Clinical Policy: Epoetin alfa (Epogen and Procrit), Epoetin alfa-epbx (Retacrit

Reference Number: PA.CP.PHAR.237
Effective Date: 01/18
Last Review Date: 04/19

Coding Implications
Revision Log

Description
The following are erythropoiesis-stimulating agents (ESA) requiring prior authorization: epoetin alfa (Epogen® and Procrit®) and epoetin alfa-epbx (Retacrit™).

FDA Approved Indication(s)
Epogen and Procrit are indicated for:

- Treatment of anemia due to:
  - Chronic kidney disease (CKD) in patients on dialysis and not on dialysis.
  - Zidovudine in patients with HIV-infection.
  - 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 (RBC) transfusions in patients undergoing elective, noncardiac, nonvascular surgery.

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

Policy/Criteria
It is the policy of Pennsylvania Health and Wellness® that Epogen or 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. Diagnosis of anemia of chronic kidney disease (CKD) (dialysis and non-dialysis members);
2. Prescribed by or in consultation with a hematologist or nephrologist;

3. Adequate iron stores as indicated by current (within the last 3 months) serum ferritin level ≥ 100mcg/L or serum transferrin saturation ≥ 20%;
4. Pretreatment hemoglobin level < 10g/dL;

Approval Duration: 6 months

B. Anemia due to Zidovudine in HIV-infected Patients (must meet all)**:**

1. Diagnosis of zidovudine induced anemia;
2. Prescribed by or in consultation with a hematologist or HIV specialist;
3. Member is HIV-positive;
4. Dose of zidovudine is ≤ 4200mg/week;
5. Endogenous serum erythropoietin levels ≤ 500 mUnits/mL;
6. Adequate iron stores as indicated by current (within the last 3 months) serum ferritin level ≥ 100mcg/L or serum transferrin saturation ≥ 20%;
7. Pretreatment hemoglobin level < 10g/dL;

Approval Duration: 6 months

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

1. Diagnosis of anemia due to chemotherapy;
2. Prescribed by or in consultation with a hematologist or oncologist;
3. Age ≥ 5 years;
4. Adequate iron stores as indicated by current (within the last 3 months) serum ferritin level ≥ 100mcg/L or serum transferrin saturation ≥ 20%;
5. Pretreatment hemoglobin < 10g/dL;

Approval Duration: 6 months or until the completion 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. Perioperative hemoglobin > 10 to ≤ 13g/dL;
3. Adequate iron stores as indicated by current (within the last 3 months) serum ferritin level ≥ 100mcg/L or serum transferrin saturation ≥ 20%;
4. Member is unwilling or unable to donate autologous blood pre-operatively;

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

E. Anemia Associated with Myelodysplastic Syndromes (off-label) (must meet all):

1. Diagnosis of anemia from myelodysplastic syndrome (MDS);
2. Prescribed by or in consultation with a hematologist or oncologist;
3. Age ≥ 18 years;
4. Current (within the last 3 months) Serum erythropoietin (EPO) ≤ 500 mU/mL;
5. Adequate iron stores as indicated by current (within the last 3 months) serum ferritin level ≥ 100mcg/L or serum transferrin saturation ≥ 20%;
6. Pretreatment hemoglobin < 10g/dL;

Approval Duration: 6 months

F. Myelofibrosis-Associated Anemia (off-label) (must meet all)**:**
1. Diagnosis of anemia associated with myelofibrosis;
2. Prescribed by or in consultation with a hematologist or oncologist;
3. Age ≥ 18 years;
4. Current (within the last 3 months) serum EPO < 500 mU/mL;
5. Adequate iron stores as indicated by current (within the last 3 months) serum ferritin level ≥ 100 mcg/L or serum transferrin saturation ≥ 20%.

Approval Duration: 6 months

G. Other diagnoses/indications:
1. Refer to PA.CP.PMN.53 if member has adequate iron stores as indicated by current (within the last 3 months) serum ferritin level ≥ 100mcg/L or serum transferrin saturation ≥ 20%;
2. Additional Epogen/Procrit uses outlined in the NCCN compendium, and which meet NCCN category 1, 2a, or 2b are covered.

