Epoetin alfa (Procrit®, Epogen®) **Epoetin alfa-epbx (Retacrit™)**	**Place of Service** **Hospital Administration** **Office Administration** **Home Infusion Administration** **Outpatient Facility Administration** **Infusion Center Administration** **Self-Administration** **HCPCS** **Procrit/Epogen:** **J0885** per 1000 units (*Non-ESRD use*) **Q4081** per 1000 units (*ESRD on dialysis*) **Retacrit:** **Q5105** per 1000 units (*ESRD on dialysis*) **Q5106** per 1000 units (*Non-ESRD use*)

Conditions listed in policy *(see criteria for details)*:

- Anemia due to chronic renal failure
- Anemia of rheumatoid arthritis
- Anemia secondary to myelosuppressive chemotherapy under specified conditions
- Anemia secondary to ribavirin therapy in hepatitis C patients
- Anemia secondary to zidovudine therapy in HIV-infected patients
- Myelodysplastic syndromes (MDS)
- Myelofibrosis-associated anemia
- Preoperative use for the anemic patient

AHFS therapeutic class: Hematopoietic Agent

Mechanism of action: Erythropoietin (EPO) is a glycoprotein hematopoietic growth factor. EPO is synthesized by the renal tubules in response to change in blood oxygen concentration. In anemic patients, the low blood oxygen concentration induces the production of EPO, which then acts on the erythroid cell in the bone marrow to stimulate hematopoiesis. Epoetin alfa is manufactured by recombinant DNA technology and has the same biological effects as endogenous erythropoietin.

(1) Special Instructions and Pertinent Information

If covered under the Medical Benefit, please submit clinical information for prior authorization review via fax.

***Effective 1/1/2021*:** Retacrit is the BSC preferred erythropoiesis stimulating agent (ESA). For all covered indications, treatment failure, intolerance or contraindication to Retacrit (epoetin alfa-epbx) is required for members newly initiating ESA therapy.

(2) Prior Authorization/Medical Review is required for the following condition(s)

All requests for epoetin alfa must be sent for clinical review and receive authorization prior to drug administration or claim payment.

Anemia due to chronic renal failure (CRF)

1. Hgb < 10 g/dL or HCT < 30%**, AND**
2. Both Primary and Secondary ICD-10 codes (listed below) must be met, **AND**
3. ***Effective 1/1/2021***, one of the following:
    a. For Retacrit: No additional requirement, OR
    b. For Epogen or Procrit: Patient has failed, is intolerant to, or is contraindicated to Retacrit as defined by any one of the following:
        i. At the max dose of Retacrit for 8 weeks, patient does not meet Hgb target, or Hgb does not rise by at least 2g/dL
        ii. Patient has a contraindication to Retacrit that is not also a contraindication of Procrit/Epogen
        iii. Patient has known side effects to Retacrit that would not be expected with Procrit/Epogen

Covered Doses
Up to 300 units/kg/week

Coverage Period
Initial: Cover 1 year

Reauthorization criteria for CRF patients and not on hemodialysis:
Hgb < 11 g/dL or HCT <33%

Covered Doses
Up to 300 units/kg/week

Coverage Period
Reauthorization: Yearly

ICD-10:
Primary: D63.1 (Anemia in ESRD)
Secondary: N18.1-N18.9 (CRF)

Anemia of rheumatoid arthritis

1. Hgb ≤ 10g/dL or HCT ≤ 30% within the past 21 days prior to epoetin alfa use**, AND**
2. Anemia not caused by a correctable etiology (e.g. occult blood loss due to gastritis)**, AND**
3. Primary (anemia of chronic disease) and secondary (rheumatoid arthritis) ICD-10 codes are met**, AND**
4. ***Effective 1/1/2021***, one of the following:
    a. For Retacrit: No additional requirement, OR
    b. For Epogen or Procrit: Patient has failed, is intolerant to, or is contraindicated to Retacrit as defined by any one of the following:
        i. At the max dose of Retacrit for 8 weeks, patient does not meet Hgb target, or Hgb does not rise by at least 2g/dL
        ii. Patient has a contraindication to Retacrit that is not also a contraindication of Procrit/Epogen
        iii. Patient has known side effects to Retacrit that would not be expected with Procrit/Epogen

Covered Doses
Up to ≤ 900 units/kg/week (Medicare LCD)
(Note: according to AHFS, max dose is 200 units/kg/week)

Coverage Period
Initial: 6 months

Reauthorization criteria for RA: Hgb ≤12 g/dL or Hct ≤ 36%

Covered Doses

Up to ≤ 900 units/kg/week (Medicare LCD)
(Note: according to AHFS, max dose is 200 units/kg/week)

