RXADVANCE
2 Park Central Drive
Southborough, MA 01772

Clinical Policy Title:	epoetin alfa, epoetin alfa-epbx
Policy Number:	RxA.265
Drug(s) Applied:	Epogen®, Procrit®, Retacrit™
Original Policy Date:	02/07/2020
Last Review Date:	09/14/2020
Line of Business Policy Applies to:	All line of business

Background

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

- Treatment of anemia due to:
  - Chronic kidney disease (CKD) in patients on dialysis and not on dialysis.
  - Zidovudine in patients with human immunodeficiency virus -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:

- ESAs have not been shown to improve quality of life, fatigue, or patient well-being.
- ESAs 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.

Dosing Information			
Drug Name	**Indication**	**Dosing Regimen**	**Maximum Dose**
epoetin alfa (Epogen®, Procrit®) epoetin alfa-epbx (Retacrit™)	Anemia due to chronic kidney disease	Initial dose: 50 to 100 Units/kg three times weekly (adults) IV or SC and 50 Units/kg three times weekly (children on dialysis) IV or SC. Individualize maintenance dose. Intravenous route is 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 three times weekly	Varies depending on indication and frequency of administration
	Anemia due to chemotherapy	40,000 Units SC weekly or 150 Units/kg SC three times weekly (adults) until completion of a chemotherapy course; 600 Units/kg IV weekly (children 5 years of age or older) until completion of a chemotherapy course	Varies depending on indication and frequency of administration
	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	Varies depending on indication and frequency of administration
	Anemia associated with MDS†	40,000-60,000 units SC one to two times weekly	Varies depending on indication and frequency of administration
	Anemia associated with myelofibrosis†	In a clinical trial, patients initially received erythropoietin 10,000 units SC three days per week. Erythropoietin was increased to 20,000 units three 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.	Varies depending on indication and frequency of administration

† *Off-label indication*

Dosage Forms

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

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

I. Initial Approval Criteria

A. Anemia due to chronic kidney disease (must meet all):

1. Diagnosis of anemia of chronic kidney disease (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 of 100 mcg/L or serum transferrin saturation of 20% or greater;
4. Pre-treatment hemoglobin level less than 10 g/dL;
5. If Epogen® or Procrit® is requested, failure of Retacrit™ unless contraindicated or clinically significant adverse effects are experienced.

Approval Duration
Commercial: 6 months
Medicaid: 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 human immunodeficiency virus specialist;
3. Member is human immunodeficiency virus-positive;
4. Dose of zidovudine is 4,200 mg/week or less;
5. Current (within the last 3 months) endogenous serum erythropoietin levels is 500 mU/mL or less;
6. Adequate iron stores as indicated by current (within the last 3 months) serum ferritin level of 100 mcg/L or serum transferrin saturation of 20% or greater;
7. Pre-treatment hemoglobin level less than 10 g/dL;
8. If Epogen® or Procrit® is requested, failure of Retacrit™ unless contraindicated or clinically significant adverse effects are experienced.

Approval Duration
Commercial: 6 months
Medicaid: 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 of age or older;
4. Adequate iron stores as indicated by current (within the last 3 months) serum ferritin level of 100 mcg/L or greater or serum transferrin saturation of 20% or greater;
5. Pre-treatment hemoglobin level less than 10 g/dL;
6. If Epogen® or Procrit® is requested, failure of Retacrit™ unless contraindicated or clinically significant adverse effects are experienced.

Approval Duration
Commercial: Until the completion of chemotherapy course or 6 months, whichever is longer
Medicaid: Until the completion of chemotherapy course or 6 months, whichever is longer

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 is greater than 10 but not greater than 13 g/dL;
3. Adequate iron stores as indicated by current (within the last 3 months) serum ferritin level of 100 mcg/L or greater or serum transferrin saturation of 20% or greater;
4. Member is unwilling or unable to donate autologous blood pre-operatively;
5. If Epogen® or Procrit® is requested, failure of Retacrit™ unless contraindicated or clinically significant adverse effects are experienced.

