Clinical Policy: Epoetin alfa (Epogen, Procrit)
Reference Number: ERX.SPMN.136
Effective Date: 10/16
Last Review Date: 09/16

See Important Reminder at the end of this policy for important regulatory and legal information.

Policy/Criteria
It is the policy of health plans affiliated with Envolve Pharmacy Solutions® that epoetin alfa (Epogen®, Procrit®) is medically necessary when the following criteria are met:

I. Initial Approval Criteria
   A. Anemia Due to Chronic Kidney Disease (must meet all):
      1. Prescribed by or in consultation with a hematologist or nephrologist;
      2. Diagnosis of anemia of chronic kidney disease (CKD) (dialysis and non-dialysis members);
      3. Does not require immediate correction of anemia;
      4. Other causes of anemia (e.g., vitamin deficiency, metabolic or chronic inflammatory conditions, bleeding, etc.) have been corrected or excluded;
      5. Adequate iron stores as indicated by serum ferritin level ≥ 100 mcg/L or serum transferrin saturation ≥ 20%;
      6. Pretreatment hemoglobin level < 10 g/dL;
      7. For Epogen request: Prior trial and failure of Procrit, or documented clinically significant adverse effects to Procrit.

      Approval duration: 12 weeks

   B. Anemia Due to Zidovudine in HIV-infected Patients (must meet all):
      1. Prescribed by or in consultation with a hematologist or HIV specialist;
      2. Diagnosis of zidovudine-induced anemia;
      3. Member is HIV-positive;
      4. Dose of zidovudine is ≤ 4200 mg/week;
      5. Endogenous serum erythropoietin levels ≤ 500 mUnits/mL;
      6. Does not require immediate correction of anemia;
      7. Other causes of anemia (e.g., vitamin deficiency, metabolic or chronic inflammatory conditions, bleeding, etc.) have been corrected or excluded;
      8. Adequate iron stores as indicated by serum ferritin level ≥ 100 mcg/L or serum transferrin saturation ≥ 20%;
      9. Pretreatment hemoglobin level < 10 g/dL;
      10. For Epogen request: Prior trial and failure of Procrit, or documented adverse effects to Procrit.

      Approval duration: 12 weeks

   C. Anemia due to Chemotherapy in Patients with Cancer (must meet all):

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1. Prescribed by or in consultation with a hematologist or oncologist;
2. Diagnosis of anemia due to chemotherapy;
3. Member has non-myeloid malignancy;
4. Member is receiving concomitant myelosuppressive chemotherapy;
5. There is a minimum of two additional months of planned chemotherapy;
6. Chemotherapy is being given as palliative treatment.
7. Member does not require immediate correction of anemia;
8. Other causes of anemia (e.g., vitamin deficiency, metabolic or chronic inflammatory conditions, bleeding, etc.) have been corrected or excluded;
9. Adequate iron stores as indicated by serum ferritin level ≥ 100 mcg/L or serum transferrin saturation ≥ 20%;
10. Pretreatment hemoglobin < 10 g/dL;
11. For Epogen request: Prior trial and failure of Procrit, or documented adverse effects to Procrit.

Approval duration: 8 weeks or duration of chemotherapy course (whichever is less)

D. Reduction of Allogeneic Red Blood Cell Transfusions in Patients Undergoing Elective, Noncardiac, Nonvascular Surgery (must meet all):
1. Member is at high risk for perioperative blood loss from elective, noncardiac, nonvascular surgery;
2. Member does not require immediate correction of anemia;
3. Other causes of anemia (e.g., vitamin deficiency, metabolic or chronic inflammatory conditions, bleeding, etc.) have been corrected or excluded;
4. Perioperative hemoglobin > 10 to ≤ 13 g/dL;
5. Adequate iron stores as demonstrated by serum ferritin level ≥ 100 mcg/L or serum transferrin saturation ≥ 20%;
6. Member is unwilling or unable to donate autologous blood pre-operatively;
7. For Epogen request: Prior trial and failure of Procrit, or documented clinically significant adverse effects to Procrit.