Coverage Period

Reauthorization: every 6 months

ICD-10:

Primary: D63.8 (anemia of chronic disease)
Secondary: M05.00-M06.9 (RA)

Anemia secondary to myelosuppressive chemotherapy under specified conditions

1. Patient is currently on chemotherapy or has completed their last dose of chemotherapy within the past 8 weeks, **AND**
2. Hgb < 10 g/dL or HCT < 30%, **AND**
3. Patient does not have uncontrolled hypertension, **AND**
4. Patient has solid tumor, multiple myeloma, lymphoma, or lymphocytic leukemia
5. ***Effective 1/1/2021***, one of the following:
    a. For Retacrit: No additional requirement, OR
    b. For Epogen or Procrit: Patient has failed, is intolerant to, or is contraindicated to Retacrit as defined by any one of the following:
        i. At the max dose of Retacrit for 8 weeks, patient does not meet Hgb target, or Hgb does not rise by at least 2g/dL
        ii. Patient has a contraindication to Retacrit that is not also a contraindication of Procrit/Epogen
        iii. Patient has known side effects to Retacrit that would not be expected with Procrit/Epogen

Covered Doses

When administered weekly, dose does not exceed 900 units/kg/week
When administered every 2 weeks, dose does not exceed 80,000 units
When administered every 3 weeks, dose does not exceed 120,000 units

Coverage Period

Initial: Up to 12 weeks but not greater than 8 weeks after the last dose of chemotherapy.

Reauthorization criteria for anemia of cancer/myelosuppressive chemotherapy:

- Patient is currently on or has completed the last dose of chemotherapy within the previous 8-week period, or is scheduled for upcoming myelosuppressive chemotherapy**, AND**
- Hgb ≤ 12 g/dL or HCT ≤ 36% prior to the next dose of Procrit/Epogen.

Covered Doses

When administered weekly, dose does not exceed 900 units/kg/week
When administered every 2 weeks, dose does not exceed 80,000 units
When administered every 3 weeks, dose does not exceed 120,000 units

Coverage Period

Reauthorization: up to 12 weeks but not greater than 8 weeks after the last dose of chemotherapy.

ICD-10:

D63.0, D64.81, Z51.11

Anemia secondary to Ribavirin therapy in hepatitis C patients

1. On Ribavin therapy, **AND**
2. Patient had a ≥ 3gm/dL drop in Hgb within 1 month on ribavirin, **OR**
3. Hgb ≤ 12 g/dL or HCT ≤ 36%
4. ***Effective 1/1/2021***, one of the following:
    a. For Retacrit: No additional requirement, OR
    b. For Epogen or Procrit: Patient has failed, is intolerant to, or is contraindicated to Retacrit as defined by any one of the following:
        i. At the max dose of Retacrit for 8 weeks, patient does not meet Hgb target, or Hgb does not rise by at least 2g/dL
        ii. Patient has a contraindication to Retacrit that is not also a contraindication of Procrit/Epogen
        iii. Patient has known side effects to Retacrit that would not be expected with Procrit/Epogen

Covered Doses
Up to ≤ 40,000 units once weekly

Coverage Period
Approval period is the same as the patient's ribavirin treatment period

ICD-10:
B18.2, B19.20 (Hepatitis C), **AND**
D61.1 (drug-induced aplastic anemia)

Anemia secondary to zidovudine therapy in HIV-infected patients

1. On zidovudine therapy for HIV, **AND**
2. Hgb ≤ 10 g/dL or HCT ≤ 30%**, AND**
3. Both Primary and Secondary ICD-10 codes must be met**, AND**
4. ***Effective 1/1/2021***, one of the following:
    a. For Retacrit: No additional requirement, OR
    b. For Epogen or Procrit: Patient has failed, is intolerant to, or is contraindicated to Retacrit as defined by any one of the following:
        i. At the max dose of Retacrit for 8 weeks, patient does not meet Hgb target, or Hgb does not rise by at least 2g/dL
        ii. Patient has a contraindication to Retacrit that is not also a contraindication of Procrit/Epogen
        iii. Patient has known side effects to Retacrit that would not be expected with Procrit/Epogen

Covered Doses
Up to 900 units/kg/week

Coverage Period
indefinite

ICD-10:
Primary: D61.1 (drug-induced aplastic anemia)
Secondary: B20 (HIV disease)

Myelodysplastic syndromes (MDS)

