Darbepoetin (Aranesp®) **Epoetin alfa (Epogen®)** **Epoetin alfa (Procrit®)** **Methoxy polyethylene glycol-epoetin beta (Mircera®)** **Epoetin alfa-epbx (Retacrit®)**	**Medicare Part B** Blue Shield Medicare (PPO) plan **HCPCS** (not on dialysis) Aranesp®: J0881 per 1 mcg Epogen®/Procrit®: J0885 per 1000 units Mircera®: J0888 per 1 mcg Retacrit®: Q5106 per 1000 units

Special Instructions and Pertinent Information

If patient is on dialysis, then erythropoiesis stimulating agents (ESAs) are billed as a medical benefit claim for bundled services provided by the dialysis center. Part B covers these drugs as part of the end-stage renal disease (ESRD) payment to the dialysis provider.

ESA drugs are covered when used to treat a medically accepted indication as established by 1) the Centers for Medicare & Medicaid Services (CMS), and 2) step therapy requirement with the BSC-preferred drug Retacrit, when applicable,

CMS allows Medicare Advantage (MA) Plans to apply step therapy to physician-administered and other Part B drugs. Blue Shield of California (BSC) requires this drug to be reviewed for step therapy requirements in addition to CMS medical necessity requirements. Step therapy with the BSC-preferred drug Retacrit is required for members newly initiating erythropoiesis-stimulating agent (ESA) therapy, when applicable.

Food and Drug Administration (FDA)-Approved Indications

- **Anemia due to Chronic Kidney Disease (CKD) in patients not on dialysis**
  - FDA-approved drugs for this indication: Aranesp, Epogen, Mircera, Procrit, Retacrit
- **Anemia due to Zidovudine in patients with HIV-infection**
  - FDA-approved drugs for this indication: Epogen, Procrit and Retacrit
- **Anemia secondary to myelosuppressive anticancer chemotherapy for the following: Solid tumor, Multiple myeloma, Lymphoma, Lymphocytic leukemia**
  - FDA-approved drugs for this indication: Aranesp, Epogen, Procrit, Retacrit
- **Reduction of allogeneic RBC transfusions in patients undergoing elective, noncardiac, nonvascular surgery**
  - FDA-approved drugs for this indication: Epogen, Procrit and Retacrit

Note: See Section below for CMS's "Nationally Non-Covered Indications"

Coverage Criteria for (FDA)-Approved Indications

Anemia due to Chronic Kidney Disease (CKD) in patients not on dialysis

1. Patient is not on hemodialysis, **AND**
2. *For request for Aranesp, Epogen, Procrit and Mircera*: Inadequate response, intolerable side effect, or contraindication with Retacrit

Covered Doses

Aranesp :
- Adults - 0.45 mcg/kg IV/SC every 4 weeks
- Pediatrics - 0.45 mcg/kg IV/SC per week or 0.75 mcg/kg every 2 weeks

Epogen/Procrit/Retacrit:
- Adults: Initial 50 to 100 units/kg three times weekly
- Pediatrics – Initial 50 Units/kg three times weekly

Mircera:
- Adults: Initial 0.6 mcg/kg IV/SC every two weeks

Coverage Period
6 months

Anemia due to zidovudine in patients with HIV-infection

1. *For request for Epogen and Procrit*: Inadequate response, intolerable side effect, or contraindication with Retacrit

Covered Doses
Epogen/Procrit/Retacrit: 100 Units/kg three times weekly

Coverage Period
12 weeks

Anemia secondary to myelosuppressive anticancer chemotherapy

1. *For request for Aranesp, Epogen, and Procrit*: Inadequate response, intolerable side effect, or contraindication with Retacrit, **AND**
2. Has a diagnosis of solid tumor, multiple myeloma, lymphoma, or lymphocytic leukemia, and
3. Hgb level is less than 10 g/dL or HCT is less than 30%, **AND**
4. Patient does not have uncontrolled hypertension, **AND**
5. Treatment duration for each course of chemotherapy does not exceed 8 weeks following the final dose of chemotherapy

