Epoetin Alfa Products for Non-Dialysis (Epogen®, Procrit®, Retacrit®)

NDC CODE(S)

55513-0126-XX EPOGEN 2000UNIT/ML Solution (AMGEN)
55513-0144-XX EPOGEN 10000UNIT/ML Solution (AMGEN)
55513-0148-XX EPOGEN 4000UNIT/ML Solution (AMGEN)
55513-0267-XX EPOGEN 3000UNIT/ML Solution (AMGEN)
55513-0283-XX EPOGEN 10000UNIT/ML Solution (AMGEN)
55513-0478-XX EPOGEN 20000UNIT/ML Solution (AMGEN)
59676-0302-XX PROCRIT 2000UNIT/ML Solution (JANSSEN PRODUCTS)
59676-0303-XX PROCRIT 3000UNIT/ML Solution (JANSSEN PRODUCTS)
59676-0304-XX PROCRIT 4000UNIT/ML Solution (JANSSEN PRODUCTS)
59676-0310-XX PROCRIT 10000UNIT/ML Solution (JANSSEN PRODUCTS)
59676-0312-XX PROCRIT 10000UNIT/ML Solution (JANSSEN PRODUCTS)
59676-0320-XX PROCRIT 20000UNIT/ML Solution (JANSSEN PRODUCTS)
59676-0340-XX PROCRIT 40000UNIT/ML Solution (JANSSEN PRODUCTS)
00069-1305-XX RETACRIT 2000UNIT/ML Solution (PFIZER U.S.)
00069-1306-XX RETACRIT 3000UNIT/ML Solution (PFIZER U.S.)
00069-1307-XX RETACRIT 4000UNIT/ML Solution (PFIZER U.S.)
00069-1308-XX RETACRIT 10000UNIT/ML Solution (PFIZER U.S.)
00069-1309-XX RETACRIT 40000UNIT/ML Solution (PFIZER U.S.)
00069-1311-XX RETACRIT 20000UNIT/ML Solution (PFIZER U.S.)
00069-1318-XX RETACRIT 10000U/ML Solution (PFIZER U.S.)
59353-0002-XX RETACRIT 2000UNIT/ML Solution (VIFOR)
59353-0003-XX RETACRIT 3000 UNIT/ML Solution (VIFOR)
59353-0004-XX RETACRIT 4000UNIT/ML Solution (VIFOR)
59353-0010-XX RETACRIT 10000UNIT/ML Solution (VIFOR)
59353-0120-XX RETACRIT 20000UN/ML Solution (VIFOR)
59353-0220-XX RETACRIT 10000UN/ML Solution (VIFOR)

DESCRIPTION

Erythropoietin is a glycoprotein produced in the kidneys responsible for the stimulation of erythropoiesis. It increases the reticulocyte count to initiate red blood cell production and is referred to as an erythropoietin-stimulating agent or an ESA.

Manufactured by recombinant DNA technology, epoetin alfa (Epogen®/Procrit®) is a 165-amino acid manufactured in the identical amino acid sequence of isolated natural erythropoietin. Like the endogenous hormone, it stimulates increased reticulocyte production followed by red blood cells in individuals with functioning erythropoiesis.

Epoetin alfa-epbx (Retacrit®) is biosimilar to epoetin alfa. It contains the identical amino acid sequence of isolated natural erythropoietin and is also a 165-amino acid erythropoiesis-stimulating glycoprotein manufactured by recombinant DNA technology. It's use is interchangeable with epoetin alfa products.

POLICY

- Epoetin Alfa products for the treatment of anemia is considered ***medically necessary*** if the medical appropriateness criteria are met. **(See Medical Appropriateness below.)**
- Epoetin Alfa products for the treatment of other conditions/diseases is considered ***investigational.***

MEDICAL APPROPRIATENESS

INITIAL APPROVAL CRITERIA

- Patient is at least 18 years of age or older (unless otherwise specified); **AND**
- Initiation of therapy Hemoglobin (Hb) < 10 g/dL and/or Hematocrit (Hct) < 30% (unless otherwise specified); **AND**

Universal Criteria

- Lab values are obtained within 30 days of the date of administration (unless otherwise indicated); **AND**
- Patient has adequate iron stores as demonstrated by serum ferritin ≥ 100 ng/mL (mcg/L) and transferrin saturation (TSAT) ≥ 20% (measured within the previous 3 months for renewal)*; **AND**
- Other causes of anemia (e.g. hemolysis, bleeding, vitamin deficiency, etc.) have been ruled out; **AND**
- Patient does not have uncontrolled hypertension; **AND**

Anemia Secondary to Myelodysplastic Syndrome (MDS)

- Endogenous serum erythropoietin level of ≤ 500 mUnits/mL; **AND**
- Patient has lower risk disease (*i.e., defined as IPSS-R [Very Low, Low, Intermediate], IPSS [Low/Intermediate-1], WPSS [Very Low, Low, Intermediate])*; **AND**
- Patient has symptomatic anemia

