Policy Title:	**Erythropoiesis stimulating agents: Retacrit (epoetin alfa), Epogen (epoetin alfa), Procrit (epoetin alfa), Aranesp (darbepoetin alfa), Mircera (methoxy polyethylene glycol-epoetin beta) NON-ONCOLOGY POLICY**		
		Department:	PHA
Effective Date:	01/01/2020		
Review Date:	12/18/19, 1/29/20, 8/3/2020, 4/15/2021, 6/16/2022, 4/20/2023, 12/14/2023, 01/04/2024, 04/02/2025, 02/10/2026		

Purpose: To support safe, effective, and appropriate use of Erythropoiesis stimulating agents.

Scope: Medicaid, Commercial, Medicare

Policy Statement:

Erythropoiesis stimulating agents are covered under the Medical Benefit when used within the following guidelines for non-oncology indications. Use outside of these guidelines may result in non-payment unless approved under an exception process. **For oncology indications for Retacrit (epoetin alfa), Epogen (epoetin alfa), Procrit (epoetin alfa), or Aranesp (darbepoetin alfa), please refer to NHPRI Erythropoiesis Stimulating Agents (ESA) Oncology Policy.**

Procedure:

Coverage of Erythropoiesis stimulating agents will be reviewed prospectively via the prior authorization process based on criteria below.

Summary of Evidence:

Epogen Procrit Retacrit: Epoetin alfa (Epogen, Procrit, Retacrit) is an erythropoiesis-stimulating agent (ESA) used for treating anemia in chronic kidney disease (CKD) in patients on and not on dialysis, HIV Patients due to zidovudine treatment, and surgical patients to reduce need for RBC transfusions in elective, noncardiac, nonvascular surgery. However, targeting hemoglobin levels above 11 g/dL with ESAs has been associated with increased risks of mortality, myocardial infarction, stroke, and thromboembolism without added benefits. Clinical studies in adult CKD patients on dialysis showed that epoetin alfa increased hemoglobin levels and significantly reduced the need for transfusions, with over 95% of patients becoming transfusion-independent within three months. Pediatric CKD patients also responded well, with 92.3% achieving transfusion independence within 12 weeks and significantly improved hemoglobin levels compared to placebo. For CKD patients not on dialysis, four studies demonstrated a dose-dependent and sustained hemoglobin increase regardless of the administration route. In HIV patients on zidovudine with low endogenous erythropoietin levels (≤500 mUnits/mL), epoetin alfa significantly reduced transfusion needs and increased hemoglobin levels compared to placebo. Common adverse events include fever, musculoskeletal pain, rash, nausea and vomiting and flu-like symptoms.

Aranesp: Aranesp (darbepoetin alfa) is an erythropoiesis-stimulating agent (ESA) approved for treating anemia in patients with chronic kidney disease (CKD)—both on and not on dialysis. Targeting hemoglobin levels above 11 g/dL with Aranesp is associated with increased risks of mortality, myocardial

infarction, stroke, and thromboembolic events without added benefit, especially in patients with cardiovascular comorbidities. In CKD patients on dialysis, early ESA studies showed reduced red blood cell (RBC) transfusions when targeting hemoglobin around 12 g/dL. In CKD patients not on dialysis, the TREAT trial (n=4038) found fewer transfusions in the higher target group (13 g/dL) vs. control (15% vs. 25%), but no cardiovascular or renal benefits and worse safety outcomes. In anemia correction studies for treatment-naïve CKD adults, once-weekly Aranesp (0.45 mcg/kg) achieved the primary endpoint (≥1 g/dL increase and Hb ≥11 g/dL) in 72%–93% of patients across two studies. Once every two-week dosing (0.75 mcg/kg) achieved the hemoglobin goal in 85%–92% of patients. In pediatric patients, once-weekly and once-every-two-weeks regimens corrected hemoglobin to ≥10 g/dL in 98% and 84% of cases, respectively. Common adverse events include increased risk of tumor progression in cancer patients, hypertension, seizures (particularly in CKD), pure red cell aplasia (PRCA), serious allergic reactions, and severe cutaneous reactions.

