Clinical Policy: Darbepoetin Alfa (Aranesp)
Reference Number: CP.CPA.320
Effective Date: 06.01.18
Last Review Date: 05.19
Line of Business: Commercial

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;
5. Failure of Procrit® unless contraindicated or clinically significant adverse effects are experienced.

Approval duration: 6 months or to member’s renewal period, whichever is longer

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;
6. Failure of Procrit unless contraindicated or clinically significant adverse effects are experienced.

Approval duration: 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 ≥ 20%;
6. Pretreatment hemoglobin < 10 g/dL;
7. Failure of Procrit unless contraindicated or clinically significant adverse effects are experienced.

Approval duration: 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 ≥ 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. Failure of Procrit unless contraindicated or clinically significant adverse effects are experienced.

Approval duration: 6 months or to member’s renewal period, whichever is longer

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): CP.CPA.09 for commercial.
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 or to the member’s renewal date, 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. 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: 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 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 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;
   3. Current hemoglobin < 10 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 or to member’s renewal period, whichever is longer

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): CP.CPA.09 for commercial.

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 – CP.CPA.09 for commercial 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.

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosing Regimen</th>
<th>Dose Limit/Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Procrit (epoetin alfa)</td>
<td>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 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 Anemia associated with MDS† 40,000 to 60,000 Units SC 1-2 times weekly</td>
<td>Varies depending on indication, frequency of administration, and individual response</td>
</tr>
</tbody>
</table>

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

V. Dosage and Administration

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anemia due to CKD</td>
<td>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</td>
<td>Varies depending on indication and frequency of administration.</td>
</tr>
<tr>
<td></td>
<td>CKD not on dialysis: starting dose 0.45 mcg/kg IV or SC at 4 week intervals</td>
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<td></td>
<td>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</td>
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<tr>
<td>Anemia due to chemotherapy in patients with cancer</td>
<td>Starting dose: 2.25 mcg/kg SC weekly, or 500 mcg SC every 3 weeks until completion of a chemotherapy course</td>
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</tr>
<tr>
<td>Anemia associated with MDS†</td>
<td>150-300 mcg SC every other week</td>
<td>500 mcg every other week</td>
</tr>
</tbody>
</table>

†Off-label NCCN recommended use

VI. Product Availability

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

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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.

<table>
<thead>
<tr>
<th>HCPSC Codes</th>
<th>Description</th>
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<tbody>
<tr>
<td>J0881</td>
<td>Injection, darbepoetin alfa, 1 mcg (non-ESRD use)</td>
</tr>
<tr>
<td>J0882</td>
<td>Injection, darbepoetin alfa, 1 mcg (for ESRD on dialysis)</td>
</tr>
</tbody>
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Reviews, Revisions, and Approvals

<table>
<thead>
<tr>
<th>Date</th>
<th>P&amp;T Approval Date</th>
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<tbody>
<tr>
<td>02.06.18</td>
<td>05.18</td>
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New policy created: split from CP.CPA.75 Hematopoietic Agents (Aranesp, Epogen, Mircera, Procrit) into individual darbepoetin alfa (Aranesp) policy; all indications: added prescriber requirement and criteria related to adequate iron stores; anemia due to CKD: added pretreatment hemoglobin requirement; 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 chemo: added age and pretreatment hemoglobin requirements; on re-auth, added continuation of ESA therapy is concurrent with myelosuppressive therapy, and requirements related to current hemoglobin; specified positive response for member who has received ≥ 8 weeks of ESA therapy; anemia associated with MDS: added age, serum EPO, and pretreatment hemoglobin requirements Added NCCN compendial/recommended use (category 2A): MF-associated anemia; references reviewed and updated.

2Q 2019 annual review: added age requirement for myelofibrosis; MDS/myelofibrosis approval duration – added “or to member’s renewal period, whichever is longer”; references reviewed and updated.

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
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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.

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