

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

Reference Number: CP.PHAR.237

Effective Date: 06.01.16

Last Review Date: 05.20

Line of Business: Commercial, 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<sup>®</sup>, Procrit<sup>®</sup>) and its biosimilar, epoetin alfa-epbx (Retacrit<sup>™</sup>), are erythropoiesis-stimulating agents (ESAs).

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

**Approval duration:**

**Medicaid/HIM** – 6 months (*see Appendix D for dose rounding guidelines*)

**Commercial** – 6 months or to member's renewal period, whichever is longer (*see Appendix D for dose rounding guidelines*)

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

**Approval duration:**

**Medicaid/HIM** – 6 months (*see Appendix D for dose rounding guidelines*)

**Commercial** – 6 months or to member's renewal period, whichever is longer (*see Appendix D for dose rounding guidelines*)

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

1. Request is for use in solid or non-myeloid malignancies in members receiving myelosuppressive chemotherapy without curative intent;
2. Prescribed by or in consultation with a hematologist or oncologist;
3. Age  $\geq 5$  years;
4. Adequate iron stores as indicated by current (within the last 3 months) serum ferritin level  $\geq 100$  mcg/L or serum transferrin saturation  $\geq 20\%$ ;
5. Pretreatment hemoglobin  $< 10$  g/dL;
6. Member meets one of the following (a or b):
  - a. If Epogen or Procrit is requested, failure of Retacrit, unless contraindicated or clinically significant adverse effects are experienced;
  - b. Request is for the treatment associated with Stage IV or metastatic cancer for a State with regulations against step therapy in advanced oncology settings (*see Appendix E*).

**Approval duration:**

**Medicaid/HIM** – 6 months or until the completion of chemotherapy course (whichever is less) (*see Appendix D for dose rounding guidelines*)

**Commercial** – Until the completion of chemotherapy course, 6 months, or to member's renewal date, whichever is longer (*see Appendix D for dose rounding guidelines*)

**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 ≥ 20%;
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;
6. Dose does not exceed one of the following (a or b):
  - a. 300 Units/kg administered daily for a total of 15 doses (*see Appendix D for dose rounding guidelines*);
  - b. 600 Units/kg for a total of 4 doses (*see Appendix D for dose rounding guidelines*).

**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 ≥ 100 mcg/L or serum transferrin saturation ≥ 20%;
6. Pretreatment hemoglobin < 10 g/dL;
7. Member meets one of the following (a or b):
  - a. If Epogen or Procrit is requested, failure of Retacrit, unless contraindicated or clinically significant adverse effects are experienced;
  - b. Request is for the treatment associated with Stage IV or metastatic cancer for a State with regulations against step therapy in advanced oncology settings (*see Appendix E*).

**Approval duration:**

**Medicaid/HIM** – 6 months (*see Appendix D for dose rounding guidelines*)

**Commercial** – 6 months or to member's renewal period, whichever is longer (*see Appendix D for dose rounding guidelines*)

**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  $\geq 100$  mcg/L or serum transferrin saturation  $\geq 20\%$ ;
6. Member meets one of the following (a or b):
  - a. If Epogen or Procrit is requested, failure of Retacrit, unless contraindicated or clinically significant adverse effects are experienced;
  - b. Request is for the treatment associated with Stage IV or metastatic cancer for a State with regulations against step therapy in advanced oncology settings (*see Appendix E*).

**Approval duration:**

**Medicaid/HIM** – 6 months (*see Appendix D for dose rounding guidelines*)

**Commercial** – 6 months or to member's renewal period, whichever is longer (*see Appendix D for dose rounding guidelines*)

**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, HIM.PHAR.21 for health insurance marketplace and CP.PMN.53 for Medicaid.

