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		

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

Scope: Medicaid, Commercial, Medicare-Medicaid Plan (MMP)

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:

Clinical trials evaluating the efficacy of ESAs in various patient populations, including those with chronic kidney disease (CKD), chemotherapy-induced anemia, and anemia associated with certain hematological disorders, have demonstrated improvements in hemoglobin levels, reduced transfusion requirements, and improvement in quality-of-life measures. There are significant warnings for these therapies that include the risk of cardiovascular events, stroke, and increased mortality.

Initial Criteria:

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

- Patient must have one of the following indications**:**
  - Anemia due to chronic kidney disease (CKD), including patients on dialysis and not on dialysis with pretreatment hemoglobin < 10 g/dL; OR
  - Anemia due to zidovudine in patients with HIV-infection with pretreatment hemoglobin < 10 g/dL; OR
  - Reduction of Allogeneic Red Blood Cell Transfusion in Patients Undergoing Elective, Non-cardiac, Nonvascular Surgery and patients 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 patients with pretreatment hemoglobin < 10 g/dL who are receiving ribavirin in combination with either interferon alfa or peginterferon alfa; OR
  - Anemia in patients whose religious beliefs forbid blood transfusions with pretreatment hemoglobin < 10 g/dL; OR
- For patients requesting Epogen (epoetin alfa) or Procrit (epoetin alfa) they must have a documented intolerable adverse event to Retacrit (epoetin alfa), and the adverse event was not an expected adverse event attributed to the active ingredient as described in the prescribing information; OR
- MMP members who have previously received this medication within the past 365 days are not subject to Step Therapy Requirements

Aranesp (darbepoetin alfa):

- Patient must have one of the following indications**:**
  - Anemia in patients with CKD with pretreatment hemoglobin < 10 g/dL; OR
  - Anemia in patients whose religious beliefs forbid blood transfusions with pretreatment hemoglobin < 10 g/dL; AND
- For patients requesting Aranesp (darbepoetin alfa) they must have a documented intolerable adverse event to Retacrit (epoetin alfa), and the adverse event was not an expected adverse event attributed to the active ingredient as described in the prescribing information; OR
- MMP 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):

- Patient must have anemia in patients with CKD with pretreatment hemoglobin < 10 g/dL; AND
- For patients requesting Mircera (methoxy polyethylene glycol-epoetin beta) they must have a documented intolerable adverse event to Retacrit (epoetin alfa), and the adverse event was not an expected adverse event attributed to the active ingredient as described in the prescribing information; OR
- MMP 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 patients 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 patient 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 patients 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 INTEGRITY 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 INTEGRITY (Medicare-Medicaid Plan) 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:

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4. Retacrit package insert. New Yok, NY: Hospira, Inc; June 2023. Accessed November 2023.
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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.