

Clinical Policy Title:	darbepoetin alfa
Policy Number:	RxA.346
Drug(s) Applied:	Aranesp®
Original Policy Date:	03/06/2020
Last Review Date:	09/14/2020
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: <ul style="list-style-type: none"> • 0.45 mcg/kg IV or SC weekly, • 0.75 mcg/kg IV or SC every 2 weeks. • IV recommended for patients on hemodialysis CKD not on dialysis, starting dose:	Varies depending on indication and frequency of administration.

This clinical policy has been developed to authorize, modify, or determine coverage for individuals with similar conditions. Specific care and treatment may vary depending on individual need and benefits covered by the plan. This policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. This document may contain prescription brand name drugs that are trademarks of pharmaceutical manufacturers that are not affiliated with RxAdvance.

		<ul style="list-style-type: none"> 0.45 mcg/kg IV or SC at 4 week intervals <p>Pediatric patients with CKD, starting dose:</p> <ul style="list-style-type: none"> 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 	
Darbepoetin alfa (Aranesp®)	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	
Darbepoetin alfa (Aranesp®)	Anemia associated with Myelodysplastic syndrome [†]	150-300 mcg SC every other week	500 mcg every other week

[†]Off-label NCCN recommended use

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.

I. Initial Approval Criteria

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

- Diagnosis of anemia of CKD (dialysis and non-dialysis members);
- Prescribed by or in consultation with a hematologist or nephrologist;
- Adequate iron stores as indicated by current (within the last 3 months) serum ferritin level ≥ 100 mcg/L or serum transferrin saturation $\geq 20\%$;
- Pretreatment hemoglobin level < 10 g/dL;
- 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):

- Diagnosis of anemia due to chemotherapy;

2. Prescribed by or in consultation with a hematologist or oncologist;
3. Age 18 years of age or older;
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. 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 of age or older;
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. 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 of age or older;
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 $\geq 20\%$;
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 $\geq 20\%$.

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 $\geq 20\%$.

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 $\geq 20\%$.

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 $\geq 20\%$.

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

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/
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		Maximum Dose
Procrit (epoetinalfa)	<p>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</p> <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>	Varies depending on indication, frequency of administration, and individual response

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.

References

1. Aranesp Prescribing Information. Thousand Oaks, CA: Amgen Inc.; January 2019. Available at <http://www.aranesp.com/>. Accessed July 22, 2020.
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 July 22, 2020.
3. Darbepoetin alfa. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at [NCCN.org](http://www.nccn.org). Accessed January 24, 2019.
4. Myelodysplastic Syndromes (Version 2.2019). In: National Comprehensive Cancer Network Guidelines. Available at [www.NCCN.org](http://www.nccn.org). Accessed July 22, 2020.
5. Myeloproliferative Neoplasms (Version 3.2019). In National Comprehensive Cancer Network Guidelines. Available at www.nccn.org. Accessed July 22, 2020.
6. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2017. Available at: <http://www.clinicalpharmacology-ip.com/>. Accessed July 22, 2020.
7. Micromedex® Healthcare Series [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed July 22, 2020.
8. Hematopoietic growth factors (Version 2.2020). In National Comprehensive Cancer Network Guidelines. Available at www.nccn.org. Accessed July 28, 2020.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	01/2020	03/06/2020
Policy was reviewed: <ol style="list-style-type: none"> 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