Anemia Secondary to Myeloproliferative Neoplasms (MPN) - Myelofibrosis

- Endogenous serum erythropoietin level of < 500 mUnits/mL

Anemia Secondary to Chemotherapy Treatment

- Patient is at least 5 years of age; **AND**
- Patient is receiving concomitant myelosuppressive chemotherapy; **AND**
- Patient's chemotherapy is not intended to cure their disease (i.e., palliative treatment); **AND**
- There are a minimum of two additional months of planned chemotherapy

Anemia Secondary to Chronic Kidney Disease (Non-Dialysis Patients)

- Patient is at least 1 month of age

Anemia Secondary to Zidovudine-Treated, HIV-Infected Patients

- Patient is at least 8 months of age; **AND**
- Endogenous serum erythropoietin level of ≤ 500 mUnits/mL; **AND**
- Patient is receiving zidovudine administered at ≤ 4200 mg/week

Reduction of Allogeneic Blood Transfusions in Elective, Non-Cardiac, Non-Vascular Surgery

- Hemoglobin (Hb) >10 g/dL and <13 g/dL and/or Hematocrit (Hct) >30% and <39%; **AND**
- Patient is at high-risk of blood-loss from surgery that is elective, non-cardiac and nonvascular; **AND**
- Patient is unwilling or unable to participate in an autologous blood donation program prior to surgery

RENEWAL CRITERIA

- Patient continues to meet universal and other indication-specific relevant criteria identified in the Initial Approval Criteria; **AND**
- Previous dose was administered within the past 60 days; **AND**
- Anemia response compared to pretreatment baseline; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: the following: severe cardiovascular events (stroke, myocardial infarction, congestive heart failure, thromboembolism, etc.), uncontrolled hypertension, increased risk of tumor progression/recurrence in patients with cancer, seizures, pure red cell aplasia, serious allergic reactions (anaphylaxis, angioedema, bronchospasm, etc.), severe cutaneous reactions (erythema multiforme, Stevens-Johnson Syndrome [SJS]/Toxic Epidermal Necrolysis [TEN], etc.), "gasping syndrome" (central nervous system depression, metabolic acidosis, gasping respirations) due to benzyl alcohol preservative, etc.; **AND**

Anemia Secondary to Myelodysplastic Syndrome (MDS):

- Hemoglobin (Hb) <12 g/dL and/or Hematocrit (Hct) <36%

Anemia Secondary to Myeloproliferative Neoplasms - Myelofibrosis

- Hemoglobin (Hb) <10 g/dL and/or Hematocrit (Hct) <30%

Reduction of Allogeneic Blood Transfusions in Elective, Non-Cardiac, Non-Vascular Surgery

- Coverage may not be renewed.

Anemia Secondary to Chemotherapy Treatment

- Refer to Initial Approval Criteria for criteria (age was met initially)

Anemia Secondary to Zidovudine Treated, HIV-Infected Patients:

- Hemoglobin (Hb) < 12 g/dL and/or Hematocrit (Hct) < 36%; **AND**
- Patient is receiving zidovudine administered at ≤ 4200 mg/week

Anemia Secondary to Chronic Kidney Disease:

- **Pediatric patients:** Hemoglobin (Hb) < 12 g/dL and/or Hematocrit (Hct) < 36%
- **Adults:** Hemoglobin (Hb) < 11 g/dL and/or Hematocrit (Hct) < 33%

** Intravenous iron supplementation may be taken into account when evaluating iron status*
• Functional iron deficiency (i.e., adequate iron stores with an insufficient supply of available iron) may occur in patients with chronic diseases, cancer, and/or in those currently receiving ESAs. • Iron is not generally recommended in anemic patients with a Ferritin >500 ng/mL • Anemic patients with a Ferritin ≤500 ng/mL AND TSAT <50% may derive benefit from IV iron therapy in conjunction with ESA

DOSAGE/ADMINISTRATION

INDICATION	DOSE
Anemia due to CKD – non-dialysis §	• Adult patients: 50-100 units/kg intravenously or subcutaneously three times weekly • Pediatric patients: 50 units/kg intravenously or subcutaneously three times weekly
Anemia due to HIV on zidovudine§	• 100 units/kg intravenously or subcutaneously three times weekly • May titrate up to 300 units/kg per dose
Anemia due to chemotherapy§	• Adult patients: 150 units/kg subcutaneously three times weekly or 40,000 units subcutaneously once weekly ○ May titrate up to 300 units/kg subcutaneously three times weekly or 60,000 units subcutaneously once weekly • Pediatric patients (5-18 years): 600 units/kg intravenously once weekly ○ May titrate up to 900 units/kg intravenously once weekly
Perioperative use	• 300 units/kg/day subcutaneously for 10 days before surgery, on the day of surgery, and for 4 days after surgery (15 days total) -OR- • 600 units/kg/dose subcutaneously on days 21, 14, and 7 before surgery plus 1 dose on the day of surgery (4 total doses)
Anemia due to MDS§	• 40,000 to 60,000 units subcutaneously once to twice weekly
Anemia due to myeloproliferative neoplasms (MPN)§	• 10,000 units subcutaneously three times weekly • May increase dose to 20,000 units subcutaneously three times weekly
Most commonly initiated dose	40,000 units weekly

