Erythropoietin Stimulating Agents: Darbepoetin alfa (Aranesp®), Epoetin alfa (Procrit®), Epoetin Alfa (Epogen®) Epoetin alfa-epbx (Retacrit®)

Prior Authorization Drug Coverage Policy

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Lines of Business: Commercial
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This Drug Coverage Policy provides parameters for the coverage of Darbepoetin alfa (Aranesp®), Epoetin alfa (Procrit®), Epoetin alfa (Epogen®), Epoetin alfa-epbx (Retacrit®). Consideration of medically necessary indications are based upon U.S. Food and Drug Administration (FDA) indications, recommended uses within the Centers of Medicare & Medicaid Services (CMS) five recognized compendia, including the National Comprehensive Cancer Network (NCCN) Drugs & Biologics Compendium (Category 1 or 2A recommendations), and peer-reviewed scientific literature eligible for coverage according to the CMS, Medicare Benefit Policy Manual, Chapter 15, section 50.4.5 titled, "Off-Label Use of Anti-Cancer Drugs and Biologics." This policy evaluates whether the drug therapy is proven to be effective based on published evidence-based medicine.

Drug Description[1]

Aranesp®, Procrit®, Epogen®, and Retacrit® stimulate erythropoiesis by the same mechanism as endogenous erythropoietin and are known collectively as erythropoietin-stimulating agents (ESAs).

FDA Indications[1]

Darbepoetin alfa (Aranesp®), Epoetin alfa (Procrit®), and Epoetin alfa-epbx (Retacrit®) are FDA indicated for the following:

- Indicated for the treatment of anemia due to chronic kidney disease (CKD), including patients on dialysis and patients not on dialysis.
- Indicated for the treatment of anemia in patients with non-myeloid malignancies where anemia is due to the effect of concomitant myelosuppressive chemotherapy, and upon initiation, there is a minimum of two additional months of planned chemotherapy.

NCCN Compendium Supported Indications [5-7]

- Treatment for Myelodysplastic Syndrome

Coverage Determinations

Darbepoetin alfa (Aranesp®), Epoetin alfa (Procrit®), Epoetin alfa (Epogen®), Epoetin alfa-epbx (Retacrit®) will require prior authorization. These agents are considered medically necessary for the following oncology-related indications if all criteria below are met:

Chemotherapy-Induced Anemia[1-7]

- The member has a diagnosis of non-myeloid, non-erythroid malignancy **AND**
- The member must be receiving concurrent myelosuppressive chemotherapy without curative intent **AND**
- ESA is initiated when the member has a minimum of two additional months of planned chemotherapy **AND**
- The member's hemoglobin level immediately prior to ESA initiation or within the last four weeks of maintenance ESA treatment is < 10g/dL and/or hematocrit is < 30% **AND**
- Iron stores must be replete with a transferrin saturation (TSAT) ≥ 20% or a ferritin ≥ 100 ng/mL within the last 4 months

Recommended dosage:

- Use the lowest dose necessary to avoid RBC transfusions.
- After 8 weeks of therapy, if there is no response as measured by hemoglobin levels or if RBC transfusions are still required, discontinue ESA.
- Discontinue following the completion of chemotherapy course
- Evaluate the iron status in all patients before and during treatment. Supplemental iron therapy may be considered when serum ferritin is less than 100 ng/mL or when serum transferrin saturation is less than 20%.

Darbepoetin alfa (Aranesp®)

- Recommended Starting Dose Adults:
  - 2.25 mcg/kg every week subcutaneously until completion of a chemotherapy course.
  - 500 mcg every 3 weeks subcutaneously until completion of a chemotherapy course.
  - Refer to prescribing information for dose escalation and reduction guidelines.

Epoetin alfa (Procrit®), Epoetin alf-epbx (Retacrit®), Epoetin alfa (Epogen®)

- Recommended Starting Dose Adults:
  - 150 Units/kg subcutaneously 3 times per week until completion of a chemotherapy course or
  - 40,000 Units subcutaneously weekly until completion of a chemotherapy course.
- Recommended Starting Dose Pediatric Patients (5 to 18 years):
  - 600 Units/kg intravenously weekly until completion of a chemotherapy course.
- Refer to prescribing information for dose escalation and reduction guidelines.

Myelodysplastic Syndrome

- The member must have a diagnosis of anemia associated with myelodysplastic syndrome (MDS) **AND**
- For initiation: The member's hemoglobin level immediately prior to ESA initiation is < 10 g/dL and/or hematocrit is < 30% **OR**
- For continuation: The member's hemoglobin level is ≤ 12 g/dL and/or hematocrit is ≤ 36% within the last four weeks of maintenance ESA treatment **AND**
- The member has a serum erythropoietin level ≤ 500 mUnits/mL **AND**
- Iron stores must be replete with a transferrin saturation (TSAT) ≥ 20% or a ferritin ≥ 100 ng/mL within the last 4 months AND

Recommended dosage:

- Use the lowest dose necessary to avoid RBC transfusions.
- After 8 weeks of therapy, if there is no response as measured by hemoglobin levels or if RBC transfusions are still required, discontinue ESA.
- Evaluate the iron status in all patients before and during treatment. Supplemental iron therapy may be considered when serum ferritin is less than 100 ng/mL or when serum transferrin saturation is less than 20%.