**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 all initial approval criteria;
2. Member is responding positively to therapy;
3. If Epogen or Procrit is requested, failure of Retacrit, unless contraindicated or clinically significant adverse effects are experienced;
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:**

**Medicaid/HIM** – 6 months (*see Appendix D for dose rounding guidelines*)

**Commercial** – 6 months or to member's renewal period, whichever is longer (*see Appendix D for dose rounding guidelines*)

**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. If Epogen or Procrit is requested, failure of Retacrit, unless contraindicated or clinically significant adverse effects are experienced;
3. Current hemoglobin level is  $\leq 12$  g/dL;
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:**

**Medicaid/HIM** – 6 months (*see Appendix D for dose rounding guidelines*)

**Commercial** – 6 months or to member's renewal period, whichever is longer (*see Appendix D for dose rounding guidelines*)

**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. Member meets one of the following (a or b):
  - a. If Epogen or Procrit is requested, failure of Retacrit, unless contraindicated or clinically significant adverse effects are experienced;
  - b. Request is for the treatment associated with Stage IV or metastatic cancer for a State with regulations against step therapy in advanced oncology settings (*see Appendix E*).
3. Continuation of ESA therapy is concurrent with myelosuppressive chemotherapy;
4. If member has received  $\geq 8$  weeks of ESA therapy, member meets both of the following (a and b):
  - a. Documented response to therapy as evidenced by a rise in hemoglobin levels  $>1$  g/dL;
  - b. No RBC transfusions are required;
5. Current hemoglobin  $< 10$  g/dL;
6. 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:**

**Medicaid/HIM** – 6 months or until the completion of chemotherapy course (whichever is less) (*see Appendix D for dose rounding guidelines*)

**Commercial** – Until the completion of chemotherapy course, 6 months, or to member's renewal date, whichever is longer (*see Appendix D for dose rounding guidelines*)

**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. Member meets one of the following (a or b):
  - a. If Epogen or Procrit is requested, failure of Retacrit, unless contraindicated or clinically significant adverse effects are experienced;
  - b. Request is for the treatment associated with Stage IV or metastatic cancer for a State with regulations against step therapy in advanced oncology settings (*see Appendix E*).
4. Current hemoglobin  $\leq 12$  g/dL;
5. Adequate iron stores as indicated by current (within the last 3 months) serum ferritin level  $\geq 100$  mcg/L or serum transferrin saturation  $\geq 20\%$ .

**Approval duration:**

**Medicaid/HIM** – 6 months (*see Appendix D for dose rounding guidelines*)

**Commercial** – 6 months or to member's renewal period, whichever is longer (*see Appendix D for dose rounding guidelines*)

**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. Member meets one of the following (a or b):
  - a. If Epogen or Procrit is requested, failure of Retacrit, unless contraindicated or clinically significant adverse effects are experienced;
  - b. Request is for the treatment associated with Stage IV or metastatic cancer for a State with regulations against step therapy in advanced oncology settings (*see Appendix E*).
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:**

**Medicaid/HIM** – 6 months (*see Appendix D for dose rounding guidelines*)

**Commercial** – 6 months or to member's renewal period, whichever is longer (*see Appendix D for dose rounding guidelines*)

**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, 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 – CP.CPA.09 for commercial, 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

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
- 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

*Appendix D: Dose Rounding Guidelines*

| Weight-based Dose Range      | Vial Quantity Recommendation                                            |
|------------------------------|-------------------------------------------------------------------------|
| ≤ 2,099.99 units             | 1 vial of 2,000 units                                                   |
| 2,100 units-3,149.99 units   | 1 vial of 3,000 units                                                   |
| 3,150 units-4,199.99 units   | 1 vial of 4,000 units                                                   |
| 4,200 units-6,299.99 units   | 1 vial of 4,000 units and 1 vial of 2,000 units                         |
| 6,300 units-7,349.99 units   | 1 vial of 4,000 units and 1 vial of 3,000 units                         |
| 7,350 units-8,399.99 units   | 2 vials of 4,000 units                                                  |
| 8,400 units-10,499 units     | 1 vial of 10,000 units                                                  |
| 10,500 units-12,599.99 units | 1 vial of 2,000 units and 1 vial of 10,000 units                        |
| 12,600 units-13,649.99 units | 1 vial of 3,000 units and 1 vial of 10,000 units                        |
| 13,650 units-14,699.99 units | 1 vial of 4,000 units and 1 vial of 10,000 units                        |
| 14,700 units-16,799.99 units | 1 vial of 2,000 units, 1 vial of 4,000 units and 1 vial of 10,000 units |
| 16,800 units-17,849.99 units | 1 vial of 3,000 units, 1 vial of 4,000 units and 1 vial of 10,000 units |
| 17,849 units-18,899.99 units | 2 vials of 4,000 units and 1 vial of 10,000 units                       |
| 18,900 units-20,999 units    | 2 vials of 10,000 units                                                 |

