Darbepoetin Alfa for Non-Dialysis (Aranesp®)

NDC CODE(S)

55513-0002-XX ARANESP 25MCG/ML Solution (AMGEN)
55513-0003-XX ARANESP 40MCG/ML Solution (AMGEN)
55513-0004-XX ARANESP 60MCG/ML Solution (AMGEN)
55513-0005-XX ARANESP 100MCG/ML Solution (AMGEN)
55513-0006-XX ARANESP 200MCG/ML Solution (AMGEN)
55513-0021-XX ARANESP 40MCG/0.4ML Solution Prefilled Syringe (AMGEN)
55513-0023-XX ARANESP 60MCG/0.3ML Solution Prefilled Syringe (AMGEN)
55513-0025-XX ARANESP 100MCG/0.5ML Solution Prefilled Syringe (AMGEN)
55513-0027-XX ARANESP 150MCG/0.3ML Solution Prefilled Syringe (AMGEN)
55513-0028-XX ARANESP 200MCG/0.4ML Solution Prefilled Syringe (AMGEN)
55513-0032-XX ARANESP 500MCG/ML Solution Prefilled Syringe (AMGEN)
55513-0057-XX ARANESP 25MCG/0.42ML Solution Prefilled Syringe (AMGEN)
55513-0098-XX ARANESP 10MCG/0.4ML Solution Prefilled Syringe (AMGEN)
55513-0110-XX ARANESP 300MCG/ML Solution (AMGEN)
55513-0111-XX ARANESP 300MCG/0.6ML Solution Prefilled Syringe (AMGEN)
55513-0002-XX ARANESP 25MCG/ML Solution (AMGEN)

DESCRIPTION

Erythropoietin is a glycoprotein produced in the kidneys responsible for the stimulation of red blood cell production. Darbepoetin alfa is produced through recombinant DNA technology and serves as a synthetic form of erythropoietin. With the addition of two additional oligosaccharide chains it remains in systemic circulation approximately three times longer than another synthetic formulation of erythropoietin, epoetin alfa.

Darbepoetin alfa has the same amino acid sequence as endogenous erythropoietin. Like the endogenous hormone, it stimulates increased production of red blood cells in individuals with functioning erythropoiesis and is referred to as an erythropoietin-stimulating agent or an ESA.

POLICY

- Darbepoetin alfa for the treatment of anemia is considered ***medically necessary*** if the medical appropriateness criteria are met. **(See Medical Appropriateness below.)**
- Darbepoetin alfa for the treatment of other conditions/diseases is considered ***investigational.***

MEDICAL APPROPRIATENESS

INITIAL APPROVAL CRITERIA

- Patient is at least 18 years of age (unless otherwise specified); **AND**
- Initiation of therapy Hemoglobin (Hb) < 10 g/dL and/or Hematocrit (Hct) < 30%; **AND**

Universal Criteria

- Lab values are obtained within 30 days of the date of administration (unless otherwise indicated); **AND**
- Patient has adequate iron stores as demonstrated by serum ferritin ≥ 100 ng/mL (mcg/L) and transferrin saturation (TSAT) ≥ 20% (measured within the previous 3 months for renewal)*; **AND**
- Other causes of anemia (e.g. hemolysis, bleeding, vitamin deficiency, etc.) have been ruled out; **AND**
- Patient does not have uncontrolled hypertension; **AND**

Anemia Secondary to Myelodysplastic Syndrome (MDS)

- Endogenous serum erythropoietin level of ≤ 500 mUnits/mL; **AND**
- Patient has lower risk disease *(i.e., defined as IPSS-R [Very Low, Low, Intermediate], IPSS [Low/Intermediate-1], WPSS [Very Low, Low, Intermediate])*; **AND**
- Patient has symptomatic anemia

Anemia Secondary to Myeloproliferative Neoplasms (MPN) - Myelofibrosis

- Endogenous serum erythropoietin level of < 500 mUnits/mL

Anemia Secondary to Chemotherapy Treatment

- Patient is receiving concomitant myelosuppressive chemotherapy; **AND**
- Patient's chemotherapy is not intended to cure their disease (i.e., palliative treatment); **AND**
- There are a minimum of two additional months of planned chemotherapy