Mircera: Mircera (methoxy polyethylene glycol-epoetin beta) is an erythropoiesis-stimulating agent (ESA) indicated for the treatment of anemia associated with chronic kidney disease (CKD) in adult patients on dialysis, adult patients not on dialysis, and pediatric patients aged 5 to 17 years on hemodialysis who are converting from another ESA after hemoglobin stabilization. Clinical studies in adult patients with CKD on dialysis have demonstrated that ESAs reduce the need for RBC transfusions. In early trials, patients with baseline hemoglobin around 7.5 g/dL who were titrated to 12 g/dL required fewer transfusions. In the NHS study, transfusion rates were 51.5% in patients with hemoglobin targets of 10 g/dL compared to 32.4% for those with 14 g/dL. For CKD patients not on dialysis, the TREAT trial showed that targeting 13 g/dL hemoglobin reduced transfusions (15%) versus control (25%).. Across three key outcome trials—NHS, CHOIR, and TREAT—higher hemoglobin targets led to worse cardiovascular outcomes without reducing progression to end-stage renal disease (ESRD), further highlighting the safety concerns with aggressive ESA therapy. In clinical trials evaluating Mircera's efficacy and safety, six open-label studies compared Mircera to other ESAs. Two of these involved ESA-naïve patients (CKD not on dialysis and on dialysis), and four involved patients already on ESA therapy. In ESA-naïve patients, Mircera administered every two weeks (0.6 mcg/kg SC or 0.4 mcg/kg IV) was comparable to darbepoetin alfa or epoetin in achieving hemoglobin goals (≥1 g/dL increase and ≥11 g/dL without transfusion), with transfusion rates below 3% in all groups. In patients already receiving ESA therapy, Mircera administered either every two or four weeks-maintained hemoglobin levels (10–13.5 g/dL) similarly to comparator ESAs administered more frequently. Safety precautions include controlling hypertension prior to and during treatment. Seizures have been reported in CKD patients receiving Mircera, warranting increased monitoring. If severe anemia and low reticulocyte counts develop, Mircera should be withheld and patients evaluated for pure red cell aplasia (PRCA). Additionally, serious allergic reactions and severe cutaneous reactions necessitate discontinuation of therapy.

Initial Criteria:

Retacrit (epoetin alfa), Epogen (epoetin alfa), Procrit (epoetin alfa):

- Member must have one of the following indications**:**
    - Anemia due to chronic kidney disease (CKD), including members on dialysis and not on dialysis with pretreatment hemoglobin < 10 g/dL; OR
    - Anemia due to zidovudine in members with HIV-infection with pretreatment hemoglobin < 10 g/dL; OR

- Reduction of Allogeneic Red Blood Cell Transfusion in Members Undergoing Elective, Non-cardiac, Nonvascular Surgery and members are scheduled to have an elective, non-cardiac, nonvascular surgery when the pretreatment hemoglobin is > 10 to ≤ 13 g/dL; OR
  - Anemia in congestive heart failure (CHF) with pretreatment hemoglobin < 9 g/dL; OR
  - Anemia in rheumatoid arthritis (RA) with pretreatment hemoglobin < 10 g/dL; OR
  - Anemia due to hepatitis C treatment in members with pretreatment hemoglobin < 10 g/dL who are receiving ribavirin in combination with either interferon alfa or peginterferon alfa; OR
  - Anemia in members whose religious beliefs forbid blood transfusions with pretreatment hemoglobin < 10 g/dL; OR
- For members requesting Epogen (epoetin alfa) they must have a documented intolerable adverse event to Retacrit (epoetin alfa) or Procrit (epoetin alfa), and the adverse event was not an expected adverse event attributed to the active ingredient as described in the prescribing information; OR
- Medicare members who have previously received this medication within the past 365 days are not subject to Step Therapy Requirements

Aranesp (darbepoetin alfa):

