) approved indications.</td>
</tr>
<tr>
<td>December 2011</td>
<td>Annual review and update</td>
</tr>
<tr>
<td>June 2012</td>
<td>Add “or reduced,” to “if the hemoglobin level exceeds this level then the prescribing physician must confirm that the dose will be held or reduced until the hemoglobin level returns to the required level.</td>
</tr>
<tr>
<td>December 2012</td>
<td>Annual review and update</td>
</tr>
<tr>
<td>March 2014</td>
<td>Annual review and update.</td>
</tr>
<tr>
<td>March 2014</td>
<td>Removal of TSAT level requirement</td>
</tr>
<tr>
<td>December 2015</td>
<td>Annual editorial review and reference update</td>
</tr>
<tr>
<td>December 2016</td>
<td>Annual review and reference update</td>
</tr>
<tr>
<td>September 2017</td>
<td>Policy code changed from 5.10.06 to 5.85.06</td>
</tr>
</tbody>
</table>
Addition of requirement to anemia secondary to chemotherapy: Patient’s anemia cannot be managed by transfusions
Addition of not used in combination with another erythropoiesis stimulating agent

January 2018
Re-worded the requirements for Anemia secondary to chemotherapy: “Patient’s anemia cannot be managed by transfusions” changed to “Prescriber agrees that transfusions are NOT an option for treatment (i.e. end organ failure, CKD, high risk bacterial infections) and “Must discontinue use of agent upon completion of the chemotherapy” changed to “Prescriber agrees to discontinue use of Epogen/Procrit upon completion of the chemotherapy”

March 2018
Annual review

June 2018
Addition of Retacrit biosimilar to criteria
Change of criteria name to “Epoetin alfa”

September 2018
Annual review and reference update
Addition of off-label indications to Retacrit, addition of requirement of endogenous serum erythropoietin level ≤ 500 mUnits/mL to anemia secondary to zidovudine, and removal of anticipated outcome of therapy is not cure of cancer per SME

September 2019
Annual review

December 2019
Annual review and reference update. Addition of requirement to trial preferred product. Changed required hemoglobin level for patients not on dialysis to be < 11 g/dL from < 10 g/dL

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on December 6, 2019 and is effective on January 1, 2020.