Corporate Medical Policy: Erythropoiesis-Stimulating Agents (ESAs)

Restricted Product(s):

- epoetin alfa (Epogen®) intravenous or subcutaneous injection for administration by a healthcare professional
- epoetin alfa (Procrit®) intravenous or subcutaneous injection for administration by a healthcare professional
- epoetin alfa-epbx (Retacrit®) intravenous or subcutaneous injection for administration by a healthcare professional
- darbepoetin alfa (Aranesp®) intravenous or subcutaneous injection for administration by a healthcare professional
- methoxy polyethylene glycol (PEG) epoetin-beta (Mircera®) for intravenous or subcutaneous injection for administration by a healthcare professional

FDA Approved Use:

- Epoetin alfa (Epogen®)
    - Treatment of anemia due to
        - Chronic Kidney Disease (CKD) in patients on dialysis and not on dialysis
        - Zidovudine in patients with HIV-infection
        - The effects of concomitant myelosuppressive chemotherapy, and upon initiation, there is a minimum of two additional months of planned chemotherapy
    - Reduction of allogeneic RBC transfusions in patients undergoing elective, noncardiac, nonvascular surgery
- Epoetin alfa (Procrit®)
    - Treatment of anemia due to
        - Chronic Kidney Disease (CKD) in patients on dialysis and not on dialysis
        - Zidovudine in patients with HIV-infection
        - The effects of concomitant myelosuppressive chemotherapy, and upon initiation, there is a minimum of two additional months of planned chemotherapy
    - Reduction of allogeneic RBC transfusions in patients undergoing elective, noncardiac, nonvascular surgery
- Epoetin alfa (Retacrit®)
    - Treatment of anemia due to
        - Chronic Kidney Disease (CKD) in patients on dialysis and not on dialysis
        - Zidovudine in patients with HIV-infection
        - The effects of concomitant myelosuppressive chemotherapy, and upon initiation, there is a minimum of two additional months of planned chemotherapy
    - Reduction of allogeneic RBC transfusions in patients undergoing elective, noncardiac, nonvascular surgery

- Darbepoetin alfa (Aranesp®)
    - Treatment of anemia due to:
        - Chronic Kidney Disease (CKD) in patients on dialysis and patients not on dialysis
        - The effects of concomitant myelosuppressive chemotherapy, and upon initiation, there is a minimum of two additional months of planned chemotherapy
- Methoxy polyethylene glycol (PEG) epoetin-beta (Mircera®)
    - Treatment of anemia associated with chronic kidney disease (CKD) in:
        - Adult patients on dialysis and adult patients not on dialysis
        - Pediatric patients 3 months to 17 years of age on dialysis or not on dialysis who are converting from another ESA after their hemoglobin level was stabilized with an ESA

Criteria for Medical Necessity:

The restricted product(s) may be considered medically necessary when the following criteria are met:

Criteria for Approval of Restricted Product(s):

1. The patient's transferrin saturation, serum ferritin, and hemoglobin have been evaluated (in the last 4 weeks); **AND**
2. For patients with a serum ferritin of < 100 mcg/L or a serum transferrin saturation < 20%, supplemental iron therapy has been initiated; **AND**
3. The patient will be using the product to reduce allogeneic transfusions; **AND**
    a. The patient is a candidate for elective, noncardiac, nonvascular surgery; **AND**
    b. The patient's hemoglobin is > 10 g/dL and ≤ 13 g/dL; **OR**
4. The patient will be using for anemia due to myelosuppressive chemotherapy; **AND**
    a. The patient has a non-myeloid malignancy; **AND**
    b. The patient's hemoglobin is < 10 g/dL (in the last 4 weeks); **AND**
    c. The patent is currently on or has received chemotherapy in the last 6 months; **AND**
    d. Chemotherapy is not intended to be curative; **AND**
    e. The requested medication is NOT Mircera; **OR**
5. The patient will be using for anemia associated with chronic kidney disease; **AND**
    a. The patient has been diagnosed with chronic kidney disease; **AND**
    b. The patient is on dialysis with a hemoglobin of < 10 g/dL (in the last 4 weeks); **OR**