- Member must have one of the following indications**:**
  - Anemia in members with CKD with pretreatment hemoglobin < 10 g/dL; OR
  - Anemia in members whose religious beliefs forbid blood transfusions with pretreatment hemoglobin < 10 g/dL; AND
- For members requesting Aranesp (darbepoetin alfa) they must have a documented intolerable adverse event to Retacrit (epoetin alfa) or Procrit (epoetin alfa), and the adverse event was not an expected adverse event attributed to the active ingredient as described in the prescribing information; OR
- Medicare members who have previously received this medication within the past 365 days are not subject to Step Therapy Requirements

Mircera (methoxy polyethylene glycol-epoetin beta):

- Member must have anemia in members with CKD with pretreatment hemoglobin < 10 g/dL; AND
- For members requesting Mircera (methoxy polyethylene glycol-epoetin beta) they must have a documented intolerable adverse event to Retacrit (epoetin alfa) or Procrit (epoetin alfa, and the adverse event was not an expected adverse event attributed to the active ingredient as described in the prescribing information; OR
- Medicare members who have previously received this medication within the past 365 days are not subject to Step Therapy Requirements

Renewal Coverage (Retacrit (epoetin alfa), Epogen (epoetin alfa), Procrit (epoetin alfa), Aranesp (darbepoetin alfa) Mircera (methoxy polyethylene glycol-epoetin beta):

For all indications below: all members (including new members) requesting authorization for continuation of therapy after at least 12 weeks of ESA treatment must show a response with a rise in hemoglobin of ≥ 1 g/dL. Members who completed less than 12 weeks of ESA treatment and have not yet responded with a rise in hemoglobin of ≥ 1 g/dL may be granted authorization of up to 12 weeks to allow sufficient time to demonstrate a response.

- Anemia due to CKD and the current hemoglobin is ≤ 12 g/dL;
- Anemia due to zidovudine in members with HIV-infection with current hemoglobin ≤ 12 g/dL;
- Anemia in CHF or RA and current hemoglobin is ≤ 12 g/dL;
- Anemia due to Hepatitis C treatment and member meets all of the following criteria:
    - The member is receiving ribavirin in combination with either interferon alfa or peginterferon alfa
    - The current hemoglobin is ≤ 12 g/dL
- Anemia in members whose religious beliefs forbid blood transfusions and current hemoglobin is ≤ 12 g/dL

Dosage and Administration:
Retacrit (epoetin alfa), Epogen (epoetin alfa), Procrit (epoetin alfa)

Indication	Dose
Anemia due to CKD	• Adults: 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 three times weekly • May titrate up to 300 units/kg
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) • 600 units/kg/dose subcutaneously on days 21, 14, and 7 before surgery plus 1 dose on the day of surgery (4 total doses)
All other indications	Dosing varies; generally up to 150 units/kg intravenously or subcutaneously three times weekly

Dosage and Administration:
Aranesp (darbepoetin alfa)

Indication	Dose
Anemia due to CKD-Not on dialysis	Adults • Initiate at 0.45 mcg/kg intravenously or subcutaneously every 28 days

	Pediatric patients • Initiate at 0.45 mcg/kg intravenously or subcutaneously every 7 days or 0.75 mcg/kg every 14 days
Most common weekly dose	• Up to 200 mcg
Most common every 2-week dose	• Up to 300 mcg
Most common every 3-week dose	• Up to 500 mcg

Mircera (methoxy polyethylene glycol-epoetin beta):

Indication	Dose
Anemia due to CKD-Not on dialysis	• Starting dose: 0.6 mcg/kg IV or SC once every 2 weeks • Maintenance dose: Once monthly dosing at twice the every-two-week dose once Hb has been stabilized. Most commonly 120 to 360 mcg every 4 weeks

Billable Units:

Drug	Billable unit
Epogen/Procrit (non-ESRD use)	1000 IU = 1 billable unit
Retacrit (non-ESRD use)	1000 IU = 1 billable unit
Aranesp (non-ESRD use)	1mcg = 1 billable unit
Mircera (non-ESRD use)	1mcg = 1 billable unit

Coverage durations: 12 weeks

Per §§ 42 CFR 422.101, this clinical medical policy only applies to Medicare in the absence of National Coverage Determination (NCD) or Local Coverage Determination (LCD).