*Appendix E: States with Regulations against Redirections in Stage IV or Metastatic Cancer*

| State | Step Therapy Prohibited? | Notes                                                                                                                                                                                     |
|-------|--------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| FL    | Yes                      | For stage 4 metastatic cancer and associated conditions.                                                                                                                                  |
| GA    | Yes                      | For stage 4 metastatic cancer                                                                                                                                                             |
| IA    | Yes                      | For standard of care stage 4 cancer drug use, supported by peer-reviewed, evidence-based literature, and approved by FDA.                                                                 |
| LA    | Yes                      | For stage 4 advanced, metastatic cancer or associated conditions. Exception if “clinically equivalent therapy, contains identical active ingredient(s), and proven to have same efficacy. |
| PA    | Yes                      | For stage 4 advanced, metastatic cancer                                                                                                                                                   |
| TN    | Yes                      | For advanced metastatic cancer and associated conditions                                                                                                                                  |
| TX    | Yes                      | For stage 4 advanced, metastatic cancer and associated conditions                                                                                                                         |

**V. 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 | Varies depending on indication and |

| Indication                                                                                                           | Dosing Regimen                                                                                                                                                                                                                                                                                             | Maximum Dose                |
|----------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------|
|                                                                                                                      | times weekly (children on dialysis) IV or SC. Individualize maintenance dose. IV route recommended for patients on hemodialysis                                                                                                                                                                            | 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 $\geq 5$ 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 <sup>†</sup>                                                                              | 40,000-60,000 units SC one to two times weekly                                                                                                                                                                                                                                                             |                             |
| Anemia associated with myelofibrosis <sup>†</sup>                                                                    | 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. |                             |

<sup>†</sup> Off-label indication

## VI. Product Availability

| Drug Name                    | Availability                                                                                                                                                                                                                                          |
|------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Epoetin alfa (Epogen)        | <ul style="list-style-type: none"> <li>Single-dose vial: 2,000 units/mL, 3,000 units/mL, 4,000 units/mL, and 10,000 units/mL</li> <li>Multiple-dose vial containing benzyl alcohol: 20,000 units/2 mL and 20,000 units/mL</li> </ul>                  |
| Epoetin alfa (Procrit)       | <ul style="list-style-type: none"> <li>Single-dose vial: 2,000 units/mL, 3,000 units/mL, 4,000 units/mL, 10,000 units/mL, and 40,000 units/mL</li> <li>Multiple-dose vial containing benzyl alcohol: 20,000 units/2 mL and 20,000 units/mL</li> </ul> |
| Epoetin alfa-epbx (Retacrit) | <ul style="list-style-type: none"> <li>Single-dose vial: 2,000 units/mL, 3,000 units/mL, 4,000 units/mL, 10,000 units/mL, 40,000 units/mL</li> <li>Multiple-dose vial containing benzyl alcohol: 20,000 units/2 mL and 20,000 units/mL</li> </ul>     |

