Clinical Policy: Darbepoetin Alfa (Aranesp)

Reference Number: ERX.SPA.89
Effective Date: 10.01.16
Last Review Date: 05.22
Line of Business: Commercial, Medicaid

Revision Log

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

Description

Darbepoetin alfa (Aranesp®) is an erythropoiesis-stimulating agent (ESA).

FDA Approved Indication(s)

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 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
- As a substitute for red blood cell transfusions in patients who require immediate correction of anemia

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.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Aranesp is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

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

1. Diagnosis of anemia of CKD (dialysis and non-dialysis members);
2. Prescribed by or in consultation with a hematologist or nephrologist;
3. Adequate iron stores as indicated by current (within the last 3 months) serum ferritin level ≥ 100 mcg/L or serum transferrin saturation ≥ 20%;
4. Pretreatment hemoglobin level < 10 g/dL;
5. Failure of Retacrit®, unless contraindicated or clinically significant adverse effects are experienced.
   **Prior authorization may be required for Retacrit*

Approval duration: 6 months

B. Anemia Due to Chemotherapy in Patients with Cancer (must meet all)**:**

1. Request is for use in solid or non-myeloid malignancies in members receiving myelosuppressive chemotherapy without curative intent;

2. Prescribed by or in consultation with a hematologist or oncologist;
3. Age ≥ 18 years;
4. Adequate iron stores as indicated by current (within the last 3 months) serum ferritin level ≥ 100 mcg/L or serum transferrin saturation ≥ 20%;
5. Pretreatment hemoglobin < 10 g/dL;
6. Member meets one of the following (a or b):
   a. Failure of Retacrit, unless contraindicated or clinically significant adverse effects are experienced;
      **Prior authorization may be required for Retacrit*
   b. Request is for treatment associated with cancer for a State with regulations against step therapy in certain oncology settings (see *Appendix D*).

Approval duration: 6 months or until the completion of chemotherapy course (whichever is less)

C. Anemia Associated with Myelodysplastic Syndrome (off-label) (must meet all)**:**
1. Diagnosis of anemia from myelodysplastic syndrome (MDS);
2. Prescribed by or in consultation with a hematologist or oncologist;
3. Age ≥ 18 years;
4. Current (within the last 3 months) serum erythropoietin (EPO) ≤ 500 mU/mL;
5. Adequate iron stores as indicated by current (within the last 3 months) serum ferritin level ≥ 100 mcg/L or serum transferrin saturation ≥ 20%;
6. Pretreatment hemoglobin < 10 g/dL;
7. Member meets one of the following (a or b):
   a. Failure of Retacrit, unless contraindicated or clinically significant adverse effects are experienced;
      **Prior authorization may be required for Retacrit*
   b. Request is for treatment associated with cancer for a State with regulations against step therapy in certain oncology settings (see *Appendix D*).

Approval duration: 6 months

D. Myelofibrosis-Associated Anemia (off-label) (must meet all)**:**
1. Diagnosis of anemia associated with myelofibrosis;
2. Prescribed by or in consultation with a hematologist or oncologist;
3. Age ≥ 18 years;
4. Current (within the last 3 months) serum EPO < 500 mU/mL;
5. Adequate iron stores as indicated by current (within the last 3 months) serum ferritin level ≥ 100 mcg/L or serum transferrin saturation ≥ 20%;
6. Member meets one of the following (a or b):
   a. Failure of Retacrit, unless contraindicated or clinically significant adverse effects are experienced;
      **Prior authorization may be required for Retacrit*
   b. Request is for treatment associated with cancer for a State with regulations against step therapy in certain oncology settings (see *Appendix D*).

Approval duration: 6 months

E. Other diagnoses/indications (must meet all)**:**
1. Member meets one of the following (a or b):
   a. Failure of Retacrit, unless contraindicated or clinically significant adverse effects are experienced;
      **Prior authorization may be required for Retacrit*
   b. Request is for treatment associated with cancer for a State with regulations against step therapy in certain oncology settings (see *Appendix D*);
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

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

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. Failure of Retacrit®, unless contraindicated or clinically significant adverse effects are experienced;
   **Prior authorization may be required for Retacrit*
4. Adequate iron stores as indicated by current (within the last 3 months) serum ferritin level ≥ 100 mcg/L or serum transferrin saturation ≥ 20%.