Covered Doses
Initial dosing: Epogen/Procrit/Retacrit: Up to 150 units/kg three x weekly
Aranesp: Up to 2.25 mcg/kg SC weekly
Maintenance dosing:
- Up to 150 units/kg three x weekly for Epogen/Procrit/Retacrit and up to to 2.25 mcg/kg SC weekly for Aranesp if HGB level remains below 10g/dL or HCT is less than 30% 4 weeks after starting the drug and rise in Hgb is less then 1 g/dl (Hct rise is less than 3%)
- For patients whose hemoglobin rises < 1g/dl (hematocrit rise < 3%) compared to pretreatment baseline over 4 weeks of treatment and whose hemoglobin level remains < 10 g/dL after the 4 weeks of treatment (or the hematocrit is < 30%), the recommended FDA label starting dose may be increased once by 25%.
- Continued use of the drug is not reasonable and necessary if the hemoglobin rises < 1g/dl (hematocrit rise < 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 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%).
- Continuation and reinstitution of ESA therapy must include a dose reduction of 25% from the previously administered dose.

Coverage Period
12 weeks and no more than 8 weeks after last dose of chemotherapy

Reduction of allogeneic RBC transfusions in patients undergoing elective, noncardiac, nonvascular surgery

1. For request for Epogen and Procrit: Inadequate response, intolerable side effect, or contraindication with Retacrit

   Covered Doses
   Epogen/Procrit/Retacrit: 300 units/kg per day daily for 15 days or 600 units/kg weekly

   Coverage Period
   1 month

Nationally Non-Covered Indications

ESA treatment is not reasonable and necessary for beneficiaries with certain clinical conditions, either because of a deleterious effect of the ESA on their underlying disease or because the underlying disease increases their risk of adverse effects related to ESA use. These conditions include:

- 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;
- 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-type resistance due to neutralizing antibodies; and
- Anemia due to cancer treatment if patients have uncontrolled hypertension.

How Supplied

Aranesp®

- 25, 40, 60, 100, 200, 300 mcg (single-dose vials)
- 10 mcg/0.4 mL, 25 mcg/0.42 mL, 40 mcg/0.4 mL, 60 mcg/0.3 mL, 100 mcg/0.5 mL, 150 mcg/0.3 mL, 200 mcg/0.4 mL, 300 mcg/0.6 mL, and 500 mcg/1 mL (single-dose prefilled syringes)

Epogen®

- 2000, 3000, 4000, 10,000 units/ml (1 ml single-dose, preservative-free vials)
- 20,000 Units/2 mL (10,000 units/mL) and 20,000 units/mL (multiple-dose vials containing benzyl alcohol)

Procrit®

- 2000, 3000, 4000, 10,000, 40,000 units/ml (1 ml single-dose, preservative-free vial)
- 10,000 units/mL (2 ml multidose, Preserved vial)
- 20,000 units/mL (1 ml multidose, Preserved vial)

Mircera®

- 30 mcg, 50 mcg, 75 mcg, 100 mcg, 120 mcg, 150 mcg, 200 mcg, or 250 mcg (in 0.3 mL solution in single-dose prefilled syringes)

Retacrit®

- 2000, 3000, 4000, 10,000, 40,000 units/ml (1 ml single-dose vial)
- 20,000 Units/2 mL (10,000 units/mL) and 20,000 units/mL (multiple-dose vials containing benzyl alcohol)

References

- Aranesp® (darbepoetin alfa) [Prescribing information]. Thousand Oaks, CA: Amgen, Inc. 1/2019.
- CMS Memorandum titled "Prior Authorization and Step Therapy for Part B Drugs in Medicare Advantage", dated August 7, 2018 see: https://www.cms.gov/Medicare/Health-Plans/HealthPlansGenInfo/Downloads/MA_Step_Therapy_HPMS_Memo_8_7_2018.pdf
- CMS National Coverage Determinations (NCDs): NCD 110.21 Erythropoiesis Stimulating Agents (ESAs) in Cancer and Related Neoplastic Conditions.
- Epogen® (epoetin alfa) [Prescribing information]. Thousand Oaks, CA: Amgen, Inc. 7/2018.
- Mircera® (methoxy polyethylene glycol-epoetin beta) [Prescribing Information]. St. Gallen, Switzerland: Vifor (International) Inc. 6/2018.
- Procrit® (epoetin alfa) [Prescribing Information]. Thousand Oaks, CA: Amgen, Inc. 7/2018.
- Retacrit™ (epoetin alfa-epbx) [Prescribing Information]. NY, NY. Pfizer, Inc. 8/2020.

Policy Update

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- No clinical change to policy following revision.