   c. The patient is not on dialysis with a hemoglobin of <10 g/dL (in the last 4 weeks) and is steadily decreasing, indicating a high likelihood for RBC transfusion; **OR**
6. The patient will be using for anemia due to myelodysplastic syndrome; **AND**
   a. The patient has been diagnosed with myelodysplastic syndrome; **AND**
   b. The patient's hemoglobin is < 12 g/dL when starting ESA therapy; **OR**
   c. The patient's hemoglobin is ≤12 g/dL while receiving and stable on ESA therapy; **OR**
7. The patient will be using for anemia related to zidovudine treatment; **AND**
   a. The patient has been diagnosed with HIV/AIDS; **AND**
   b. The patient is being treated with zidovudine; **AND**
   c. The patient's hemoglobin is < 12 g/dL when starting ESA therapy; **OR**
   d. The patient's hemoglobin is ≤ 12 g/dL while receiving and stable on ESA therapy; **OR**
8. The prescriber has submitted documentation in support of the use of the prescribed ESA for the intended diagnosis which has been reviewed and approved by the Clinical Review pharmacist; **AND**
   a. The patient's hemoglobin is < 12 g/dL when starting ESA therapy; **OR**
   b. The patient's hemoglobin is ≤ 12 g/dL while receiving and stable on ESA therapy; **AND**
9. If the request is for Epogen or Procrit, the patient has tried and had an inadequate response to Retacrit OR has an intolerance, FDA labeled contraindication, or hypersensitivity to Retacrit **[medical record documentation required]**; **AND**
10. The requested quantity does NOT exceed the maximum units allowed for the duration of approval (see table below).

Duration of Approval:

Reduction of allogenic blood transfusion: 180 days
Anemia due to myelosuppressive chemotherapy: 180 days
All other diagnoses: 365 days

NOTE:
Use of Erythropoiesis-Stimulating Agents (ESAs) may be considered medically necessary for clinical indications not listed above when the drug is prescribed for the treatment of **cancer** either:

1. In accordance with FDA label (when clinical benefit has been established, and it is not determined to be investigational as defined in the Blue Cross NC Corporate Medical Policy (CMP), “Investigational (Experimental) Services.” [please refer to CMP “Investigational (Experimental) Services” for a summary of evidence standards from nationally recognized compendia]; **OR**

2. In accordance with specific strong endorsement or support by nationally recognized compendia, when such recommendation is based on strong/high levels of evidence, and/or uniform consensus of clinical appropriateness has been reached.

FDA Label Reference				
Medication	**Indication**	**Dosing**	**HCPCS**	**Maximum Units***
Epoetin alfa (Epogen®)	Treatment of anemia due to: Chronic Kidney Disease (CKD) in patients on dialysis and not on dialysis Zidovudine in patients with HIV-infection The effects of concomitant myelosuppressive chemotherapy, and upon initiation, there is a minimum of two additional months of planned chemotherapy Reduction of allogeneic RBC transfusions in patients undergoing elective, noncardiac, nonvascular surgery	**Patients with CKD:** Initial dose: 50 to 100 Units/kg 3 times weekly (adults) and 50 Units/kg 3 times weekly (pediatric patients). Individualize maintenance dose. Intravenous route recommended for patients on hemodialysis **Patients on Zidovudine due to HIV-infection:** 100 Units/kg 3 times weekly **Patients with Cancer on Chemotherapy:** 40,000 Units weekly or 150 Units/kg 3 times weekly (adults); 600 Units/kg intravenously weekly (pediatric patients ≥ 5 years) **Surgery Patients:** 300 Units/kg per day daily for 15 days or 600 Units/kg weekly	**Q4081(for CKD dialysis only)** **J0885 (for non-dialysis)**	**CKD:** 15600 **Patients on Zidovudine:** 1560 **Cancer patients on chemotherapy:** 1170 **Reduction of allogenic RBC transfusions:** 450

FDA Label Reference				
Medication	**Indication**	**Dosing**	**HCPCS**	**Maximum Units***
Epoetin alfa (Procrit®)	Treatment of anemia due to: Chronic Kidney Disease (CKD) in patients on dialysis and not on dialysis Zidovudine in patients with HIV-infection The effects of concomitant myelosuppressive chemotherapy, and upon initiation, there is a minimum of two additional months of planned chemotherapy Reduction of allogeneic RBC transfusions in patients undergoing elective, noncardiac, nonvascular surgery	**Patients with CKD:** Initial dose: 50 to 100 Units/kg 3 times weekly (adults) and 50 Units/kg 3 times weekly (pediatric patients). Individualize maintenance dose. Intravenous route recommended for patients on hemodialysis **Patients on Zidovudine due to HIV-infection:** 100 Units/kg 3 times weekly **Patients with Cancer on Chemotherapy:** 40,000 Units weekly or 150 Units/kg 3 times weekly (adults); 600 Units/kg intravenously weekly (pediatric patients ≥ 5 years) **Surgery Patients:** 300 Units/kg per day daily for 15 days or 600 Units/kg weekly	**Q4081(for CKD dialysis only)** **J0885 (for non-dialysis**	**CKD:** 15600 **Patients on Zidovudine:** 1560 **Cancer patients on chemotherapy:** 1170 **Reduction of allogenic RBC transfusions:** 450
Epoetin alfa-epbx (Retacrit®)	Treatment of anemia due to: Chronic Kidney Disease (CKD) in patients not on dialysis Zidovudine in patients with HIV-infection	**Patients with CKD:** Initial dose: 50 to 100 Units/kg 3 times weekly (adults) and 50 Units/kg 3 times weekly (pediatric patients). Individualize maintenance dose. **Patients on Zidovudine due to HIV-infection:** 100 Units/kg 3 times weekly	**Q5106 (for non-dialysis)**	**CKD:** 15600 **Patients on Zidovudine:** 1560 **Cancer patients on chemotherapy:** 1170