Policy Rationale:
Epogen/Procrit, Retacrit, Aranesp, and Mircera were reviewed by the Neighborhood Health Plan of Rhode Island Pharmacy & Therapeutics (P&T) Committee. Neighborhood adopted the following clinical coverage criteria to ensure that its members use Epogen/Procrit, Retacrit, Aranesp, and Mircera according to Food and Drug Administration (FDA) approved labeling and/or relevant clinical literature. Neighborhood worked with network prescribers and pharmacists to draft these criteria. These criteria will help ensure its members are using this drug for a medically accepted indication, while minimizing the risk for adverse effects and ensuring more cost-effective options are used first, if applicable and appropriate. For Medicare members, these coverage criteria will only apply in the absence of National Coverage Determination (NCD) or Local Coverage Determination (LCD) criteria. Neighborhood will

give individual consideration to each request it reviews based on the information submitted by the prescriber and other information available to the plan.

Investigational use: All therapies are considered investigational when used at a dose or for a condition other than those that are recognized as medically accepted indications as defined in any one of the following standard reference compendia: American Hospital Formulary Service Drug information (AHFS-DI), Thomson Micromedex DrugDex, Clinical Pharmacology, Wolters Kluwer Lexi-Drugs, or Peer-reviewed published medical literature indicating that sufficient evidence exists to support use. Neighborhood does not provide coverage for drugs when used for investigational purposes.

Applicable Codes:
Below is a list of billing codes applicable for covered treatment options. The below tables are provided for reference purposes and may not be all inclusive. Requests received with codes from tables below do not guarantee coverage. Requests must meet all criteria provided in the procedure section.

The following HCPCS/CPT codes are:

HCPCS/CPT Code	Description
Q5106	Injection, epoetin alfa, biosimilar, (retacrit) (for non-esrd use), 1000 units
J0885	Injection, epoetin alfa, (for non-esrd use), 1000 units
J0881	Injection, darbepoetin alfa, 1 mcg (non-esrd use)
J0888	Injection, epoetin alfa, 1mcg (non-esrd use)

Note: The following HCPCS codes Q5105, Q4081 & J0882 & J0887 are NOT covered under this policy, but are covered under the dialysis bundle.

References:

1. Aranesp package insert. Thousand Oaks, CA; Amgen, Inc; December 2024. Accessed January 2026.
2. Epogen package insert. Thousand Oaks, CA: Amgen Inc.; November 2025. . Accessed January 2026.
3. Procrit package insert. Horsham, PA: Janssen Products, LP; April 2025. Accessed January 2026.
4. Retacrit package insert. New Yok, NY: Hospira, Inc; June 2025. Accessed January 2026.
5. Mircera package insert. Switerland: Vifor Pharma; June 2024. Accessed January 2026.
6. Micromedex Solutions [database online]. Ann Arbor, MI: Truven Health Analytics Inc. Updated periodically. www.micromedexsolutions.com [available with subscription]. Accessed September 19, 2018.
7. AHFS DI (Adult and Pediatric) [database online]. Hudson, OH: Lexi-Comp, Inc.; http://online.lexi.com/lco/action/index/dataset/complete_ashp [available with subscription]. Accessed September 19, 2018.
8. Kidney Disease: Improving Global Outcomes (KDIGO) Anemia Work Group. KDIGO Clinical Practice Guideline for Anemia in Chronic Kidney Disease. Kidney Int. 2012;Suppl 2:279-335.

9. National Kidney Foundation. KDOQI Clinical Practice Guideline and Clinical Practice Recommendations for Anemia in Chronic Kidney Disease: 2007 Update of Hemoglobin Target. http://www2.kidney.org/professionals/KDOQI/guidelines_anemiaUP/. Accessed September 19, 2018.
10. Qaseem A, Humphrey LL, Fitterman N, Starkey M, Shekelle P, for the Clinical Guidelines Committee of the American College of Physicians. Treatment of Anemia in Patients with Heart Disease: A Clinical
11. Cervantes F, Alvarez-Larran A, Hernandez-Boluda JC, et al. Erythropoietin treatment of the anemia of myelofibrosis with myeloid metaplasia: results in 20 patients and review of the literature. Br J Haematol. 2004;127(4):399-403.