Approval Duration
Commercial: 15 days (for 300 Units/kg daily) or 21 days (for 600 Units/kg in 4 doses)
Medicaid: 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 of age or older;
4. Current (within the last 3 months) endogenous serum erythropoietin (EPO) is 500 mU/mL or less;
5. Adequate iron stores as indicated by current (within the last 3 months) serum ferritin level of 100 mcg/L or greater or serum transferrin saturation of 20% or greater;
6. Pre-treatment hemoglobin level less than 10 g/dL;
7. If Epogen® or Procrit® is requested, failure of Retacrit™ unless contraindicated or clinically significant adverse effects are experienced.

Approval Duration
Commercial: 6 months
Medicaid: 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 of age or older;
4. Current (within the last 3 months) endogenous serum erythropoietin (EPO) is 500 mU/mL or less;
5. Adequate iron stores as indicated by current (within the last 3 months) serum ferritin level of 100 mcg/L or greater or serum transferrin saturation of 20% or greater;
6. If Epogen® or Procrit® is requested, failure of Retacrit™ unless contraindicated or clinically significant

adverse effects are experienced.

Approval Duration
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

A. Anemia due to chronic kidney disease (must meet all):
1. Currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy;
2. Member is responding positively to therapy;
3. Adequate iron stores as indicated by current (within the last 3 months) serum ferritin level of 100 mcg/L or greater or serum transferrin saturation of 20% or greater.

Approval Duration
Commercial: 6 months
Medicaid: 6 months

B. Anemia due to zidovudine in HIV-infected patients (must meet all):
1. Currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy;
2. Current hemoglobin level is 12 g/dL or less;
3. Adequate iron stores as indicated by current (within the last 3 months) serum ferritin level of 100 mcg/L or greater or serum transferrin saturation of 20% or greater.

Approval Duration
Commercial: 6 months
Medicaid: 6 months

C. Anemia due to chemotherapy in patients with cancer (must meet all):
1. Currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy;
2. Continuation of ESA therapy is concurrent with myelosuppressive chemotherapy;
3. If member has received greater than or equal to 8 weeks of ESA therapy, member meets both of the following (a and b):
    a. Documented evidence of response to therapy as evidenced by rise in hemoglobin levels of 1g/dL or greater;
    b. No RBC transfusions are required;
4. Current hemoglobin less than 10 g/dL;
5. Adequate iron stores as indicated by current (within the last 3 months) serum ferritin level of 100 mcg/L or greater or serum transferrin saturation of 20% or greater.

Approval Duration
Commercial: Until the completion of chemotherapy course or 6 months, whichever is longer
Medicaid: Until the completion of chemotherapy course or 6 months, whichever is longer

D. Reduction of allogeneic red blood cell transfusions in patients undergoing elective, noncardiac, nonvascular Surgery
1. Re-authorization is not permitted.

Approval Duration: Not Applicable

E. Anemia Associated with myelodysplastic syndrome (off-label) (must meet all):

1. Currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy;
2. Member is responding positively to therapy;
3. Current hemoglobin is 12 g/dL or less;
4. Adequate iron stores as indicated by current (within the last 3 months) serum ferritin level of 100 mcg/L or greater or serum transferrin saturation of 20% or greater.

Approval Duration
Commercial: 6 months
Medicaid: 6 months

F. Myelofibrosis-associated anemia (off-label) (must meet all):

1. Currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy;
2. Member is responding positively to therapy;
3. Adequate iron stores as indicated by current (within the last 3 months) serum ferritin level of 100 mcg/L or greater or serum transferrin saturation of 20% or greater.

Approval Duration
Commercial: 6 months
Medicaid: 6 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
CKD: Chronic Kidney Disease
ESA: Erythropoiesis-Stimulating Agent
FDA: Food and Drug Administration
HIV: Human Immunodeficiency Virus
IV: Intravenous
RBC: Red Blood Cell
SC: Subcutaneous

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):
  - Erythropoiesis-stimulating agents increase the risk of death, myocardial infarction, stroke, venous thromboembolism, thrombosis of vascular access and tumor progression or recurrence

References

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Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	01/2020	02/07/2020
Policy Reviewed. 1. Formatting updated. 2. References updated. 3. Clinical policy title updated. 4. Drug(s) Applied updated. 5. Line of Business updated. 6. Continued therapy criteria updated.	06/30/2020	9/14/2020