

Clinical Policy: Darbepoetin Alfa (Aranesp)

Reference Number: CP.PHAR.236

Effective Date: 07.01.16

Last Review Date: 05.22

Line of Business: Commercial, HIM, Medicaid

[Coding Implications](#)[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.

It is the policy of health plans affiliated with Centene Corporation[®] 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 $\geq 20\%$;
4. Pretreatment hemoglobin level < 10 g/dL;
5. 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. If Retacrit is unavailable due to shortage, failure of Epogen[®], unless contraindicated or clinically significant adverse effects are experienced.
**Prior authorization may be required for Epogen*

Approval duration:

Medicaid/HIM – 6 months

Commercial – 6 months or to member's renewal period, whichever is longer

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 $\geq 20\%$;
5. Pretreatment hemoglobin < 10 g/dL;
6. Member meets one of the following (a or b):
 - a. One of the following (i or ii):
 - i. Failure of Retacrit, unless contraindicated or clinically significant adverse effects are experienced;
**Prior authorization may be required for Retacrit*
 - ii. If Retacrit is unavailable due to shortage, failure of Epogen, unless contraindicated or clinically significant adverse effects are experienced;
**Prior authorization may be required for Epogen*
 - 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:

Medicaid/HIM – 6 months or until the completion of chemotherapy course (whichever is less)

Commercial – Until the completion of chemotherapy course, 6 months, or to member's renewal date, whichever is longer

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 $\geq 20\%$;
6. Pretreatment hemoglobin < 10 g/dL;
7. Member meets one of the following (a or b):
 - a. One of the following (i or ii):
 - i. Failure of Retacrit, unless contraindicated or clinically significant adverse effects are experienced;
**Prior authorization may be required for Retacrit*

- ii. If Retacrit is unavailable due to shortage, failure of Epogen, unless contraindicated or clinically significant adverse effects are experienced;
**Prior authorization may be required for Epogen*
- 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:

Medicaid/HIM – 6 months

Commercial – 6 months or to member's renewal period, whichever is longer

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 \geq 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 \geq 100 mcg/L or serum transferrin saturation \geq 20%;
- 6. Member meets one of the following (a or b):
 - a. One of the following (i or ii):
 - i. Failure of Retacrit, unless contraindicated or clinically significant adverse effects are experienced;
**Prior authorization may be required for Retacrit*
 - ii. If Retacrit is unavailable due to shortage, failure of Epogen, unless contraindicated or clinically significant adverse effects are experienced;
**Prior authorization may be required for Epogen*
 - 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:

Medicaid/HIM – 6 months

Commercial – 6 months or to member's renewal period, whichever is longer

E. Other diagnoses/indications (must meet all):

- 1. Member meets one of the following (a or b):
 - a. One of the following (i or ii):
 - i. Failure of Retacrit, unless contraindicated or clinically significant adverse effects are experienced;
**Prior authorization may be required for Retacrit*
 - ii. If Retacrit is unavailable due to shortage, failure of Epogen, unless contraindicated or clinically significant adverse effects are experienced;
**Prior authorization may be required for Epogen*
 - 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 the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

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

1. Currently receiving medication via Centene benefit or member has previously met all initial approval criteria;
2. Member is responding positively to therapy;
3. 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. If Retacrit is unavailable due to shortage, failure of Epogen, unless contraindicated or clinically significant adverse effects are experienced;
**Prior authorization may be required for Epogen*
4. Adequate iron stores as indicated by current (within the last 3 months) serum ferritin level ≥ 100 mcg/L or serum transferrin saturation $\geq 20\%$.

Approval duration:

Medicaid/HIM – 6 months

Commercial – 6 months or to member's renewal period, whichever is longer

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

1. Currently receiving medication via Centene benefit or member has previously met all initial approval criteria;
2. Member meets one of the following (a or b):
 - a. One of the following (i or ii):
 - i. Failure of Retacrit, unless contraindicated or clinically significant adverse effects are experienced;
**Prior authorization may be required for Retacrit*
 - ii. If Retacrit is unavailable due to shortage, failure of Epogen, unless contraindicated or clinically significant adverse effects are experienced;
**Prior authorization may be required for Epogen*
 - 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 $\geq 20\%$.

Approval duration:

Medicaid/HIM – 6 months or until the completion of chemotherapy course (whichever is less)

Commercial – Until the completion of chemotherapy course, 6 months, or to member's renewal date, whichever is longer

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

1. Currently receiving medication via Centene benefit or member has previously met all initial approval criteria;
2. Member meets one of the following (a or b):
 - a. One of the following (i or ii):
 - i. Failure of Retacrit, unless contraindicated or clinically significant adverse effects are experienced;
**Prior authorization may be required for Retacrit*
 - ii. If Retacrit is unavailable due to shortage, failure of Epogen, unless contraindicated or clinically significant adverse effects are experienced;
**Prior authorization may be required for Epogen*
 - 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 $\geq 20\%$.

