# Clinical Policy: Darbepoetin Alfa (Aranesp)

Reference Number: CP.PHAR.236
Effective Date: 06.01.16
Last Review Date: 05.18
Line of Business: 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 ≥ 20%;
4. Pretreatment hemoglobin level < 10 g/dL.

**Approval duration: 6 months**

**B. Anemia due to Chemotherapy in Patients with Cancer** (must meet all)**:**
1. Diagnosis of anemia due to chemotherapy;
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.

**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.

**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. Current (within the last 3 months) serum EPO < 500 mU/mL;
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**
1. 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): HIM.PHAR.21 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. 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 Centene benefit or member has previously met all initial approval criteria;
2. Continuation of ESA therapy is concurrent with myelosuppressive chemotherapy;
3. If member has received ≥ 8 weeks of ESA therapy, both (a and b):
   a. Member is responding positively to therapy as evidenced by a rise in hemoglobin levels > 1 g/dL;
   b. No red blood cell transfusions are required;
4. Current hemoglobin < 10 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 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 Centene benefit or member has previously met all initial approval criteria;
2. Member is responding positively to therapy;
3. Current hemoglobin ≤ 12 g/dL;
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**

**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;
3. 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 1 or 2)**:**
1. 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
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): HIM.PHAR.21 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 – HIM.PHAR.21 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*
Not applicable

## V. Dosage and Administration

| Indication | Dosing Regimen | Maximum Dose |
|---|---|---|
| Anemia due to CKD | • Recommended starting dose for patients with CKD on dialysis: 0.45 mcg/kg intravenously or subcutaneously weekly, or 0.75 mcg/kg intravenously or subcutaneously every 2 weeks Intravenous route is recommended for patients on hemodialysis<br>• Recommended starting dose for patients with CKD not on dialysis: 0.45 mcg/kg intravenously or subcutaneously at 4 week intervals<br>• Recommended starting dose for pediatric patients with CKD: 0.45 mcg/kg intravenously or subcutaneously 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 | • Recommended starting dose for patients with cancer on chemotherapy: 2.25 mcg/kg subcutaneously weekly, or 500 mcg subcutaneously every 3 weeks until completion of a chemotherapy course | |
| Anemia associated with MDS† | • 150-300 mcg subcutaneously every other week | In some institutions, darbepoetin alfa has been administered using doses up to 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, and 500 mcg/1 mL, and 150 mcg/0.75 mL

- 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.; April 2017. Available at http://www.aranesp.com/. Accessed December 18, 2017.
2. Rizzo, JD., Brouwers, M., Hurley, P., et al. American Society of Hematology/American Society of Clinical Oncology clinical practice guideline update on the use of epoetin and darbepoetin in adult patients with cancer. Blood, 116(20), 4045-4059. Accessed January 4, 2018. https://doi.org/10.1182/blood-2010-08-300541.
3. Darbepoetin alfa. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at NCCN.org. Accessed December 18, 2017.
4. Myelodysplastic Syndromes (Version 1.2018). In: National Comprehensive Cancer Network Guidelines. Available at www.NCCN.org. Accessed December 18, 2017.
5. Myeloproliferative Neoplasms (Version 2.2018). In National Comprehensive Cancer Network Guidelines. Available at www.nccn.org. Accessed December 18, 2017.
6. Micromedex® Healthcare Series [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed January 4, 2018.
7. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2017. Available at: http://www.clinicalpharmacology-ip.com/.

**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 |
|---|---|---|
| Policy split from CP.PHAR.10.<br>Criteria: Added serious allergic reaction as a contraindication; added adequate iron stores requirement for chemo, MDS; removed ESA APPRISE Oncology Program requirement from criteria for chemo; removed negative del (5q) requirement from MDS criteria.<br>Re-auth: added iron stores and reasons to discontinue requirements; Anemia of CKD: removed specific dose adjustment questions but retained upper limit Hgb requirement for patients on and not on dialysis; added Hgb requirement for pediatric patients; Anemia due to chemo: added current Hgb < 10g/dL requirement per CMS policy; Anemia due to MDS: removed questions about to specific hemoglobin | 05.16 | 06.16 |

| Reviews, Revisions, and Approvals | Date | P&T Approval Date |
|---|---|---|
| levels but retained current Hgb ≤ 12g/dL requirement. References updated. | | |
| Removed requirement related to prior trial and failure of Epogen | 09.16 | |
| Initial and re-auth: indicated that iron lab should be within the last 3 months.<br>Initial: removed serious allergic reactions to Aranesp; anemia due to chemo-added requirement that anemia cannot be managed by transfusion; added NCCN recommended use (myelofibrosis-associated anemia); re-auth: removed requirements for reasons to discontinue; updated limitations of use. | 05.17 | 06.17 |
| 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 |

**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.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

**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.

**For Health Insurance Marketplace members**, when applicable, this policy applies only when the prescribed agent is on your health plan approved formulary. Request for non-formulary drugs must be reviewed using the formulary exception policy.