1. Symptomatic anemia (Hgb ≤ 10 g/dL or HCT <30%), **AND**
2. Baseline serum EPO ≤ 500 mU/ml drawn prior to epoetin alfa therapy, **AND**
3. ***Effective 1/1/2021***, one of the following:
    a. For Retacrit: No additional requirement, OR
    b. For Epogen or Procrit: Patient has failed, is intolerant to, or is contraindicated to Retacrit as defined by any one of the following:
        i. At the max dose of Retacrit for 8 weeks, patient does not meet Hgb target, or Hgb does not rise by at least 2g/dL
        ii. Patient has a contraindication to Retacrit that is not also a contraindication of Procrit/Epogen
        iii. Patient has known side effects to Retacrit that would not be expected with Procrit/Epogen

Covered Doses
Up to 120,000 units/week

Coverage Period
Initial: 6 months

Reauthorization criteria for MDS:

- Assess for response to therapy (e.g. reticulocyte response, rise in hemoglobin of ≥1.5 g/dL, or reduction in # of blood transfusions), **AND**
- Hgb ≤ 12 gm/dL or HCT ≤ 36% prior to the next dose of epoetin alfa.

Covered Doses
Up to 120,000 units/week

Coverage Period:
Reauthorization: every 6 months

ICD-10:
D46.0, D46.1, D46.2, D46.21, D46.22, D46.4, D46.A, D46.B, D46.C, D46.9, D46.Z

Myelofibrosis-associated anemia

1. Symptomatic anemia (Hgb ≤ 10 g/dL or HCT ≤ 30%)**, AND**
2. Baseline serum EPO < 500 mU/ml drawn prior to epoetin alfa therapy
3. ***Effective 1/1/2021***, one of the following:
    a. For Retacrit: No additional requirement, OR
    b. For Epogen or Procrit: Patient has failed, is intolerant to, or is contraindicated to Retacrit as defined by any one of the following:
        i. At the max dose of Retacrit for 8 weeks, patient does not meet Hgb target, or Hgb does not rise by at least 2g/dL
        ii. Patient has a contraindication to Retacrit that is not also a contraindication of Procrit/Epogen
        iii. Patient has known side effects to Retacrit that would not be expected with Procrit/Epogen

Covered Doses
Up to 180,000 units/week

Coverage Period
Initial: 3 months

Reauthorization criteria for myelofibrosis-associated anemia:

- Response to therapy [e.g. sustained increase in hgb levels (>2g/dl) or >50% reduction in transfusion requirements within 12 weeks], **AND**
- Hgb ≤ 12 gm/dL or HCT ≤ 36% prior to the next dose of epoetin alfa

Covered Doses
Up to 180,000 units/week

Coverage Period
Reauthorization: every 3 months

ICD-10:
C94.40-C94.42, D47.4, D75.81

Pre-operative prevention in anemic patients

1. Patient is mildly anemic (Hgb ≤ 13 g/dL), **AND**
2. Patient is scheduled to undergo elective, non-cardiac, or non-vascular surgery, **AND**
3. Patient is at high risk for perioperative transfusion with significant, anticipated blood loss (2 units of blood or more), and patient is not a candidate for blood transfusion
4. ***Effective 1/1/2021***, one of the following:
    a. For Retacrit: No additional requirement, OR
    b. For Epogen or Procrit: Patient has failed, is intolerant to, or is contraindicated to Retacrit as defined by any one of the following:
        i. At the max dose of Retacrit for 8 weeks, patient does not meet Hgb target, or Hgb does not rise by at least 2g/dL
        ii. Patient has a contraindication to Retacrit that is not also a contraindication of Procrit/Epogen
        iii. Patient has known side effects to Retacrit that would not be expected with Procrit/Epogen

Covered Dose
Patient is scheduled for elective surgery, **AND** dose is ≤ 600 units/kg/week for 4 weekly doses, or 300 units/kg/day for 15 days

Coverage Period
Coverage period is 2 months per surgery. Total length of epoetin alfa therapy not to exceed 15 days for daily dosing or 4 weekly doses for once weekly dosing.

ICD-10:
D64.9 (Anemia, unspecified)

(3) The following condition(s) DO NOT require Prior Authorization/Preservice
All requests for Epoetin alfa/alfa-epbx must be sent for clinical review and receive authorization prior to drug administration or claim payment.