FDA Label Reference				
Medication	**Indication**	**Dosing**	**HCPCS**	**Maximum Units***
	The effects of concomitant myelosuppressive chemotherapy, and upon initiation, there is a minimum of two additional months of planned chemotherapy Reduction of allogeneic RBC transfusions in patients undergoing elective, noncardiac, nonvascular surgery	**Patients with Cancer on Chemotherapy:** 40,000 Units weekly or 150 Units/kg 3 times weekly (adults); 600 Units/kg intravenously weekly (pediatric patients ≥ 5 years) **Surgery Patients:** 300 Units/kg per day daily for 15 days or 600 Units/kg weekly		**Reduction of allogenic RBC transfusions:** 450
Darbepoetin alfa (Aranesp®)	Treatment of anemia due to: Chronic Kidney Disease (CKD) in patients on dialysis and patients not on dialysis The effects of concomitant myelosuppressive chemotherapy, and upon initiation, there is a minimum of two additional months of planned chemotherapy	**Starting dose for patients with CKD on dialysis**: 0.45 mcg/kg intravenously or subcutaneously weekly, OR 0.75 mcg/kg intravenously or subcutaneously every 2 weeks **Starting dose for patients with CKD not on dialysis**: 0.45 mcg/kg intravenously or subcutaneously at 4 week intervals **Starting dose for pediatric patients with CKD**: 0.45 mcg/kg intravenously or subcutaneously weekly. **Pediatric patients with CKD not on dialysis may also be** initiated at 0.75 mcg/kg every 2 weeks	**J0882 (for CKD dialysis only** **J0881 (for non-dialysis)**	**CKD on dialysis:** 2340 **Adult CKD not on dialysis:** 585 **Pediatric CKD patients:** 2340 **Cancer Patients on chemotherapy:** 5850

FDA Label Reference				
Medication	**Indication**	**Dosing**	**HCPCS**	**Maximum Units***
		Starting dose for patients with cancer on chemotherapy: 2.25 mcg/kg subcutaneously weekly, or - 500 mcg subcutaneously every 3 weeks		
Methoxy polyethylene glycol (PEG) epoetin-beta (Mircera®)	Treatment of anemia associated with chronic kidney disease (CKD) in: Adults on dialysis and not on dialysis. Pediatric patients 3 months to 17 years of age on dialysis or not on dialysis who are converting from another ESA after their hemoglobin level was stabilized with an ESA.	**Adults** Initial treatment (not currently treated with an ESA): • CKD patients on dialysis: 0.6 mcg/kg body weight administered once every two weeks • CKD patients not on dialysis: 1.2 mcg/kg body weight administered once every month as a single subcutaneous injection. Alternatively, a starting dose of 0.6 mcg/kg body weight may be administered once every two weeks as a single intravenous or subcutaneous injection. Conversion from another ESA: Dosed once monthly or once every two weeks based on total weekly epoetin alfa or darbepoetin alfa dose at time of conversion. **Pediatric Patients** Conversion from another ESA: Dosed once every 4 weeks based on total weekly	**J0887 (for CKD dialysis only** **J0888 (for non dialysis)**	**1560**

FDA Label Reference				
Medication	**Indication**	**Dosing**	**HCPCS**	**Maximum Units***
		epoetin alfa or darbepoetin alfa dose at time of conversion. In patients < 6 years old, maintain the same route of administration as the previous ESA when switching from another ESA to Mircera.		

***Maximum units allowed for duration of approval**

References: all information referenced is from FDA package insert unless otherwise noted below.

Policy Implementation/Update Information: Criteria and treatment protocols are reviewed annually by the Blue Cross NC P&T Committee, regardless of change. This policy is reviewed in Q3 annually.

November 2024: Criteria update (Mircera): Expanded FDA labeled age to pediatric patients 3 months to 17 years of age on dialysis or not on dialysis, and added associated dosing in FDA label reference table. Other minor updates made throughout policy for clarity with no change to policy intent.
April 2022: Criteria update: Added Retacrit dosing for CKD patients not on dialysis to FDA label dosing table.
March 2022: Criteria change: Removed HCPCS code Q5105 from FDA label dosing table.
June 2021: Criteria change: Added requirement of evaluation of patient's transferrin saturation, serum ferritin, and hemoglobin; requirement of supplemental iron for low ferritin or transferrin; removal of Omontys; defined surgical candidate for reduce allogeneic transfusions as elective, noncardiac, nonvascular; added maximum units; medical policy formatting change. **Policy notification given 4/16/2021 for effective date 6/16/2021**.
*Further historical criteria changes and updates available upon request from Medical Policy and/or Corporate Pharmacy