II. Continued Approval

A. Anemia due to CKD (must meet all):
1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met initial approval criteria or the Continuity of Care policy applies;
2. Member is responding positively to therapy;
3. Adequate iron stores as indicated by current (within the last 3 months) serum ferritin level ≥ 100mcg/L or serum transferrin saturation ≥ 20%;

Approval Duration: 6 months

B. Anemia due to Zidovudine in HIV-infected Patients (must meet all)**:**
1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met initial approval criteria or the Continuity of Care policy applies;
2. Current hemoglobin level is ≤ 12g/dL;
3. Adequate iron stores as indicated by current (within the last 3 months) serum ferritin level ≥ 100mcg/L or serum transferrin saturation ≥ 20%.

Approval Duration: 6 months

C. Anemia due to Chemotherapy in Patients with Cancer (must meet all):
1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met initial approval criteria or the Continuity of Care policy applies;
2. Continuation of ESA therapy is concurrent with myelosuppressive chemotherapy;
3. If member has received ≥ 8 weeks of ESA therapy and both of the following (a and b):
   a. Documented evidence of response to therapy as measured by rise in hemoglobin levels >1g/dL;
   b. No RBC transfusions are required;
4. Current hemoglobin < 12g/dL;

5. Adequate iron stores as indicated by current (within the last 3 months) serum ferritin level ≥ 100mcg/L or serum transferrin saturation ≥ 20%.

Approval Duration:
6 months or until the 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 Associated with Myelodysplastic Syndrome (off-label) (must meet all):
1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met initial approval criteria or the Continuity of Care policy applies;
2. Member is responding positively to therapy;
3. Current hemoglobin ≤ 12g/dL;
4. Adequate iron stores as indicated by current (within the last 3 months) serum ferritin level ≥ 100mcg/L or serum transferrin saturation ≥ 20%.

Approval Duration: 6 months

F. Myelofibrosis-Associated Anemia (off-label) (must meet all)**:**
1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met initial approval criteria or the Continuity of Care policy applies;
2. Member is responding positively to therapy;
3. Adequate iron stores as indicated by current (within the last 3 months) serum ferritin level ≥ 100 mcg/L or serum transferrin saturation ≥ 20%.

Approval duration: 6 months

G. Other diagnoses/indications: (1 or 2)
1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met initial approval criteria or the Continuity of Care policy applies;
   Approval Duration: duration of request or 6 months (whichever is less); or
2. Refer to PA.CP.PMN.53

III. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CKD: chronic kidney disease
ESA: erythropoiesis-stimulating agent
FDA: Food and Drug Administration
HIV: human immunodeficiency virus
RBC: red blood cell

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s):

- Uncontrolled hypertension
- Pure red cell aplasia (PRCA) that begins after treatment with erythropoietin protein drugs
- Allergic reactions
- Epogen/Procrit - Use of the multiple-dose vials containing benzyl alcohol in neonates, infants, pregnant women, and lactating women

- Boxed warning(s): ESAs increase the risk of death, myocardial infarction, stroke, venous thromboembolism, thrombosis of vascular access and tumor progression or recurrence

IV. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Anemia due to CKD	Initial dose: 50 to 100 Units/kg 3 times weekly (adults) IV or SC and 50 Units/kg 3 times weekly (children on dialysis) IV or SC. Individualize maintenance dose. IV route recommended for patients on hemodialysis	Varies depending on indication and frequency of administration
Anemia due to zidovudine in HIV-infected patients	100 Units/kg IV or SC 3 times weekly	
Anemia due to chemotherapy	40,000 Units SC weekly *or* 150 Units/kg SC 3 times weekly (adults) until completion of a chemotherapy course; 600 Units/kg IV weekly (children ≥ 5 years) until completion of a chemotherapy course	
Reduction of allogeneic red blood cell transfusions in patients undergoing elective, noncardiac, nonvascular surgery	300 Units/kg per day SC daily for 15 days total: administered daily for 10 days before surgery, on the day of surgery, and for 4 days after surgery or 600 Units/kg SC weekly in 4 doses administered 21, 14, and 7 days before surgery and on the day of surgery	
Anemia associated with MDS†	40,000-60,000 units SC one to two times weekly	
Anemia associated with myelofibrosis†	In a clinical trial, patients initially received erythropoietin 10,000 units SC 3 days per week. Erythropoietin was increased to 20,000 units 3 days per week if a response was not obtained after 2 months and erythropoietin was discontinued in patients who did not experience a response at 3 months.	