## VII. References

1. Epogen Prescribing Information. Thousand Oaks, CA: Amgen Inc.; July 2018. Available at <http://www.epogen.com/>. Accessed July 8, 2020.
2. Procrit Prescribing Information. Thousand Oaks, CA: Amgen Inc.; July 2018. Available at <http://www.procrit.com/>. Accessed July 8, 2020.
3. Bohlius J, Bohlke K, Castelli R, et al. American Society of Hematology/American Society of Clinical Oncology clinical practice guideline update: Management of Cancer-Associated Anemia With Erythropoiesis-Stimulating Agents. J Clin Oncol 37:1336-1351. Available at: <https://ascopubs.org/doi/pdf/10.1200/JCO.18.02142>. Accessed February 13, 2020.
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 February 13, 2020.
7. Myelodysplastic Syndromes (Version 1.2020). In: National Comprehensive Cancer Network Guidelines. Available at [www.nccn.org](http://www.nccn.org). Accessed February 13, 2020.
8. Myeloproliferative Neoplasms (Version 3.2019). In National Comprehensive Cancer Network Guidelines. Available at [www.nccn.org](http://www.nccn.org). Accessed February 13, 2020.
9. Hematopoietic Growth Factors (Version 2.2020). In National Comprehensive Cancer Network Guidelines. Available at [www.nccn.org](http://www.nccn.org). Accessed February 13, 2020.
10. Cancer and Chemotherapy Induced Anemia (Version 3.2018). In National Comprehensive Cancer Network Guidelines. Available at [www.nccn.org](http://www.nccn.org). Accessed February 13, 2020.
11. Epoetin Alfa Drug Monograph. Clinical Pharmacology. Accessed February 13, 2020. <http://www.clinicalpharmacology-ip.com>.
12. DRUGDEX<sup>®</sup> System [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed February 13, 2020.
13. Retacrit Prescribing Information. Lake Forest, IL: Hospira, Inc., June 2020. Available at <https://www.pfizerpro.com/product/retacrit/hcp>. Accessed July 8, 2020.

## 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 |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------|-------------------|
| 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. 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 $\leq$ 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 $\leq$ 12g/dL. References updated. | 05.16    | 06.16             |
| Removed requirement related to prior trial and failure of Epogen (for Procrit request).                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 09.16    |                   |
| 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.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | 05.17    | 06.17             |
| 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.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | 02.06.18 | 05.18             |
| 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 | 02.19             |
| 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             |
| Added Commercial line of business; retire CP.CPA.321; for Epogen and Procrit, added redirection to Retacrit per existing clinical guidance                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 10.01.19 |                   |

| Reviews, Revisions, and Approvals                                                                                                                                                                                                                                                                                                                                                                                                               | Date     | P&T Approval Date |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------|-------------------|
| and SDC recommendation; removed reference to HIM.PA.103 for Retacrit requests.                                                                                                                                                                                                                                                                                                                                                                  |          |                   |
| 2Q 2020 annual review: for anemia with chemotherapy, modified diagnosis requirement to confirm request is for use in solid or non-myeloid malignancies in members receiving myelosuppressive chemotherapy without curative intent consistent with NCCN and ASCO recommendations; added appendix D: dose rounding guidelines; added reference to appendix D within criteria; references reviewed and updated.                                    | 02.13.20 | 05.20             |
| RT4: added new multiple-dose vial formulation for Retacrit and updated Appendix C with benzyl alcohol-related contraindication. Added to Section II for continued therapy, redirection to Retacrit for Epogen and Procrit requests.                                                                                                                                                                                                             | 08.18.20 |                   |
| Allowed by-passing of redirection if state regulations do not allow step therapy in Stage IV or metastatic cancer settings.                                                                                                                                                                                                                                                                                                                     | 09.15.20 |                   |
| Removed AR from appendix E (“For metastatic cancer, <b>unless</b> the preferred drug is consistent with “best practices” (1) used for treatment under (A) FDA-approved indication, or (B) National Comprehensive Cancer Network Drugs & Biologics Compendium; or (2) using evidence-based, peer-reviewed, recognized medical literature.<br>Note – may not require step therapy a second time for same Rx drug”) to minimize misinterpretation. | 11.16.20 |                   |

### **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.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

**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.

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