Clinical Policy: Blood Formation, Coagulation, and Thrombosis Agents: Hematopoietic Agents

Reference Number: OH.PHAR.PPA.24
Effective Date: 01.2020
Last Review Date: 11.21
Line of Business: Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

The following are erythropoiesis-stimulating agents (ESA) requiring prior authorization:

BLOOD AGENTS: HEMATOPOIETIC AGENTS

CLINICAL PA REQUIRED "PREFERRED"	PA REQUIRED "NON-PREFERRED"
EPOGEN® (epoetin alfa) RETACRIT® (epoetin alfa-epbx) MIRCERA® (methoxy polyethylene glycol-epoetin beta)	ARANESP® (darbepoetin alfa) PROCRIT® (epoetin alfa)

FDA Approved Indication(s): Varies by drug product, please see package insert; clinical pharmacology or other appropriate clinical reference.

Epogen, Procrit, and Retacrit are indicated for:

- **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 red blood cell (RBC) transfusions in patients undergoing elective, noncardiac, nonvascular surgery.

Limitation(s) of use:

- Epogen, Procrit, and Retacrit have not been shown to improve quality of life, fatigue, or patient well-being.
- **Epogen, Procrit, and Retacrit are not indicated for use:**
  - In patients with cancer receiving hormonal agents, biologic products, or radiotherapy, unless also receiving concomitant myelosuppressive chemotherapy.
  - In patients with cancer receiving myelosuppressive chemotherapy when the anticipated outcome is cure.
  - In patients with cancer receiving myelosuppressive chemotherapy in whom the anemia can be managed by transfusion.
  - In patients scheduled for surgery who are willing to donate autologous blood.
  - In patients undergoing cardiac or vascular surgery.
  - As a substitute for RBC transfusions in patients who require immediate correction of anemia.

Aranesp is indicated for the treatment of:

- Anemia due to chronic kidney disease (CKD), including patients on dialysis and patients not on dialysis.
- 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.

Limitation(s) of use: Aranesp has not been shown to improve quality of life, fatigue, or patient well-being. Aranesp is not indicated for use:

- In patients with cancer receiving myelosuppressive chemotherapy when the anticipated outcome is cure.
- In patients with cancer receiving myelosuppressive chemotherapy in whom the anemia can be managed by transfusion.
- As a substitute for red blood cell transfusions in patients who require immediate correction of anemia.

Mircera is indicated for the treatment of:

- anemia associated with chronic kidney disease (CKD) in Adult patients on dialysis and patients not on dialysis
- anemia associated with chronic kidney disease (CKD) in Pediatric patients 5 to 17 years of age on hemodialysis who are converting from another ESA after their hemoglobin level was stabilized with an ESA.

Limitation(s) of use:

- Mircera is not indicated and is not recommended for use:
  - In the treatment of anemia due to cancer chemotherapy
  - As a substitute for red blood cell (RBC) transfusions in patients who require immediate correction of anemia.
- Mircera has not been shown to improve symptoms, physical functioning or health-related quality of life.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of Buckeye Health Plan® that Epogen; Retacrit; Mircera Aranesp; Procrit is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria for Non-preferred (Mircera)

A. Anemia of Chronic Kidney Disease (must meet all):

1. **Diagnosis of anemia of CKD and member meets one of the following (a or b):**
   a. Age ≥ **18 years** (dialysis status is irrelevant);
   b. Age = **5 - 17 years,** on hemodialysis, and will be converting from another ESA agent (e.g., epoetin alfa, darbepoetin alfa)
2. **Member has failed therapeutic trials of 14 days with preferred medications unless one of the following (a,b, or c)**
   a. Allergy to all medications not requiring prior approval
   b. Contraindication to all medications not requiring prior approval
   c. History of unacceptable/toxic side effects to medications not requiring prior approval