(4) This Medication is NOT medically necessary for the following condition(s)

Blue Shield's research indicates there is inadequate clinical evidence to support off-label use of this drug for the following conditions (Health and Safety Code 1367.21):

- Treatment is not covered when Hgb > 12 g/dL or HCT > 36% for all indications
- (280.0) Iron deficiency anemias; secondary to blood loss (chronic)
- (280.9) Iron deficiency anemia, unspecified
- (281.9) Unspecified deficiency anemia
- (283.0) Autoimmune hemolytic anemias
- (284.9) Aplastic anemia,
- (285.9) Anemia, unspecified (except for EPO for preoperative use)
- (288.0) Agranulocytosis
- (289.9) Unspecified diseases of blood and blood forming organs
- (451.9) Phlebitis and thrombophlebitis of deep vessels of lower extremities
- (V59.01) Donors; blood; whole blood
- (205.00-205.91) Myeloid leukemia
- (206.00-206.91) Monocytic leukemia
- (207.00-208.91) Other specified and unspecified leukemias

Anemias due to:

- Hemolysis
- Nutritional deficiencies
- Untreated underlying infections
- Refractory anemia such as thalassemia or sickle cell disease
- Cofactor deficiencies
- Hemorrhage
- Most patients with GI bleeding
- Cancer radiotherapy
- Congestive heart failure
- Folate deficiency anemia
- Porphyria
- Postpartum
- Prematurity
- Athletic performance mgmt
- Beta-thalassemia
- Blood transfusion reduction
- Insulin resistance
- Sexual dysfunction
- Sickle-cell anemia
- Transfusional iron overload

Coverage for a Non-FDA approved indication, requires that criteria outlined in Health and Safety Code § 1367.21, including objective evidence of efficacy and safety are met for the proposed indication.

Please refer to the Provider Manual and User Guide for more information.

(5) Additional Information

How supplied:
Epogen/Procrit:
1ml Single-dose, preservative-free vial: 2000/ml, 3000/ml, 4000/ml or 10,000 Units/ml
1ml Single-dose, preservative-free vial: 40,000 Units/mL
2ml Multidose, Preserved Vial: 10,000 Units/mL
1ml Multidose, Preserved Vial: 20,000 Units/mL
Retacrit:
2,000 Units/mL single-dose 1 ml vials
3,000 Units/mL single-dose 1 ml vials
4,000 Units/mL single-dose 1 ml vials
10,000 Units/mL single-dose 1 ml vials
40,000 Units/mL single-dose 1 ml vials

Key:

Hgb = hemoglobin level, measured in grams per deciliter (g/dL)
HCT = hematocrit level, reported in %
EPO = Erythropoietin level, reported in microunits per milliliter (mU/ml)

Concurrent iron supplementation is recommended.

(6) References

- AHFS®. Available by subscription at http://www.lexi.com
- Cancer and chemotherapy-Induced Anemia, Erythropoietic Therapy. National Comprehensive Cancer Network (NCCN) Practice Guidelines in Oncology v.2.2018. Available at http://www.nccn.com.
- DrugDex®. Available by subscription at http://www.micromedexsolutions.com/home/dispatch
- Epogen® (epoetin alfa) Prescribing Information. Amgen, Inc., Thousand Oaks, CA. 2018.
- National Comprehensive Cancer Network. Hematopoietic Growth Factors (Version 1.2020). Available at http://www.nccn.com.
- Myelodysplastic Syndromes. National Comprehensive Cancer Network (NCCN) Practice Guidelines in Oncology v.1.2020. Available at http://www.nccn.com.
- Myeloproliferative Neoplasms. National Comprehensive Cancer Network (NCCN) Practice Guidelines in Oncology v.3.2019. Available at http://www.nccn.org.
- Procrit® (epoetin alfa) Prescribing Information. Amgen, Inc., Thousand Oaks, CA. 2018.
- Retacrit™ (epoetin alfa-epbx) Prescribing Information. Pfizer, Inc. 2019.
- Rizzo JD, Brouwers M, Hurley P et al. American Society of Clinical Oncology/American Society of Hematology clinical practice guideline update on the use of epoetin and darbepoetin in adult patients with cancer. J Clin Oncol. 2010;28(33):4996-5010.
- Tsiara SN, Chaidos A, Bourantas LK et al. Recombinant human erythropoietin for the treatment of anemia in patients with chronic myelofibrosis. Acta Haematol 2007; 117(3): 156-61.

(7) Policy Update

Date of initial review: 4Q2020
Date of next review: 1Q2021
Changes from previous policy version:

- ***For Procrit or Epogen, and effective 1/1/2021***, all indications will require an intolerable side effect with the preferred erythropoiesis stimulating agent (ESA) Retracrit that is not expected with Procrit/Epogen, or contraindication to Retacrit.