

Clinical Policy: Epoetin Alfa (Epogen and Procrit)

Reference Number: CP.PHAR.237

Effective Date: 06.01.16

Last Review Date: 05.18

Line of Business: HIM, Medicaid

[Coding Implications](#)

[Revision Log](#)

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

Description

Epoetin alfa (Epogen[®] and Procrit[®]) is an erythropoiesis-stimulating agent (ESA).

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

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 and Procrit 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.

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 ≤ 4200 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.

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 ≥ 100 mcg/L or serum transferrin saturation $\geq 20\%$;
5. Pretreatment hemoglobin < 10 g/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 ≤ 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.

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 (off-label) (must meet all):

1. Diagnosis of anemia secondary to combination ribavirin and interferon-alfa therapy for treatment of hepatitis C;
2. Age ≥ 18 years;

3. Pretreatment hemoglobin < 10 g/dL, despite ribavirin dose reduction;
4. 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 duration of ribavirin treatment (whichever is less)

F. 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.

Approval duration: 6 months

G. 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. Current (within the last 3 months) serum EPO < 500 mU/mL;
4. 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

H. 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): HIM.PHAR.21 for health insurance marketplace and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Anemia due to CKD (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. 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

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

1. Currently receiving medication via Centene benefit or member has previously met all 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 \geq 100 mcg/L or serum transferrin saturation \geq 20%.

Approval Duration: 6 months

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, both (a and b):
 - a. Documented evidence of response to therapy as measured 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: 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 Secondary to Combination Ribavirin and Interferon-Alfa Therapy in Patients Infected with Hepatitis C Virus (off-label) (must meet all):

1. Currently receiving medication via Centene benefit or member has previously met all initial approval criteria;
2. Current hemoglobin ≤ 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 duration of ribavirin therapy, whichever is less.

F. 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

G. Myelofibrosis-Associated Anemia (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. 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

H. 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): HIM.PHAR.21 for health insurance marketplace and CP.PMN.53 for Medicaid.

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 policies – HIM.PHAR.21 for health insurance marketplace and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CKD: chronic kidney disease

EPO: erythropoietin

ESA: erythropoiesis-stimulating agent

FDA: Food and Drug Administration

MDS: myelodysplastic syndrome

Appendix B: Therapeutic Alternatives

Not applicable

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) until completion of a chemotherapy course	

Indication	Dosing Regimen	Maximum Dose
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 <i>or</i> 600 Units/kg SC weekly in 4 doses administered 21, 14, and 7 days before surgery and on the day of surgery	
Anemia secondary to combination ribavirin and interferon-alfa therapy in patients infected with hepatitis C virus [†]	40,000 units SC once weekly maintained the ribavirin dose in anemic patients with chronic hepatitis C virus; After 4 weeks, if the hemoglobin had not increased by at least 1 g/dL, the weekly dose was increased to 60,000 units SC.	
Anemia associated with MDS [†]	150—300 units/kg SC 3 times weekly has been shown to improve anemia in about 20% of patients with MDS. When epoetin alfa is given in combination with granulocyte-macrophage colony stimulating or granulocyte colony stimulating factor, response increases to about 50% of MDS patients.	
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 (Epoegen)	<ul style="list-style-type: none"> Single-dose vial: 2000, 3000, 4000, 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: 2000, 3000, 4000, 10,000, and 40,000 units/mL Multiple-dose vial containing benzyl alcohol: 20,000 units/2 mL and 20,000 units/mL

VII. References

1. Epoegen Prescribing Information. Thousand Oaks, CA: Amgen Inc.; September 2017. Available at <http://www.epoegen.com/>. Accessed January 11, 2018.
2. Procrit Prescribing Information. Thousand Oaks, CA: Amgen Inc.; September 2017. Available at <http://www.procrit.com/>. Accessed January 11, 2018.
3. Rizzo, J. D., Brouwers, M., Hurley, 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*, 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 11, 2018.
7. Myelodysplastic Syndromes (Version 1.2018). In: National Comprehensive Cancer Network Guidelines. Available at www.NCCN.org. Accessed January 11, 2018.
8. Epoetin Alfa Drug Monograph. *Clinical Pharmacology*. Accessed January 2018. <http://www.clinicalpharmacology-ip.com>.

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

Reviews, Revisions, and Approvals	Date	P&T Approval Date
<p>Policy split from CP.PHAR.10. Criteria: added contraindications of serious allergic reaction to Procrit/Epogen and use of the multi-dose vials in neonates, infants, pregnant women, and nursing mothers; added adequate iron stores requirement to criteria for allogeneic blood transfusion in surgery patients and anemia due to: chemo, zidovudine, MDS, and HCV treatment; removed ESA APPRISE Oncology Program requirement from chemo criteria; added duration of ribavirin treatment (whichever is less) to initial approval duration for HCV treatment; removed negative del (5q) requirement from MDS criteria.</p> <p>Re-auth: added iron stores and reasons to discontinue requirements; Anemia of CKD: removed Hgb dose adjustments but kept upper limit Hgb for patients on and not on dialysis; Zidovudine-induced anemia: simplified specific Hgb levels to Hgb ≤ 12g/dL; Anemia due to chemo: added current Hgb < 10g/dL per CMS policy; Anemia due to MDS or HCV: removed questions relating to specific Hgb levels but kept current Hgb ≤ 12g/dL. References updated.</p>	05.16	06.16
<p>Removed requirement related to prior trial and failure of Epogen (for Procrit request).</p>	09.16	
<p>Initial and re-auth: indicated that iron lab should be current (within the last 3 months). Initial: anemia due to chemo-added requirement that anemia cannot be managed by transfusion; added NCCN recommended use (myelofibrosis-associated anemia); re-auth: anemia due to zidovudine -added approval duration; updated limitations of use. For off-label uses, added that member must have adequate iron stores. Added Appendix B Dosage and Administration.</p>	05.17	06.17
<p>2Q 2018 annual review: HIM added; removed subjective criteria across all indications since specialist requirement is added; 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.</p>	02.06.18	05.18

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.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

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 discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. 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 clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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Note:

For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

For Health Insurance Marketplace members, when applicable, this policy applies only when the prescribed agent is on your health plan approved formulary. Request for non-formulary drugs must be reviewed using the formulary exception policy.

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