Approval duration: 6 months

B. Anemia Due to Chemotherapy in Patients with Cancer (must meet all)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
2. Member meets one of the following (a or b):
   a. Failure of Retacrit, unless contraindicated or clinically significant adverse effects are experienced;
      **Prior authorization may be required for Retacrit*
   b. Request is for treatment associated with cancer for a State with regulations against step therapy in certain oncology settings (see *Appendix D*);
3. Continuation of ESA therapy is concurrent with myelosuppressive chemotherapy;
4. If member has received ≥ 8 weeks of ESA therapy, member meets both of the following (a and b):
   a. Documented response to therapy as evidenced by a rise in hemoglobin levels > 1 g/dL;
   b. No RBC transfusions are required;
5. Current hemoglobin < 10 g/dL;
6. Adequate iron stores as indicated by current (within the last 3 months) serum ferritin level ≥ 100 mcg/L or serum transferrin saturation ≥ 20%.

Approval duration: 6 months or until the completion of chemotherapy course, whichever is less

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

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
2. Member meets one of the following (a or b):
   a. Failure of Retacrit, unless contraindicated or clinically significant adverse effects are experienced;
      **Prior authorization may be required for Retacrit*
   b. Request is for treatment associated with cancer for a State with regulations against step therapy in certain oncology settings (see *Appendix D*);
3. If member has received ≥ 12 weeks of ESA therapy, member meets one of the following (a or b):
   a. Documented response to therapy as evidenced by a rise in hemoglobin levels > 1.5 g/dL;
   b. Decrease of RBC transfusions requirement;
4. Current hemoglobin ≤ 12 g/dL;
5. Adequate iron stores as indicated by current (within the last 3 months) serum ferritin level ≥ 100 mcg/L or serum transferrin saturation ≥ 20%.

Approval duration: 6 months

D. Myelofibrosis-Associated Anemia (off-label) (must meet all)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;

2. Member is responding positively to therapy (examples may include, but are not limited to: for transfusion-independent members with a baseline hemoglobin < 10 g/dL, a ≥ 2 g/dL increase in hemoglobin; or for previously transfusion-dependent members, transitioning to become transfusion-independent);
3. Member meets one of the following (a or b):
   a. Failure of Retacrit, unless contraindicated or clinically significant adverse effects are experienced;
      **Prior authorization may be required for Retacrit*
   b. Request is for treatment associated with cancer for a State with regulations against step therapy in certain oncology settings (see *Appendix D*);
4. Adequate iron stores as indicated by current (within the last 3 months) serum ferritin level ≥ 100 mcg/L or serum transferrin saturation ≥ 20%.

Approval duration: 6 months

E. Other diagnoses/indications (must meet all)**:**
1. Member meets one of the following (a or b):
   a. Failure of Retacrit, unless contraindicated or clinically significant adverse effects are experienced;
      **Prior authorization may be required for Retacrit*
   b. Request is for treatment associated with cancer for a State with regulations against step therapy in certain oncology settings (see *Appendix D*);
2. Member meets one of the following (a or b):
   a. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
      Approval duration: Duration of request or 6 months (whichever is less); or
   b. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

A. 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 policy – ERX.PA.01 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CKD: chronic kidney disease
EPO: erythropoietin
ESA: erythropoiesis-stimulating agent
FDA: Food and Drug Administration
MDS: myelodysplastic syndrome

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): uncontrolled hypertension, pure red cell aplasia that begins after treatment with Aranesp or other erythropoietin protein drugs, serious allergic reactions
- Boxed warning(s): ESAs increase the risk of death, myocardial infarction, stroke, venous thromboembolism, thrombosis of vascular access and tumor progression or recurrence

Appendix D: States with Regulations against Redirections in Certain Oncology Settings

State	Step Therapy Prohibited?	Notes
FL	Yes	For stage 4 metastatic cancer and associated conditions.
GA	Yes	For stage 4 metastatic cancer
IA	Yes	For standard of care stage 4 cancer drug use, supported by peer-reviewed, evidence-based literature, and approved by FDA.