Approval duration: 180 days

II. Initial Approval Criteria for Preferred: (Epogen; Retacrit) and Non-preferred: (Procrit)

A. Anemia due to Chronic Kidney Disease(must meet all)**:**

1. Diagnosis of Anemia of CKD (dialysis and non-dialysis members)
2. **If prescribed drug is Non-preferred medication, member has failed therapeutic trials of 14 days with preferred medications unless one of the following (a,b, or c)**
   a. Allergy to all medications not requiring prior approval
   b. Contraindication to all medications not requiring prior approval
   c. History of unacceptable/toxic side effects to medications not requiring prior approval
3. **Member on Dialysis**-pretreatment hemoglobin level < or equal to **11 g/dL;**
4. **Member not on Dialysis** pretreatment hemoglobin level < or equal to **10 g/dL;**

Approval duration: 12 months

B. Cancer chemotherapy-induced Anemia;

1. **Diagnosis of anemia due to chemotherapy**
2. **Age ≥ 5 years**
3. **If prescribed drug is Non-preferred medication, member has failed therapeutic trials of 14 days with preferred medications unless one of the following (a,b, or c)**
   a. Allergy to all medications not requiring prior approval
   b. Contraindication to all medications not requiring prior approval
   c. History of unacceptable/toxic side effects to medications not requiring prior approval
4. **Pretreatment hemoglobin level < or equal to 10 g/dL**

Approval duration: 90 days

C. Anemia Associated with Myelodysplastic Syndromes (off-label) (must meet all):

1. Diagnosis of anemia from myelodysplastic syndrome (MDS)
2. Age ≥ 18 years
3. **If prescribed drug is Non-preferred medication, member has failed therapeutic trials of 14 days with preferred medications unless one of the following (a,b, or c)**
   a. Allergy to all medications not requiring prior approval
   b. Contraindication to all medications not requiring prior approval
   c. History of unacceptable/toxic side effects to medications not requiring prior approval
4. Pretreatment hemoglobin level < or equal to 11 g/dL

Approval duration: 180 days

D. Anemia due to Zidovudine in HIV-infected Patients (must meet all):

1. **Diagnosis of zidovudine induced anemia;**
2. **If prescribed drug is Non-preferred medication, member has failed therapeutic trials of 14 days with preferred medications unless one of the following (a,b, or c)**
   a. Allergy to all medications not requiring prior approval
   c. History of unacceptable/toxic side effects to medications not requiring prior approval
3. Pretreatment hemoglobin level < or equal to 11 g/dL

Approval duration: 180 days

E. Autologous blood donation, patient will require blood transfusions (must meet all):

1. **Member is at high risk for perioperative blood loss**
2. **If prescribed drug is Non-preferred medication, member has failed therapeutic trials of 14 days with preferred medications unless one of the following (a,b, or c)**
   a. Allergy to all medications not requiring prior approval
   b. Contraindication to all medications not requiring prior approval
   c. History of unacceptable/toxic side effects to medications not requiring prior approval
3. **Perioperative hemoglobin > 10 to ≤ 13 g/dL;**
   Approval Duration: 30 days

F. Anemia of prematurity, age < or = 6 months

1. **Diagnosis of Anemia of prematurity, age <=6 months**
2. **If prescribed drug is Non-preferred medication, member has failed therapeutic trials of 14 days with preferred medications unless one of the following (a,b, or c)**
   a. Allergy to all medications not requiring prior approval
   b. Contraindication to all medications not requiring prior approval

c. History of unacceptable/toxic side effects to medications not requiring prior approval

Approval Duration: 42 days

G. Anemia associated with chronic inflammatory disorders (e.g., rheumatoid arthritis)

1. **Diagnosis of Anemia associated with chronic inflammatory disorders**
2. **If prescribed drug is Non-preferred medication, member has failed therapeutic trials of 14 days with preferred medications unless one of the following (a,b, or c)**
   a. Allergy to all medications not requiring prior approval
   b. Contraindication to all medications not requiring prior approval
   c. History of unacceptable/toxic side effects to medications not requiring prior approval
3. **Pretreatment hemoglobin level < or equal to 11 g/dL**

