

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

Reference Number: CP.CPA.321

Effective Date: 06.01.18

Last Review Date: 05.19

Line of Business: Commercial

[Coding Implications](#)
[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

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, Procrit, and Retacrit 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, Procrit, and Retacrit have not been shown to improve quality of life, fatigue, or patient well-being.
- Epogen Procrit, and Retacrit 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

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

It is the policy of health plans affiliated with Centene Corporation® that Epogen, Procrit, and Retacrit are **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 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 ≥ 100 mcg/L or serum transferrin saturation $\geq 20\%$;
4. Pretreatment hemoglobin level < 10 g/dL;
5. If Epogen or Retacrit is requested, failure of Procrit unless contraindicated or clinically significant adverse effects are experienced.

Approval duration: 6 months or to member's renewal period, whichever is longer

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 $\leq 4,200$ mg/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 ≥ 100 mcg/L or serum transferrin saturation $\geq 20\%$;
7. Pretreatment hemoglobin level < 10 g/dL;
8. If Epogen or Retacrit is requested, failure of Procrit unless contraindicated or clinically significant adverse effects are experienced.

Approval duration: 6 months or to member's renewal period, whichever is longer

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 ≥ 100 mcg/L or serum transferrin saturation $\geq 20\%$;
5. Pretreatment hemoglobin < 10 g/dL;
6. If Epogen or Retacrit is requested, failure of Procrit unless contraindicated or clinically significant adverse effects are experienced.

Approval duration: Until the completion of chemotherapy course, 6 months, or to member's renewal date, 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 > 10 to ≤ 13 g/dL;
3. Adequate iron stores as indicated by current (within the last 3 months) serum ferritin level ≥ 100 mcg/L or serum transferrin saturation $\geq 20\%$;
4. Member is unwilling or unable to donate autologous blood pre-operatively;

5. If Epogen or Retacrit is requested, failure of Procrit unless contraindicated or clinically significant adverse effects are experienced.

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 \geq 18 years;
4. Current (within the last 3 months) serum erythropoietin (EPO) \leq 500 mU/mL;
5. Adequate iron stores as indicated by current (within the last 3 months) serum ferritin level \geq 100 mcg/L or serum transferrin saturation \geq 20%;
6. Pretreatment hemoglobin $<$ 10 g/dL;
7. If Epogen or Retacrit is requested, failure of Procrit unless contraindicated or clinically significant adverse effects are experienced.

Approval duration: 6 months or to member's renewal period, whichever is longer

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 \geq 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 \geq 100 mcg/L or serum transferrin saturation \geq 20%;
6. If Epogen or Retacrit is requested, failure of Procrit unless contraindicated or clinically significant adverse effects are experienced.

Approval duration: 6 months or to member's renewal period, whichever is longer

G. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial.

II. Continued Therapy

A. Anemia due to Chronic Kidney Disease (must meet all):

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. Adequate iron stores as indicated by current (within the last 3 months) serum ferritin level \geq 100 mcg/L or serum transferrin saturation \geq 20%.

Approval duration: 6 months or to the member's renewal date, whichever is longer

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

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Current hemoglobin level is \leq 12 g/dL;

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

Approval duration: 6 months or to the member's renewal date, whichever is longer

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

1. Currently receiving medication via Centene benefit or member has previously met all initial approval criteria;
2. Continuation of ESA therapy is concurrent with myelosuppressive chemotherapy;
3. If member has received ≥ 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 >1 g/dL;
 - b. No RBC transfusions are required;
4. Current hemoglobin < 10 g/dL;
5. Adequate iron stores as indicated by current (within the last 3 months) serum ferritin level ≥ 100 mcg/L or serum transferrin saturation $\geq 20\%$.

Approval duration: Until the completion of chemotherapy course, 6 months, or to member's renewal date, whichever is longer

D. Reduction of Allogeneic Red Blood Cell Transfusions in Patients Undergoing Elective, Noncardiac, Nonvascular Surgery

1. Re-authorization is not permitted. Members must meet the initial approval criteria.

Approval duration: Not applicable

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

1. Currently receiving medication via Centene benefit or member has previously met all initial approval criteria;
2. Member is responding positively to therapy;
3. Current hemoglobin ≤ 12 g/dL;
4. Adequate iron stores as indicated by current (within the last 3 months) serum ferritin level ≥ 100 mcg/L or serum transferrin saturation $\geq 20\%$.

Approval Duration: 6 months or to the member's renewal date, whichever is longer

F. Myelofibrosis-Associated Anemia (off-label) (must meet all):

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
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 $\geq 20\%$.

Approval duration: 6 months or to the member's renewal date, whichever is longer

G. Other diagnoses/indications (must meet 1 or 2):

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.

Approval duration: Duration of request or 6 months (whichever is less); or

2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial.

III. Diagnoses/Indications for which coverage is NOT authorized:

- A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – CP.CPA.09 for commercial or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

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

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

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Anemia due to CKD	Initial dose: 50 to 100 units/kg 3 times weekly (adults) intravenously (IV) or subcutaneously (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 <i>or</i> 150 units/kg SC 3 times weekly (adults) until completion of a chemotherapy course; 600 units/kg IV weekly (children ≥ 5 years)	

Indication	Dosing Regimen	Maximum Dose
	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

VI. Product Availability

Drug Name	Availability
Epoetin alfa (Epogen)	<ul style="list-style-type: none"> 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)	<ul style="list-style-type: none"> 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)	<ul style="list-style-type: none"> Single-dose vial: 2,000 units/mL, 3,000 units/mL, 4,000 units/mL, 10,000 units/mL, 40,000 units/mL

VII. 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
Q5105	Injection, epoetin alfa, biosimilar, (Retacrit) (for ESRD on dialysis), 100 units
Q5106	Injection, epoetin alfa, biosimilar, (Retacrit) (for non-ESRD use), 1000 units

Reviews, Revisions, and Approvals	Date	P&T Approval Date
New policy created: split from CP.CPA.75 Hematopoietic Agents (Aranesp, Epogen, Mircera, Procrit); added specialist requirement and criteria related to adequate iron stores; anemia due to CKD: added requirement for pretreatment hemoglobin level; removed requirement related to dosage reduction per hemoglobin level on re-auth since it is not a hard stop to discontinue and specialist is involved in care; anemia due to zidovudine: added requirements related to HIV status, dose of zidovudine, serum EPO and	01.12.18	05.18

Reviews, Revisions, and Approvals	Date	P&T Approval Date
pretreatment hemoglobin levels; anemia due to chemotherapy: added age requirement as safety and effectiveness in pediatrics < 5 years have not been established; added requirement for pretreatment hemoglobin level; reduction of RBC transfusion in surgery patients: added perioperative hemoglobin requirement per PI; anemia secondary to ribavirin/interferon alfa: added age and pretreatment hemoglobin requirements; anemia associated with MDS: added requirements related age, serum EPO and pretreatment hemoglobin levels; added NCCN compendial/recommended use (category 2A): MF-associated anemia; references reviewed and updated.		
Added Retacrit to criteria; removed myelofibrosis-associated anemia, anemia due to myelodysplastic syndrome, anemia secondary to combination ribavirin and interferon-alfa therapy in patients infected with hepatitis C virus off label uses since DrugDex IIb not covered; references reviewed and updated.	06.26.18	11.18
2Q 2019 annual review: added NCCN compendium supported uses for myelofibrosis-associated anemia and anemia due to myelodysplastic syndrome; references reviewed and updated	01.30.19	05.19

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. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

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This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a

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