# Clinical Policy: Darbepoetin alfa (Aranesp)

Reference Number: PA.CP.PHAR.236
Effective Date: 01/18
Last Review Date: 04/19

Coding Implications
Revision Log

**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**
It is the policy of Pennsylvania Health and Wellness® 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 chronic kidney disease (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 ≥ 100mcg/L or serum transferrin saturation ≥ 20%;
4. Pretreatment hemoglobin level < 10g/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 ≥ 100mcg/L or serum transferrin saturation ≥ 20%;
5. Pretreatment hemoglobin < 10g/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 ≥ 100mcg/L or serum transferrin saturation ≥ 20%;
6. Pretreatment hemoglobin < 10g/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:** Refer to PA.CP.PMN.53.
1. Additional Aranesp uses outlined in the NCCN compendium, and which meet NCCN category 1, 2a, or 2b are covered.

## II. Continued Approval

**A. Anemia due to CKD** (must meet all):

1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met initial approval criteria or the Continuity of Care policy applies;
2. Member is responding positively to therapy;
3. Adequate iron stores as indicated by current (within the last 3 months) serum ferritin level ≥ 100mcg/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 Pennsylvania Health and Wellness benefit or member has previously met initial approval criteria or the Continuity of Care policy applies;
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 < 10g/dL;
5. Adequate iron stores as indicated by current (within the last 3 months) serum ferritin level ≥ 100mcg/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** (must meet all):

1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met initial approval criteria or the Continuity of Care policy applies;
2. Member is responding positively to therapy
3. Current hemoglobin < 12g/dL;
4. Adequate iron stores as indicated by current (within the last 3 months) serum ferritin level ≥ 100mcg/L or serum transferrin saturation ≥ 20%.

**Approval Duration: 6 months**

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

1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met initial approval criteria or the Continuity of Care policy applies;
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**

**D. Other diagnoses/indications:** (1 or 2)

1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met initial approval criteria or the Continuity of Care policy applies;

**Approval duration: Duration of request or 6 months (whichever is less);** or

2. Refer to PA.CP.PMN.53

## III. 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

## IV. 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<br><br>CKD not on dialysis: starting dose 0.45 mcg/kg IV or SC at 4 week intervals<br><br>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 | |
| Anemia associated with MDS† | 150-300 mcg SC every other week | 500 mcg every other week |

†*Off-label NCCN recommended use*

## V. 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

## VI. References

1. Aranesp Prescribing Information. Thousand Oaks, CA: Amgen Inc.; December 2018. Available at http://www.aranesp.com/. Accessed January 24, 2019.
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 2010, 116(20), 4045-4059. Accessed April 27, 2017. 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 January 24, 2019.
4. Myelodysplastic Syndromes (Version 2.2019). In: National Comprehensive Cancer Network Guidelines. Available at www.NCCN.org. Accessed January 24, 2019.
5. Myeloproliferative Neoplasms (Version 2.2019). In National Comprehensive Cancer Network Guidelines. Available at www.nccn.org. Accessed January 24, 2019.
6. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2017. Available at: http://www.clinicalpharmacology-ip.com/. Accessed January 24, 2019.
7. Micromedex® Healthcare Series [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed January 24, 2019.

## 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 | Approval Date |
|---|---|---|
| 2Q 2018 annual review: 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 | |
| 2Q 2019 annual review: references reviewed and updated. | 04/19 | |