§

- For patients with CKD,
  - ➢ Dose increases of 25% can be considered if after 4 weeks of initial therapy the hemoglobin has increased less than 1 g/dL and the current hemoglobin level is less than the indication specific level noted above.
  - ➢ Dose decreases of 25% or more can be considered if the hemoglobin rises rapidly by more than 1 g/dL in any 2-week period.
  - ➢ Dose and frequency requested are the minimum necessary for the patient to avoid RBC transfusions.
  - ➢ Avoid frequent dose adjustments. Do not increase the dose more frequently than once every 4 weeks; decreases can occur more frequently.
  - ➢ If patients fail to respond over a 12-week dose escalation period, further doses increases are unlikely to improve response and discontinuation of therapy should be considered.
- For patients with MDS:
  - ➢ After 3 to 4 months of therapy, if there is no response as measured by at least a 1.5 g/dL increase in hemoglobin or a decrease in RBC transfusions, discontinuation of therapy should be considered.
- For patients with MPN:
  - ➢ After 3 months of therapy, if there is no response as measured by at least a 2 g/dL increase in hemoglobin or a decrease in RBC transfusions, discontinuation of therapy should be considered.
- For patients on Cancer Chemotherapy
  - ➢ After 8 weeks of therapy, if there is no response as measured by hemoglobin levels or if RBC transfusions are still required, discontinue therapy.
- For zidovudine treated HIV infected patients
  - ➢ If the patient fails to respond after 8 weeks of therapy, increase dose by approximately 50-100 U/kg at 4- to 8- week intervals until the hemoglobin reaches levels needed to avoid transfusion or max dose of 300 U/kg is reached.
  - ➢ If the hemoglobin exceeds the indication specific level noted above, withhold therapy and resume therapy once level declines to <11 g/dL, at a dose 25% below the previous dose.

LENGTH OF AUTHORIZATION

Coverage will be provided for 45 days and may be renewed unless otherwise specified.

- Reduction of Allogeneic Blood Transfusions in Elective, Non-Cardiac, Non-Vascular Surgery: Coverage may not be renewed.

DOSING LIMITS

Max Units (per dose and over time) [HCPCS Unit]:

- MDS: 120 billable units every 7 days
- Surgery patients: 600 billable units every 15 days
- All other indications: 60 billable units every 7 days

APPLICABLE TENNESSEE STATE MANDATE REQUIREMENTS

BlueCross BlueShield of Tennessee's Medical Policy complies with Tennessee Code Annotated Section 56-7-2352 regarding coverage of off-label indications of Food and Drug Administration (FDA) approved drugs when the off-label use is recognized in one of the statutorily recognized standard reference compendia or in the published peer-reviewed medical literature.

IMPORTANT REMINDER

We develop Medical Policies to provide guidance to Members and Providers. This Medical Policy relates only to the services or supplies described in it. The existence of a Medical Policy is not an authorization, certification, explanation of benefits or a contract for the service (or supply) that is referenced in the Medical Policy. For a determination of the benefits that a Member is entitled to receive under his or her health plan, the Member's health plan must be reviewed. If there is a conflict between the Medical Policy and a health plan, the express terms of the health plan will govern.

ADDITIONAL INFORMATION

For appropriate chemotherapy regimens, dosage information, contraindications, precautions, warnings, and monitoring information, please refer to one of the standard reference compendia (e.g., the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) published by the National Comprehensive Cancer Network®, Drugdex Evaluations of Micromedex Solutions at Truven Health, or The American Hospital Formulary Service Drug Information).

SOURCES

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2. Epogen [package insert]. Thousand Oaks, CA; Amgen, Inc; July 2018. Accessed April 2021.
3. Retacrit [package insert]. Lake Forest, IL; Hospira, Inc; January 2020. Accessed April 2021.
4. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) epoetin alfa. National Comprehensive Cancer Network, 2021. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc." To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed April 2021.

5. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Hematopoietic Growth Factors – Management of Cancer-and Chemotherapy-Induced Anemia Version 2.2021. National Comprehensive Cancer Network, 2021. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc." To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed April 2021.
6. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Myelodysplastic Syndrome Version 3.2021. National Comprehensive Cancer Network, 2021. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc." To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed April 2021.
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EFFECTIVE DATE 8/31/2021

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