Approval duration: 15 days (for 300 units/kg daily) OR 21 days (for 600 units/kg in 4 doses)

E. Anemia Secondary to Combination Ribavirin and Interferon-Alfa Therapy in Patients Infected with Hepatitis C Virus (must meet all):
1. Diagnosis of anemia secondary to combination ribavirin and interferon-alfa therapy for treatment of hepatitis C;
2. Member does not require immediate correction of anemia;
3. Other causes of anemia (e.g., vitamin deficiency, metabolic or chronic inflammatory conditions, bleeding, etc.) have been corrected or excluded;
4. Pretreatment hemoglobin < 10 g/dL, despite ribavirin dose reduction;
5. Adequate iron stores as indicated by serum ferritin level ≥ 100 mcg/L or serum transferrin saturation ≥ 20%;
6. For Epogen request: Prior trial and failure of Procrit, or documented clinically significant adverse effects to Procrit.
**Approval duration: 12 weeks, or duration of ribavirin treatment (whichever is less)**

**F. Anemia Associated with Myelodysplastic Syndromes** (must meet all):
1. Diagnosis of anemia from myelodysplastic syndrome;
2. Serum erythropoietin ≤ 500 mU/mL;
3. Member does not require immediate correction of anemia;
4. Other causes of anemia (e.g., vitamin deficiency, metabolic or chronic inflammatory conditions, bleeding, etc.) have been corrected or excluded;
5. Adequate iron stores as indicated by serum ferritin level ≥ 100 mcg/L or serum transferrin saturation ≥ 20%;
6. Pretreatment hemoglobin < 10 g/dL;
7. For Epogen request: Prior trial and failure of Procrit, or documented clinically significant adverse effects to Procrit.

**Approval duration: 12 weeks**

**G. Other diagnoses/indications:** Refer to ERX.SPMN.16 - Global Biopharm Policy.

**II. Continued Approval**

**A. Anemia due to CKD** (must meet all):
1. Currently receiving medication via health plan benefit or member has previously met all initial approval criteria;
2. Hemoglobin is responsive to erythropoiesis-stimulant agent (ESA) therapy;
3. Documented evidence of adequate iron stores as indicated by serum ferritin level
   \[ \geq 100 \text{ mcg/L or serum transferrin saturation } \geq 20\% \text{ within the last 3 months}; \]
4. Current hemoglobin is one of the following:
   a. If on dialysis: \( \leq 11 \text{ g/dL} \);
   b. Not on dialysis: \( \leq 10 \text{ g/dL} \).

**Approval duration: 12 weeks**

**B. Anemia due to Zidovudine in HIV-infected Patients** (must meet all):
1. Currently receiving medication via health plan benefit or member has previously met all initial approval criteria;
2. Current hemoglobin level is \( \leq 12 \text{ g/dL} \);
3. Documented evidence of adequate iron stores as indicated by serum ferritin level
   \[ \geq 100 \text{ mcg/L or serum transferrin saturation } \geq 20\% \text{ within the last 3 months}. \]

**Approval duration: 12 weeks**

**C. Anemia due to Chemotherapy in Patients with Cancer** (must meet all):
1. Currently receiving medication via health plan benefit or member has previously met all initial approval criteria;
2. Continuation of ESA therapy is concurrent with myelosuppressive chemotherapy;
3. Length of therapy is one of the following:
   a. Has received < 8 weeks of ESA therapy;
   b. Has received ≥ 8 weeks of ESA therapy and both of the following:
      i. Documented evidence of response to therapy as measured by rise in hemoglobin levels > 1 g/dL;
      ii. No RBC transfusions are required;
4. Current hemoglobin < 10 g/dL;
5. Documented evidence of adequate iron stores as indicated by serum ferritin level ≥ 100 mcg/L or serum transferrin saturation ≥ 20% within the last 3 months.

Approval duration:
For member who has received < 8 weeks of ESA therapy: 8 weeks;
For member who has received ≥ 8 weeks of ESA therapy: 8 weeks or until completion of chemotherapy course, whichever is less

D. Reduction of Allogeneic Red Blood Cell Transfusions in Patients Undergoing Elective, Noncardiac, Nonvascular Surgery
   1. Continuation of therapy will not be granted for this indication.

E. Anemia Secondary to Combination Ribavirin and Interferon-Alfa Therapy in Patients Infected with Hepatitis C Virus (must meet all):
   1. Currently receiving medication via health plan benefit or member has previously met all initial approval criteria;
   2. Current hemoglobin ≤ 12 g/dL;
   3. Documented evidence of adequate iron stores as indicated by serum ferritin level ≥ 100 mcg/L or serum transferrin saturation ≥ 20% within the last 3 months.