Anemia Secondary to Chronic Kidney Disease (Non-Dialysis Patients)

- Patient at least age is 1 month of ager older

RENEWAL CRITERIA

- Patient continues to meet universal and other indication-specific relevant criteria identified in the Initial Approval Criteria; **AND**
- Previous dose was administered within the past 60 days; **AND**
- Anemia response compared to pretreatment baseline; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: pure red cell aplasia, severe allergic reactions (anaphylaxis, angioedema, bronchospasm, etc.), severe cardiovascular events (stroke, myocardial infarction, congestive heart failure, thromboembolism, etc.),, uncontrolled hypertension), seizures, increased risk of tumor progression/recurrence in patients with cancer, severe cutaneous reactions (erythema multiforme, Stevens-Johnson Syndrome [SJS]/Toxic Epidermal Necrolysis [TEN], etc.), etc.; **AND**

Anemia Secondary to Myelodysplastic Syndrome (MDS):

- Hemoglobin (Hb) < 12 g/dL and/or Hematocrit (Hct) < 36%

Anemia Secondary to Myeloproliferative Neoplasms - Myelofibrosis

- Hemoglobin (Hb) < 10 g/dL and/or Hematocrit (Hct) < 30%

Anemia Secondary to Chemotherapy Treatment
- Refer to the Initial Approval Criteria

Anemia Secondary to Chronic Kidney Disease:
- **Pediatric patients**: Hemoglobin (Hb) < 12 g/dL and/or Hematocrit (Hct) < 36%
- **Adults**: Hemoglobin (Hb) < 11 g/dL and/or Hematocrit (Hct) < 33%

** Intravenous iron supplementation may be taken into account when evaluating iron status*
• Functional iron deficiency (i.e., adequate iron stores with an insufficient supply of available iron) may occur in patients with chronic diseases, cancer, and/or in those currently receiving ESAs. • Iron is not generally recommended in anemic patients with a Ferritin >500 ng/mL • Anemic patients with a Ferritin ≤500 ng/mL AND TSAT <50% may derive benefit from IV iron therapy in conjunction with ESA

DOSAGE/ADMINISTRATION

INDICATION	DOSE
Anemia due to myelosuppressive chemotherapy**§**	Initial Dose: 2.25 mcg/kg subcutaneously every 7 days -OR- 500 mcg subcutaneously every 21 days **Maximum Dose:** May increase up to 4.5 mcg/kg subcutaneously every 7 days for insufficient response
Anemia due to CKD-Not on dialysis**§**	**Initial Dose in Adult and Pediatric Patients:** 0.45 mcg/kg intravenously or subcutaneously every 28 days **-OR-** 0.75 mcg/kg intravenously or subcutaneously every 14 days **Maximum Dose:** Adult patients: May increase to a maximum dose of 600 mcg every 28 days Pediatric patients: Dose will not exceed maximum initial dosing indicated above
Anemia due to MDS**§**	**Initial Dose:** 150 to 300 mcg subcutaneously every other week **Maximum Dose:** May increase up to 500 mcg every other week
Anemia due to myeloproliferative neoplasms (MPN)**§**	**Initial Dose:** 150 mcg subcutaneously every 7 days **Maximum Dose:** May increase up to 300 mcg every 7 days

§

- For patients with CKD:,
  - Dose increases of 25% can be considered if after 4 weeks of initial therapy the hemoglobin has increased less than 1 g/dL and the current hemoglobin level is less than the indication specific level noted above.
  - Dose decreases of 25% or more can be considered if the hemoglobin rises rapidly by more than 1 g/dL in any 2- week period.
  - Dose and frequency requested are the minimum necessary for the patient to avoid RBC transfusions.
  - Avoid frequent dose adjustments. Do not increase the dose more frequently than once every 4 weeks; decreases can occur more frequently.
  - If patients fail to respond over a 12-week dose escalation period, further dose increases are unlikely to improve response and discontinuation of therapy should be considered.
- For patients with MDS:
  - After 3 to 4 months of therapy, if there is no response as measured by at least a 1.5 g/dL increase in hemoglobin or a decrease in RBC transfusions, discontinuation of therapy should be considered.
- For patients with MPN:
  - After 3 months of therapy, if there is no response as measured by at least a 2 g/dL increase in hemoglobin or a decrease in RBC transfusions, discontinuation of therapy should be considered.
- For patients on Cancer Chemotherapy:
  - After 8 weeks of therapy, if there is no response as measured by hemoglobin levels or if RBC transfusions are quired or following completion of a chemotherapy course discontinue therapy.

