Reference number(s)
5563-A

Jurisdiction Specific Medicare Part B Epogen-Procrit-Retacrit

Products Referenced by this Document

Drugs that are listed in the following table include both brand and generic and all dosage forms and strengths unless otherwise stated. Over-the-counter (OTC) products are not included unless otherwise stated.

Brand Name	Generic Name
Epogen	epoetin alfa
Procrit	epoetin alfa
Retacrit	epoetin alfa-epbx

Covered Uses

The indications below are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

- Anemia in patients with non-myeloid malignancies where anemia is specifically due to concomitantly administered chemotherapy
- Anemia related to end-stage renal disease (ESRD) and Stages IIIb, IV and V chronic kidney disease (CKD)
- Anemia induced by AZT (Zidovudine) used in HIV/AIDS therapy
- Anemia related to low prognostic risk myelodysplastic syndrome (MDS) and some myeloproliferative neoplasms in select patients
- Peri-surgical adjuvant therapy for purposes of allogenic red blood cell (RBC) transfusion reduction

All other indications will be assessed on an individual basis. Submissions for indications other than those listed in this criteria should be accompanied by supporting evidence from Medicare approved compendia.

Exclusions

Coverage will not be provided for members with any of the following exclusions:

- Any anemia in cancer or cancer treatment in patients due to folate deficiency, B-12 deficiency, iron deficiency, hemolysis, bleeding, or bone marrow fibrosis.
- The anemia associated with the treatment of acute and chronic myelogenous leukemias (CML, AML), or erythroid cancers.
- The anemia of cancer not related to cancer treatment.
- Any anemia associated only with radiotherapy.
- Prophylactic use to prevent chemotherapy-induced anemia.
- Prophylactic use to reduce tumor hypoxia.
- Patients with erythropoietin (EPO)-type resistance due to neutralizing antibodies.
- Non-ESRD erythropoiesis-stimulating agent (ESA) services within the context of other medical conditions for which resolution would be reasonably expected prior to starting or continuing ESA administration (including, but not limited to: iron/vitamin B12/folate deficiencies, G6PD deficiency, pyridoxine deficiency, various forms of hemolysis, hereditary spherocytosis, and pure red cell aplasias).
- HIV-infected patients due to other factors such as iron or folate deficiencies, hemolysis, or gastrointestinal bleeding, which should be managed appropriately.
- ESA use within the context of uncontrolled hypertension.
- ESA use to replace red blood cell (RBC) transfusions in members who need immediate urgent correction of anemia.

Coverage Criteria

Note: The following causes of anemia should be considered, documented, and corrected before starting or continuing ESA therapy for any of the covered indications: iron deficiency; underlying infection, inflammatory or malignant processes; underlying hematological disease; hemolysis; vitamin deficiencies (e.g., folic acid or B12); blood loss- overt or occult; aluminum intoxication; osteitis fibrosis cystica; or pure red blood cell aplasia.

Anemia of end Stage Renal Disease (ESRD) in a Member on Dialysis

Authorization of 12 weeks may be granted for treatment of anemia of ESRD in a member on dialysis when all of the following criteria are met:

- Member has a diagnosis of end stage renal disease.
- Hemoglobin (Hgb) less than 10 grams per deciliter (g/dL) or hematocrit (HCT) less than 30% at initiation of therapy.
- The provider will document the most recent creatinine within the past month prior to initiation or next dosing of ESA.

Anemia of Chronic Kidney Disease (CKD) in a Member not on Dialysis

Authorization of 12 weeks may be granted for treatment of anemia of CKD in a member not on dialysis when all of the following criteria are met:

- Hgb less than 10 g/dL or HCT less than 30% at initiation of therapy.
- Glomerular filtration rate (GFR) less than 45 mL/min/1.73m^2.
- The provider will document the most recent creatinine within the past month prior to initiation or next dosing of ESA.

Anemia due to Chemotherapy in Members with Non-Myeloid Malignancies

Authorization of 8 weeks may be granted for treatment of anemia due to chemotherapy in members with non-myeloid malignancies when all of the following criteria are met:

- Diagnosis of a non-myeloid malignancy (solid tumor, multiple myeloma, lymphoma, or lymphocytic leukemia).
- Hgb level immediately prior to initiation of ESA treatment is less than 10 g/dL (or HCT less than 30%).
- ESA treatment duration for each course of chemotherapy includes the 8 weeks following the final dose of myelosuppressive chemotherapy in a chemotherapy regimen.

Anemia Related to Treatment with Zidovudine (AZT) for HIV/AIDS

Authorization of 12 months may be granted for treatment of anemia related to AZT treatment for HIV/AIDS when all of the following criteria are met:

- Hgb less than 10 g/dL or HCT less than 30% at initiation of therapy.
- The member's AZT dose less than or equal to 4200 milligrams (mg) per week.
- The member has an endogenous baseline pre-transfusion serum erythropoietin (sEPO) level less than or equal to 500 mU/mL.

Peri-Surgical Adjuvant Therapy to Reduce Allogenic Transfusion

Authorization of 8 weeks may be granted as peri-surgical adjuvant therapy to reduce allogenic transfusion when all of the following criteria are met:

- Member is undergoing planned elective major hip or knee surgery.
- Member has presurgical anemia with Hgb between 10 g/dL and 13 g/dL at least 3 weeks prior to surgery.
- Member is not a candidate for autologous blood transfusion or is unwilling to donate autologous blood.
- There is an expectation for peri-operative blood loss of two units or more.
- Member has undergone previous evaluation to ensure that the existing anemia is likely due to chronic disease rather than another reversible condition.