Approval Duration: 180 days

H. Anemia associated with ribavirin combination therapy in hepatitis C-infected patient

1. **Diagnosis of Anemia associated with ribavirin combination therapy in hepatitis C-infected patient**
2. **If prescribed drug is Non-preferred medication, member has failed therapeutic trials of 14 days with preferred medications unless one of the following (a,b, or c)**
   a. Allergy to all medications not requiring prior approval
   b. Contraindication to all medications not requiring prior approval
   c. History of unacceptable/toxic side effects to medications not requiring prior approval
3. **Pretreatment hemoglobin level < or equal to 11 g/dL**

Approval Duration: 180 days

III. Initial Approval Criteria for Non-preferred Aranesp (Darbepoetin alfa):

A. Anemia due to Chronic Kidney Disease(must meet all)**:**

2. **If prescribed drug is Non-preferred medication, member has failed therapeutic trials of 14 days with preferred medications unless one of the following (a,b, or c)**
   a. Allergy to all medications not requiring prior approval
   b. Contraindication to all medications not requiring prior approval
   c. History of unacceptable/toxic side effects to medications not requiring prior approval
3. **Member on Dialysis**-pretreatment hemoglobin level < or equal to **11 g/dL;**
4. **Member not on Dialysis** pretreatment hemoglobin level < or equal to **10 g/dL;**

Approval duration: 12 months

B. Cancer chemotherapy-induced Anemia;
1. **Diagnosis of anemia due to chemotherapy**
2. **Age ≥ 5 years**
3. **If prescribed drug is Non-preferred medication, member has failed therapeutic trials of 14 days with preferred medications unless one of the following (a,b, or c)**
   a. Allergy to all medications not requiring prior approval
   b. Contraindication to all medications not requiring prior approval
   c. History of unacceptable/toxic side effects to medications not requiring prior approval
4. **Pretreatment hemoglobin level < or equal to 10 g/dL**

Approval duration: 90 days

C. Anemia Associated with Myelodysplastic Syndromes (off-label) (must meet all):
1. Diagnosis of anemia from myelodysplastic syndrome (MDS)
2. Age ≥ 18 years
3. **If prescribed drug is Non-preferred medication, member has failed therapeutic trials of 14 days with preferred medications unless one of the following (a,b, or c)**
   a. Allergy to all medications not requiring prior approval
   b. Contraindication to all medications not requiring prior approval
   c. History of unacceptable/toxic side effects to medications not requiring prior approval
4. **Pretreatment hemoglobin level < or equal to 11 g/dL**

D. Approval duration: 180 days

IV. Diagnoses/Indications for which coverage is NOT authorized:
Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.PMN.53 for Medicaid or evidence of coverage documents.

V. Appendices/General Information
Appendix A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
PA: Prior Authorization
ER: Extended Release

Appendix B: Therapeutic Alternatives

Appendix C: Contraindications/Boxed Warnings

- *See package insert; clinical pharmacology or other appropriate clinical reference.*

VI. Dosage and Administration:

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

Indication	Dosing Regimen	Maximum Dose
Anemia due to CKD	Initial dose: 50 to 100 Units/kg 3 times weekly (adults) IV or SC and 50 Units/kg 3 times weekly (children on dialysis) IV or SC. Individualize maintenance dose. IV route recommended for patients on hemodialysis	Varies depending on indication and frequency of administration
Anemia due to zidovudine in HIV-infected patients	100 Units/kg IV or SC 3 times weekly	Varies depending on indication and frequency of administration
Anemia due to chemotherapy	40,000 Units SC weekly *or* 150 Units/kg SC 3 times weekly (adults) until completion of a chemotherapy course; 600 Units/kg IV weekly (children ≥ 5 years) until completion of a chemotherapy course	Varies depending on indication and frequency of administration
Reduction of allogeneic red blood cell transfusions in patients undergoing elective, noncardiac, nonvascular surgery	300 Units/kg per day SC daily for 15 days total: administered daily for 10 days before surgery, on the day of surgery, and for 4 days after surgery or 600 Units/kg SC weekly in 4 doses administered 21, 14, and 7 days before surgery and on the day of surgery	Varies depending on indication and frequency of administration
Anemia associated with MDS†	40,000-60,000 units SC one to two times weekly	Varies depending on indication and frequency of administration
Anemia associated with myelofibrosis †	In a clinical trial, patients initially received erythropoietin 10,000 units SC 3 days per week. Erythropoietin was increased to 20,000 units 3 days per week if a response was not obtained after 2 months and erythropoietin was discontinued in patients who did not experience a response at 3 months.	Varies depending on indication and frequency of administration

