Clinical Policy Title:	darbepoetin alfa
Policy Number:	RxA.346
Drug(s) Applied:	Aranesp®
Original Policy Date:	03/06/2020
Last Review Date:	09/14/2021
Line of Business Policy Applies to:	All lines of business

Background

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

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
darbepoetin alfa (Aranesp®)	Anemia due to chronic kidney disease	CKD on dialysis, starting dose: • 0.45 mcg/kg intravenously or subcutaneously weekly, • 0.75 mcg/kg intravenously or subcutaneously every 2 weeks. • Intravenous recommended for patients on hemodialysis CKD not on dialysis, starting dose: • 0.45 mcg/kg intravenously or subcutaneously at 4-week intervals	Varies depending on indication and frequency of administration.

Dosing Information			
Drug Name	**Indication**	**Dosing Regimen**	**Maximum Dose**
		Pediatric patients with CKD, starting dose: • 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	
darbepoetin alfa (Aranesp®)	Anemia due to chemotherapy in patients with cancer	Starting dose: 2.25 mcg/kg subcutaneously weekly, or 500 mcg subcutaneously every 3 weeks until completion of a chemotherapy course	
darbepoetin alfa (Aranesp®)	Anemia associated with Myelodysplastic syndrome †	150-300 mcg subcutaneously every other week	500 mcg every other week

Dosage Forms

- 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

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

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

Commercial: 6 months
Medicaid: 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;
6. Failure of Procrit unless contraindicated or clinically significant adverse effects are experienced.

Approval duration
Commercial: Until the completion of chemotherapy course or 6 months
Medicaid: Until the completion of chemotherapy course or 6 months

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
Commercial: 6 months
Medicaid: 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. Failure of Procrit unless contraindicated or clinically significant adverse effects are experienced.

Approval duration
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

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

1. Member is currently receiving medication that has been authorized by RxAdvance or the member has met initial approval criteria listed in this policy;
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

Commercial: 6 months
Medicaid: 6 months

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

1. Member is currently receiving medication that has been authorized by RxAdvance or the member has met initial approval criteria listed in this policy;
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
Commercial: Until the completion of chemotherapy course or 6 months
Medicaid: Until the completion of chemotherapy course or 6 months

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

1. Member is currently receiving medication that has been authorized by RxAdvance or the member has met initial approval criteria listed in this policy;
2. Member is responding positively to therapy;
3. Current hemoglobin 12 g/dL or less;
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
Commercial: 6 months
Medicaid: 6 months

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

1. Member is currently receiving medication that has been authorized by RxAdvance or the member has met initial approval criteria listed in this policy;
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
Commercial: 6 months
Medicaid: 6 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
CKD: Chronic kidney disease
ESA: Erythropoiesis-stimulating agent
EPO: Erythropoietin
MDS: Myelodysplastic syndrome
FDA: Food and Drug Administration

APPENDIX B: Therapeutic Alternatives

Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Dosing Regimen	Maximum Dose
Procrit® (epoetinalfa)	**Anemia due to CKD** Initial dose: 50 to 100 Units/kg 3 times weekly (adults) intravenously or subcutaneously and 50 Units/kg 3 times weekly (pediatric patients ages 1 month or older) intravenously or subcutaneously. Individualize maintenance dose. Intravenous route recommended for patients on hemodialysis **Anemia due to chemotherapy** 40,000 Units subcutaneously weekly or 150 Units/kg subcutaneously 3 times weekly (adults); 600 Units/kg intravenously 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	Varies depending on indication, frequency of administration, and individual response

Therapeutic alternatives are listed as generic (Brand name®) when the drug is available by both generic and brand; Brand name® when the drug is available by brand only and generic name when the drug is available by generic only.
†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 deathmyocardial infarction, stroke, venous thromboembolism, thrombosis of vascular access and tumor progression or recurrence.

References

1. Aranesp® Prescribing Information. Thousand Oaks, CA: Amgen Inc.; January 2019. Available at http://www.aranesp.com/. Accessed June 2, 2021.

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 November 18, 2010, 116(20), 4045-4059.https://doi.org/10.1182/blood-2010-08-300541. Accessed June 2, 2021.
3. Darbepoetin alfa. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at NCCN.org. Accessed June 2, 2021.
4. Myelodysplastic Syndromes (Version 3. 2021). In: National Comprehensive Cancer Network Guidelines. Available at www.NCCN.org. Accessed June 2, 2021.
5. Myeloproliferative Neoplasms (Version 1. 2021). In National Comprehensive Cancer Network Guidelines. Available at www.nccn.org. Accessed June 2, 2021.
6. Clinical Pharmacology [database online]. Elsevier; Gold Standard, Inc.; 2021. Available at: https://www.clinicalkey.com/pharmacology/. Accessed June 2, 2021.
7. Micromedex® Healthcare Series [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed June 2, 2021.
8. Hematopoietic growth factors (Version 4.2021). In National Comprehensive Cancer Network Guidelines. Available at www.nccn.org. Accessed July 28, 2020. Accessed June 2, 2021.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	01/2020	03/06/2020
Policy was reviewed: 1. Policy description table was updated. 2. Continuation therapy criteria II.A.1., II.B.1., II.C.1. were rephrased to “Member is currently receiving medication that has been authorized by RxAdvance…” 3. Initial therapy and continued therapy criteria approval duration was updated for commercial and Medicaid. 4. References were updated.	07/22/2020	09/14/2020
Policy was reviewed: 1. Statement about provider sample ‘‘The provision of provider samples does not guarantee coverage…” was added to Clinical Policy. 2. Therapeutic Alternatives was rephrased to "Below are suggested therapeutic alternatives based on clinical guidance..". 3. Statement about drug listing format in Appendix B is rephrased to "Therapeutic	06/01/2021	09/14/2021

alternatives are listed as generic (Brand name®) when the drug is available by both generic and brand; Brand name® when the drug is available by brand only and generic name when the drug is available by generic only". 4. References were reviewed and updated.		