Anemia Related to Myelodysplastic Syndrome (MDS)

Authorization of 12 weeks may be granted for treatment of anemia in members with MDS when all of the following criteria are met:

- Member has a diagnosis of MDS confirmed by bone marrow aspiration and/or biopsy report.
- Hgb less than 10 g/dL (or HCT less than 30%) at initiation of therapy.
- Member meets one of the following:
  - Revised International Prognostic Scoring System (IPSS-R) score correlating to very low, low risk.
  - IPSS-R correlating to a low score intermediate risk.
  - International Prognostic Scoring System (IPSS) score of low or intermediate-1 risk.
  - WHO (World Health Organization) Prognostic Scoring System (WPSS) score of very low, low or intermediate risk.
- Member has a pretreatment EPO less than or equal to 500 mU/mL.
- Member meets one of the following:
  - MDS without del(5q).
  - MDS with del(5q) and no chromosome 7 associated abnormalities, on or before starting lenalidomide.
- Member has documented anemia-related symptoms such as fatigue, pallor, infection, bleeding or bruising or transfusion dependence.
- Member has documentation of a reasonable expectancy of longer survival with a reduced need for transfusion support.

Continuation of Therapy

Note: The following causes of anemia should be considered, documented, and corrected before starting or continuing ESA therapy for any of the covered indications: iron deficiency; underlying infection, inflammatory or malignant processes; underlying hematological disease; hemolysis; vitamin deficiencies (e.g., folic acid or B12); blood loss-overt or occult; aluminum intoxication; osteitis fibrosis cystica; or pure red blood cell aplasia.

Anemia of ESRD in a Member on Dialysis, Anemia of CKD in a Member not on Dialysis

Authorization of 12 weeks may be granted when both of the following criteria are met:

- The goal of therapy is to maintain a stable Hgb and HCT, with target ranges of 10-12 g/dL and 30-36% respectively.
- The provider will document the most recent creatinine within the past month prior to next dosing of ESA.

Anemia due to Chemotherapy in Members with Non-Myeloid Malignancies

Authorization of 12 weeks may be granted when both of the following criteria are met:

- Hgb less than 10 g/dL or HCT less than 30%.
- ESA treatment duration for each course of chemotherapy includes the 8 weeks following the final dose of myelosuppressive chemotherapy in a chemotherapy regimen.

Anemia Related to Treatment with Zidovudine (AZT) for HIV/AIDS

Authorization of 12 months may be granted when the goal of therapy is to maintain a stable Hgb and HCT, with target ranges of 10-12 g/dL and 30-36%, respectively.

Peri-Surgical Adjuvant Therapy to Reduce Allogenic Transfusion

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

Anemia Related to Myelodysplastic Syndrome (MDS)

Authorization of 12 weeks may be granted when both of the following criteria are met:

- The goal of therapy is to maintain a stable Hgb and HCT, with target ranges of 10-12 g/dL and 30-36%, respectively.
- ESAs should not be continued for more than twelve weeks if no response is observed.

Dosage and Administration

- For anemia due to chemotherapy in members with non-myeloid malignancies, the member must meet all of the following, where applicable:
    - The starting dose for ESA treatment is the recommended FDA label starting dose.
    - Maintenance of ESA therapy is the starting dose if the Hgb level remains below 10 g/dL (or HCT is less than 30%) 4 weeks after initiation of therapy and the rise in Hgb is greater than or equal to 1 g/dL (HCT greater than or equal to 3%).
    - For patients whose Hgb rises less than 1 g/dL (HCT rise less than 3%) compared to pretreatment baseline over 4 weeks of treatment and whose Hgb remains less than 10 g/dL (or HCT < 30%) after the 4 weeks of treatment, the recommended FDA label starting dose may be increased once by 25%. Continued use of the drug is not reasonable and necessary if the Hgb rises less than 1 g/dL (HCT rise less than 3%) compared to pretreatment baseline by 8 weeks of treatment.
    - Continued administration of the drug is not reasonable and necessary if there is a rapid rise in Hgb greater than 1 g/dL (HCT greater than 3%) over 2 weeks of treatment unless

the Hgb remains below or subsequently falls to less than 10 g/dL (or the HCT is less than 30%). Continuation and reinstitution of ESA therapy must include a dose reduction of 25% from the previously administered dose.

- For all other indications, the starting dose and subsequent dose adjustments must be in accordance with FDA-approved labeling or dosing provided in Billing and Coding: Erythropoiesis Stimulating Agents (A58982) or LCD – Erythropoiesis Stimulating Agents (L39237). Doses must be titrated according to the patient's response.

References

1. Erythropoiesis Stimulating Agents LCD (L39237) Original Version. Available at: https://www.cms.gov/medicare-coverage-database/indexes/national-and-local-indexes.aspx. Accessed September 9, 2024.
2. Billing and Coding: Erythropoiesis Stimulating Agents (ESA) (A58982) Version R2. Available at: https://www.cms.gov/medicare-coverage-database/indexes/national-and-local-indexes.aspx. Accessed September 9, 2024.
3. National Coverage Determination (NCD) 110.21 Erythropoiesis Stimulating Agents (ESAs) in Cancer and Related Neoplastic Conditions Version 1. Available at: https://www.cms.gov/medicare-coverage-database/indexes/national-and-local-indexes.aspx. Accessed September 9, 2024.
4. Epogen [package insert]. Thousand Oaks, CA: Amgen Inc.; April 2024.
5. Procrit [package insert]. Horsham, PA: Janssen Products; July 2018.
6. Retacrit [package insert]. New York, NY: Pfizer Labs; June 2024.