Darbepoetin alfa (Aranesp®)

- Recommended Starting Dose Adults:
  - 150-300 mcg subcutaneously every 2 weeks.
  - Refer to prescribing information for dose escalation and reduction guidelines.

Epoetin alfa (Procrit®), Epoetin alf-epbx (Retacrit®), Epoetin alfa (Epogen®)

- Recommended Starting Dose Adults:
  - 40,000 – 60,000 Units subcutaneously one to two times per week.
  - Refer to prescribing information for dose escalation and reduction guidelines.

All indications:

- Darbepoetin alfa (Aranesp®), Epoetin alfa (Procrit®), Epoetin alfa (Neupogen®), and Epoetin alfa-epbx (Retacrit®) will be approved through clinical review up to a 12-month determination.

Coverage Limitations

Treatment with Darbepoetin alfa (Aranesp®), Epoetin alfa (Procrit®), Epoetin alfa (Epogen®), and Epoetin alfa-epbx (Retacrit®) is not considered medically necessary for members with the following concomitant conditions:

- In members with cancer receiving hormonal agents, biologic products, or radiotherapy, unless also receiving concomitant myelosuppressive chemotherapy.
- In members with cancer receiving myelosuppressive chemotherapy when the anticipated outcome is cure.
- In members with cancer receiving myelosuppressive chemotherapy in whom the anemia can be managed by transfusion.

- As a substitute for RBC transfusions in patients who require immediate correction of anemia.
- Continued use of the ESA is not reasonable and necessary 8 weeks following the final dose of myelosuppressive chemotherapy in a chemotherapy regimen.
- Continued use of the ESA is not reasonable and necessary if the hemoglobin rises < 1 g/dL (hematocrit rise < 3%) compared to pretreatment baseline by 8 weeks of treatment.
- Continued administration of the ESA is not reasonable and necessary if there is a rapid rise in hemoglobin > 1g/dL (hematocrit > 3%) over 2 weeks of treatment unless the hemoglobin remains below or subsequently falls to < 10g/dL (or the hematocrit is < 30%).
- Anemia due to cancer treatment in patients with uncontrolled hypertension.
- Any anemia in cancer or cancer treatment 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.
- Indications not supported by NCCN category 2A or higher recommendations may not be considered medically necessary.

Contraindications/Warnings/Precautions[1,2,3]

- Contraindications:
  - Uncontrolled hypertension.
  - Pure red cell aplasia (PRCA) that begins after treatment with Aranesp or other erythropoietin protein drugs.
  - Serious allergic reactions.
- Warnings/Precautions:
  - **Black Box Warning**
    - Warning: ESAs increase the risk of death, myocardial infarction, stroke, venous thromboembolism, thrombosis of vascular access and tumor progression or recurrent
  - Increased Mortality, Myocardial Infarction, Stroke, and Thromboembolism
    - In controlled clinical trials of patients with CKD comparing higher hemoglobin targets (13 - 14 g/dL) to lower targets (9 - 11.3 g/dL), ESAs increased the risk of death, myocardial infarction, stroke, congestive heart failure, thrombosis of hemodialysis vascular access, and other thromboembolic events in the higher target groups.
    - Using ESA's to target a hemoglobin level of greater than 11 g/dL increases the risk of serious adverse cardiovascular reactions and has not been shown to provide additional benefit [see Clinical Studies. Use caution in patients with coexistent cardiovascular disease and stroke [see Dosage and Administration. Patients with CKD and an insufficient hemoglobin response to ESA therapy may be at even greater risk for cardiovascular reactions and mortality than other

patients. A rate of hemoglobin rise of greater than 1 g/dL over 2 weeks may contribute to these risks.
    - In controlled clinical trials of patients with cancer, ESAs increased the risks for death and serious adverse cardiovascular reactions. These adverse reactions included myocardial infarction and stroke.
- Increased Mortality and/or Increased Risk of Tumor Progression or Recurrence in Patients with Cancer.

For specific recommendations on contraindications, warnings and precautions, patient monitoring, and on dose adjustments and discontinuation, please refer to the current prescribing information.

Billing

- **Description**: Injection, darbepoetin alfa, 1 microgram
    - HCPCS: J0881 (non-ESRD)
- **Description**: Injection, epoetin alfa, 1000 units
    - HCPCS: J0885 (non-ESRD)
- **Description**: Injection, epoetin alfa, 1000 units
    - HCPCS: J0885 (non-ESRD)
- **Description**: Injection, epoetin alfa-epbx, 1000 units
    - HCPCS: Q5106 (non-ESRD)

Disclaimer

Drug Coverage Policies are developed as needed, regularly reviewed, updated at least annually, and are subject to change. Other policies and coverage determination guidelines may apply. Federal and state regulatory requirements and member specific benefit plan documents, if applicable, must be reviewed prior to this Drug Coverage Policy. This Drug Coverage Policy is for informational purposes only and does not constitute medical advice or dictate how providers should practice medicine. This policy should not be reproduced, stored in a retrieval system, or altered from its original form without written permission from Oncology Analytics, Inc.

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