Approval duration:

Medicaid/HIM – 6 months

Commercial – 6 months or to member's renewal period, whichever is longer

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

1. Currently receiving medication via Centene benefit or member has previously met all 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. One of the following (i or ii):
 - i. Failure of Retacrit, unless contraindicated or clinically significant adverse effects are experienced;
**Prior authorization may be required for Retacrit*
 - ii. If Retacrit is unavailable due to shortage, failure of Epogen, unless contraindicated or clinically significant adverse effects are experienced;
**Prior authorization may be required for Epogen*
 - 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 $\geq 20\%$.

Approval duration:

Medicaid/HIM – 6 months

Commercial – 6 months or to member's renewal period, whichever is longer

E. Other diagnoses/indications (must meet all):

1. Member meets one of the following (a or b):
 - a. One of the following (i or ii):
 - i. Failure of Retacrit, unless contraindicated or clinically significant adverse effects are experienced;
**Prior authorization may be required for Retacrit*
 - ii. If Retacrit is unavailable due to shortage, failure of Epogen, unless contraindicated or clinically significant adverse effects are experienced;
**Prior authorization may be required for Epogen*
 - 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 Centene benefit and documentation supports positive response to therapy.
Approval duration: Duration of request or 6 months (whichever is less); or
 - b. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

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 policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid 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

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

| Drug Name | Dosing Regimen | Dose Limit/ Maximum Dose |
|--|--|--|
| Retacrit (epoetin alfa-epbx), Epogen (epoetin alfa) | 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 (pediatric patients ages 1 month or older) IV or SC. Individualize maintenance dose. IV route recommended for patients on hemodialysis | Varies depending on indication, frequency of administration, and individual response |

| Drug Name | Dosing Regimen | Dose Limit/ Maximum Dose |
|-----------|--|-----------------------------|
| | <p>Anemia due to chemotherapy 40,000 Units SC weekly or 150 Units/kg SC 3 times weekly (adults); 600 Units/kg IV weekly (pediatric patients 5 to 18 years) until completion of a chemotherapy course</p> <p>Anemia associated with MDS[†] 40,000 to 60,000 Units SC 1-2 times weekly</p> <p>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.</p> | |

Therapeutic alternatives are listed as Brand name[®] (generic) when the drug is available by brand name only and generic (Brand name[®]) when the drug is available by both brand and generic.

[†]Off-label indication

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. Redirection does not refer to review of medical necessity or clinical appropriateness. |
| IA | Yes | For standard of care stage 4 cancer drug use, supported by peer-reviewed, evidence-based literature, and approved by FDA. |
| 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 |

| State | Step Therapy Prohibited? | Notes |
|-------|--------------------------|---|
| OH | Yes | <i>*Applies to Commercial and HIM requests only*</i> 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 | <p>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</p> <p>CKD not on dialysis: starting dose 0.45 mcg/kg IV or SC at 4 week intervals</p> <p>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</p> | 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 | |
| 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/1 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.

Coding Implications –

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

| HCPCS Codes | Description |
|-------------|---|
| J0881 | Injection, darbepoetin alfa, 1 mcg (non-ESRD use) |
| J0882 | Injection, darbepoetin alfa, 1 mcg (for ESRD on dialysis) |

| Reviews, Revisions, and Approvals | Date | P&T Approval Date |
|---|----------|-------------------|
| 2Q 2018 annual review: HIM added; removed subjective criteria across all indications since specialist requirement is added; added age; where relevant approval duration modified to allow no less than 6 months for initial/continued approval; anemia associated with MDS/MF: 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; references reviewed and updated. | 02.06.18 | 05.18 |
| 2Q 2019 annual review: added age requirement for myelofibrosis; references reviewed and updated. | 01.24.19 | 05.19 |
| 2Q 2020 annual review: added Commercial line of business (retired CP.CPA.320); added redirection to biosimilar ESA Retacrit per existing clinical guidance; for anemia with chemotherapy, modified diagnosis requirement to confirm request is for use in solid or non-myeloid malignancies in members receiving myelosuppressive chemotherapy without curative intent consistent with NCCN and ASCO recommendations; references reviewed and updated. | 02.13.20 | 05.20 |
| Added to Section II for continued therapy redirection to Retacrit. | 08.18.20 | |
| Added language criteria that allows by-passing of redirection if state regulations do not allow step therapy in Stage IV or metastatic cancer settings and appendix D to mirror CP.PHAR.237 policy. | 03.10.21 | |

| Reviews, Revisions, and Approvals | Date | P&T Approval Date |
|--|----------|-------------------|
| 2Q 2021 annual review: for MDS and MF associated anemia added for continued therapy hemoglobin or transfusion response criteria per NCCN; applied redirection to Retacrit to other diagnoses/indications; revised reference to HIM off-label use policy from HIM.PHAR.21 to HIM.PA.154; references reviewed and updated. | 02.22.21 | 05.21 |
| Added Nevada to Appendix D. | 08.03.21 | |
| Per SDC and previously approved clinical guidance, added redirection to Epogen if Retacrit is unavailable due to shortage. | 04.26.22 | |
| 2Q 2022 annual review: for CKD removed redirection bypass for stage IV or metastatic cancer as it is not applicable for this indication; references reviewed and updated. | 04.27.22 | 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. 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.

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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.

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