Approval duration: 12 weeks or duration of ribavirin therapy, whichever is less

F. Anemia Associated with Myelodysplastic Syndrome (must meet all):
   1. Currently receiving medication via health plan benefit or member has previously met all initial approval criteria;
   2. Current hemoglobin ≤ 12 g/dL;
   3. Documented evidence of adequate iron stores as indicated by serum ferritin level ≥ 100 mcg/L or serum transferrin saturation ≥ 20% within the last 3 months.
Approval duration: 12 weeks

G. Other diagnoses/indications (must meet 1 or 2):
   1. Currently receiving medication via health plan benefit and documentation supports positive response to therapy; or
   2. Refer to ERX.SPMN.16 - Global Biopharm Policy.

Background

Description/Mechanism of Action:
Epoetin alfa is an erythropoiesis-stimulant agent (ESA). It stimulates erythropoiesis by the same mechanism as endogenous erythropoietin.

FDA Approved Indications:
Epogen and Procrit are ESAs/injections for intravenous or subcutaneous use indicated for:
- Treatment of anemia due to:
  - CKD in patients on dialysis and not on dialysis.
  - Zidovudine in HIV-infected patients.
  - The effects of concomitant myelosuppressive chemotherapy, and upon initiation, there is a minimum of two additional months of planned chemotherapy.
- Reduction of allogeneic red blood cell transfusions in patients undergoing elective, noncardiac, nonvascular surgery.

Limitations of Use
- Epogen and Procrit have not been shown to improve quality of life, fatigue, or patient well-being.
- Epogen and Procrit are not indicated for use:
  - In patients with cancer receiving hormonal agents, biologic products, or radiotherapy, unless also receiving concomitant myelosuppressive chemotherapy.
  - In patients with cancer receiving myelosuppressive chemotherapy when the anticipated outcome is cure.
  - In patients scheduled for surgery who are willing to donate autologous blood.
  - In patients undergoing cardiac or vascular surgery.
  - As a substitute for red blood cell transfusions in patients who require immediate correction of anemia.

Appendices

Appendix A: Abbreviation Key
CKD: chronic kidney disease
ESA: erythropoiesis-stimulating agent
HIV: human immunodeficiency virus
PRCA: pure red cell aplasia
Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

<table>
<thead>
<tr>
<th>HCPCS Codes</th>
<th>Description</th>
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<tbody>
<tr>
<td>Q4081</td>
<td>Injection, epoetin alfa, 100 units (for ESRD on dialysis)</td>
</tr>
<tr>
<td>J0885</td>
<td>Injection, epoetin alfa, (for non-ESRD use), 1000 units</td>
</tr>
<tr>
<td>J0882</td>
<td>Injection, darbepoetin alfa, 1 mcg (for ESRD on dialysis)</td>
</tr>
<tr>
<td>J0881</td>
<td>Injection, darbepoetin alfa, 1 mcg (non-ESRD use)</td>
</tr>
</tbody>
</table>

Reviews, Revisions, and Approvals

| Policy split from USS.SPMN.13 Erythropoiesis Stimulating Agents and converted to new template. Removed all safety criteria and requests for documentation. Added requirement for adequate iron stores and exclusion of all other causes of anemia. -Anemia due to chemo: added requirement for current Hgb < 10 g/dL per CMS policy. -Anemia of CKD: added Hgb requirement for pediatric patients and modified criteria to allow for continued therapy after 12 weeks. -Anemia due to MDS: removed approval for members with Hgb > 12 g/dL. -Anemia due to HCV treatment: added duration of ribavirin treatment (whichever is less) to initial approval duration. -Zidovudine-induced anemia: removed dose adjustment criteria and simplified specific Hgb levels to Hgb ≤ 12 g/dL. | Date | Approval Date |
|-------------|------------------------------------------------------------------------------|------|--------------|
| 08/16       | 09/16                                                                        |

References


**Important Reminder**
This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This policy is the property of Envolve Pharmacy Solutions. Unauthorized copying, use, and distribution of this Policy or any information contained herein is strictly prohibited. By accessing this policy, you agree to be bound by the foregoing terms and conditions, in addition to the Site Use Agreement for Health Plans associated with Envolve Pharmacy Solutions.

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