† Off-label indication

Dosage and Administration: Darbepoetin Alfa (Aranesp)

Indication	Dosing Regimen	Maximum Dose
Anemia due to CKD	CKD on dialysis: starting dose 0.45 mcg/kg IV or SC weekly, or 0.75 mcg/kg IV or SC every 2 weeks. IV recommended for patients on hemodialysis CKD not on dialysis: starting dose 0.45 mcg/kg IV or SC at 4 week intervals Pediatric patients with CKD: starting dose 0.45 mcg/kg IV or SC weekly; patients with CKD not on dialysis may also be initiated at 0.75 mcg/kg every 2 weeks	Varies depending on indication and frequency of administration
Anemia due to chemotherapy in patients with cancer	Starting dose: 2.25 mcg/kg SC weekly, or 500 mcg SC every 3 weeks until completion of a chemotherapy course	Varies depending on indication and frequency of administration
Anemia associated with MDS†	150-300 mcg SC every other week	500 mcg every other week

† Off-label indication

Dosage and Administration: Methoxy polyethylene glycol-epoetin beta (Mircera

Indication	Dosing Regimen	Maximum Dose
Anemia due to CKD	**Adult patients with CKD on or not on dialysis** Initial treatment: 0.6 mcg/kg body weight SC or IV once every two weeks Maintenance treatment: dose twice that of the every-two-week dose SC or IV once monthly Conversion from another ESA: dosed SC or IV once monthly or once every two weeks based on total weekly epoetin alfa or darbepoetin alfa dose at time of conversion **Pediatric patients with CKD on hemodialysis** Conversion from another ESA: dosed IV once every four weeks based on total weekly epoetin alfa or darbepoetin alfa dose at time of conversion.	Varies

VII. Product Availability

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

Drug Name	Availability
Epoetin alfa (Epogen)	• Single-dose vial: 2,000 units/mL, 3,000 units/mL, 4,000 units/mL, and 10,000 units/mL • Multiple-dose vial containing benzyl alcohol: 20,000 units/2 mL and 20,000 units/mL
Epoetin alfa (Procrit)	• Single-dose vial: 2,000 units/mL, 3,000 units/mL, 4,000 units/mL, 10,000 units/mL, and 40,000 units/mL • Multiple-dose vial containing benzyl alcohol: 20,000 units/2 mL and 20,000 units/mL
Epoetin alfa-epbx (Retacrit)	• Single-dose vial: 2,000 units/mL, 3,000 units/mL, 4,000 units/mL, 10,000 units/mL, 40,000 units/mL

Darbepoetin Alfa (Aranesp

• Single-dose vials for injection: 25 mcg, 40 mcg, 60 mcg, 100 mcg, 200 mcg, 300 mcg
• Single dose prefilled syringes for injection: 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

Methoxy polyethylene glycol-epoetin beta (Mircera)

Injection (single-dose prefilled syringe): 30, 50, 75, 100, 120, 150, 200, or 250 mcg in 0.3 mL solution; 360 mcg in 0.6 mL solution

VIII. References. Refer to package insert.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
New policy created	10.19	
Annual review – no changes deemed necessary	11.20	
Updated preferred chart	11.21	

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.