†*Off-label indication*

V. Product Availability

Drug Name	Availability
Epoetin alfa (Epogen)	• Single-dose vial: 2,000 units/mL, 3,000 units/mL, 4,000 units/mL, and 10,000 units/mL

Drug Name	Availability
	• Multiple-dose vial containing benzyl alcohol: 20,000 units/2 mL and 20,000 units/mL
Epoetin alfa (Procrit)	• Single-dose vial: 2,000 units/mL, 3,000 units/mL, 4,000 units/mL, 10,000 units/mL, and 40,000 units/mL • Multiple-dose vial containing benzyl alcohol: 20,000 units/2 mL and 20,000 units/mL
Epoetin alfa-epbx (Retacrit)	• Single-dose vial: 2,000 units/mL, 3,000 units/mL, 4,000 units/mL, 10,000 units/mL, 40,000 units/mL

VI. References

1. Epogen Prescribing Information. Thousand Oaks, CA: Amgen Inc.; July 2018. Available at http://www.epogen.com/. Accessed January 30, 2019.
2. Procrit Prescribing Information. Thousand Oaks, CA: Amgen Inc.; July 2018. Available at http://www.procrit.com/. Accessed January 30, 2019.
3. Rizzo JD, Brouwers M, Hurley P, et al (2010). American Society of Hematology/American Society of Clinical Oncology clinical practice guideline update on the use of epoetin and darbepoetin in adult patients with cancer. Blood 2010; 116(20):4045-4059. Accessed January 4, 2018. https://doi.org/10.1182/blood-2010-08-300541.
4. Mancino P, Falasca K, Ucciferri C, Pizzigallo E, Vecchiet J. Use of Hematopoietic Growth Factor in the Management of Hematological Side Effects Associated to Antiviral Treatment for Hcv Hepatitis. Mediterranean Journal of Hematology and Infectious Diseases. 2010;2(1):e2010003. doi:10.4084/MJHID.2010.003.
5. Afdhal NH, Dieterich DT, et al. Epoetin alfa maintains ribavirin dose in HCV-infected patients: a prospective, double-blind, randomized controlled study. Gastroenterology. 2004 May;126(5):1302-11.
6. Epoetin alfa. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at NCCN.org. Accessed January 30, 2019.
7. Myelodysplastic Syndromes (Version 2.2019). In: National Comprehensive Cancer Network Guidelines. Available at www.nccn.org. Accessed January 30, 2019.
8. Myeloproliferative Neoplasms (Version 2.2019). In National Comprehensive Cancer Network Guidelines. Available at www.nccn.org. Accessed January 24, 2019.
9. Cancer and Chemotherapy Induced Anemia (Version 3.2018). In National Comprehensive Cancer Network Guidelines. Available at www.nccn.org. Accessed January 30, 2019.
10. Epoetin Alfa Drug Monograph. Clinical Pharmacology. Accessed January 30, 2019. http://www.clinicalpharmacology-ip.com.
11. DRUGDEX® System [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed January 30, 2019.
12. Retacrit Prescribing Information. Lake Forest, IL: Hospira, Inc., January 2019. Available at https://www.pfizerpro.com/product/retacrit/hcp. Accessed January 30, 2019.

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.

HCPCS Codes	Description
Q4081	Injection, epoetin alfa, 100 units (for ESRD on dialysis)
J0885	Injection, epoetin alfa, (for non-ESRD use), 1000 units
J0882	Injection, darbepoetin alfa, 1 mcg (for ESRD on dialysis)
J0881	Injection, darbepoetin alfa, 1 mcg (non-ESRD use)

Reviews, Revisions, and Approvals	Date	Approval Date
2Q 2018 annual review: added age where relevant approval duration modified to allow no less than 6 months for initial/continued approval; clarified that the lab for serum EPO should be current (within the past 3 months) for MDS; added requirement for positive response to therapy on re-auth; added criteria for MF-associated anemia; references reviewed and updated.	02.06.18	
2Q 2019 annual review: added NCCN compendium supported uses for myelofibrosis-associated anemia; added requirement for Endogenous serum erythropoietin levels ≤ 500 mUnits/mL for Anemia due to zidovudine; removed anemia secondary to combination ribavirin and interferon-alfa therapy in patients infected with hepatitis C virus off label uses since DrugDex IIb not covered; Per FFS guidance changed hemoglobin threshold to< 12g/dL in the continued approval for anemia due to chemotherapy in patients with cancer; references reviewed and updated.	04/19	