State	Step Therapy Prohibited?	Notes
LA	Yes	For stage 4 advanced, metastatic cancer or associated conditions. Exception if "clinically equivalent therapy, contains identical active ingredient(s), and proven to have same efficacy.
NV	Yes	Stage 3 and stage 4 cancer patients for a prescription drug to treat the cancer or any symptom thereof of the covered person
OH	Yes	**Applies to Commercial requests only** For stage 4 metastatic cancer and associated conditions
PA	Yes	For stage 4 advanced, metastatic cancer
TN	Yes	For advanced metastatic cancer and associated conditions
TX	Yes	For stage 4 advanced, metastatic cancer and associated conditions

V. Dosage and Administration

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	Starting dose: 2.25 mcg/kg SC weekly, or 500 mcg SC every 3 weeks until completion of a chemotherapy course	
Anemia associated with MDS†	150-300 mcg SC every other week	500 mcg every other week

†*Off-label NCCN recommended use*

VI. Product Availability

- 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/mL

VII. References

1. Aranesp Prescribing Information. Thousand Oaks, CA: Amgen Inc.; January 2019. Available at http://www.aranesp.com/. Accessed February 17, 2022.
2. Bohlius J, Bohlke K, Castelli R, et al. American Society of Hematology/American Society of Clinical Oncology clinical practice guideline update: Management of Cancer-Associated Anemia With Erythropoiesis-Stimulating Agents. 2019 May 20; J Clin Oncol 37:1336-1351. Available at: https://ascopubs.org/doi/pdf/10.1200/JCO.18.02142. Accessed February 17, 2022.
3. Darbepoetin alfa. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at www.nccn.org. Accessed February 17, 2022.
4. Myelodysplastic Syndromes (Version 3.2022). In: National Comprehensive Cancer Network Guidelines. Available at www.nccn.org. Accessed February 17, 2022.
5. Myeloproliferative Neoplasms (Version 2.2021). In National Comprehensive Cancer Network Guidelines. Available at www.nccn.org. Accessed February 17, 2022.
6. Hematopoietic Growth Factors (Version 1.2022). In National Comprehensive Cancer Network Guidelines. Available at www.nccn.org. Accessed February 17, 2022.
7. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2017. Available at: https://www.clinicalkey.com/pharmacology/. Accessed February 17, 2022.

8. Micromedex® Healthcare Series [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed February 17, 2022.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
2Q 2018 annual review: Anemia due to CKD, chemotherapy, MDS: removed criteria that are under the purview of the prescriber-"Member does not require immediate correction of anemia", and "Other causes of anemia (e.g., vitamin deficiency, metabolic or chronic inflammatory conditions, bleeding, etc.) have been corrected or excluded"; modified initial/continued approval duration to 6 months; Anemia due to CKD: removed requirement related to dosage reduction per hemoglobin level on re-auth since it is not a hard stop to discontinue and specialist is involved in care; Anemia due to chemotherapy: removed criteria that are under the purview of the prescriber-"Member has non-myeloid malignancy", a minimum of 2 additional months of planned chemotherapy, chemotherapy is being given as palliative treatment, and anemia cannot be managed by transfusion; removed "member is receiving concomitant myelosuppressive chemotherapy" since chemo is already included as part of the diagnosis; Anemia associated with MDS: added specialist requirement and clarified that the lab for serum EPO should be current (within the past 3 months); added requirement for positive response to therapy on re-auth; Added NCCN compendial/recommended use (category 2A): MF-associated anemia; References reviewed and updated.	01.05.18	05.18
2Q 2019 annual review: no significant changes; added age requirement for myelofibrosis; references reviewed and updated.	01.24.19	05.19
2Q 2020 annual review: for anemia with chemotherapy, modified diagnosis requirement to confirm request is for use in solid or non-myeloid malignancies in members receiving myelosuppresive chemotherapy without curative intent consistent with NCCN and ASCO recommendations; references reviewed and updated.	02.13.20	05.20
2Q 2021 annual review: for MDS and MF associated anemia added for continued therapy hemoglobin or transfusion response criteria per NCCN; references reviewed and updated.	02.22.21	05.21
2Q 2022 annual review: added redirection to Retacrit per formulary preferencing with optional bypass for oncology indications for states with regulations against redirections in certain oncology settings; references reviewed and updated.	02.17.22	05.22

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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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.

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