LENGTH OF AUTHORIZATION

Coverage will be provided for 45 days and may be renewed.

DOSING LIMITS

Max Units (per dose and over time) [HCPCS Unit]:

- MDS: 500 billable units every 14 days
- MPN: 300 billable units every 7 days
- CKD (Non-Dialysis Patients):
  - Initial: 100 billable units every 14 days
  - Maintenance: 600 billable units every 28 days
- Chemotherapy-induced: 600 billable units every 21 days

APPLICABLE TENNESSEE STATE MANDATE REQUIREMENTS

BlueCross BlueShield of Tennessee's Medical Policy complies with Tennessee Code Annotated Section 56-7-2352 regarding coverage of off-label indications of Food and Drug Administration (FDA) approved drugs when the off-label use is recognized in one of the statutorily recognized standard reference compendia or in the published peer-reviewed medical literature.

IMPORTANT REMINDER

We develop Medical Policies to provide guidance to Members and Providers. This Medical Policy relates only to the services or supplies described in it. The existence of a Medical Policy is not an authorization, certification, explanation of benefits or a contract for the service (or supply) that is referenced in the Medical Policy. For a determination of the benefits that a Member is entitled to receive under his or her health plan, the Member's health plan must be reviewed. If there is a conflict between the Medical Policy and a health plan, the express terms of the health plan will govern.

ADDITIONAL INFORMATION

For appropriate chemotherapy regimens, dosage information, contraindications, precautions, warnings, and monitoring information, please refer to one of the standard reference compendia (e.g., the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) published by the National Comprehensive Cancer Network®, Drugdex Evaluations of Micromedex Solutions at Truven Health, or The American Hospital Formulary Service Drug Information).

SOURCES

1. Aranesp [package insert] Thousand Oaks, CA; Amgen Inc; January 2019. Accessed April 2021.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) darbepoetin alfa. National Comprehensive Cancer Network, 2021. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed April 2021.
3. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Hematopoietic Growth Factors – Management of Cancer-and Chemotherapy-Induced Anemia Version 2.2021. National Comprehensive Cancer Network, 2021. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed April 2021.
4. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Myelodysplastic Syndrome Version 3.2021. National Comprehensive Cancer Network, 2021. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed April 2021.
5. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Myeloproliferative Neoplasms Version 1.2020. National Comprehensive Cancer Network, 2021. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed April 2021.
6. Younossi ZM, Nader FH, Bai C, et al. A phase II dose finding study of darbepoetin alpha and filgrastim for the management of anaemia and neutropenia in chronic hepatitis C treatment. Journal of Viral Hepatitis 2008; 15(5):370-8
7. Cervantes F, Alvarez-Laran A, Hernandez-Boluda JC, et al. Darbepoetin-alpha for the anaemia of myelofibrosis with myeloid metaplasia. British Journal of Haematology, 134: 184–186. doi:10.1111/j.1365-2141.2006.06142.x
8. Andre JL, Deschenes G, Boudaillies B, et al, “Darbepoetin, Effective Treatment of Anaemia in Paediatric Patients With Chronic Renal Failure,” Pediatr Nephrol, 2007, 22(5):708-14.
9. Canon JL, Vansteenkiste J, Bodoky G, et al, “Randomized, Double-Blind, Active-Controlled Trial of Every-3-Week Darbepoetin Alfa for the Treatment of Chemotherapy-Induced Anemia,” J Natl Cancer Inst, 2006, 98(4):273-84. 10. Bristoyiannis G, Germanos N, Grekas D, et al, “Unit Dosing of Darbepoetin Alfa for the

10. Treatment of Anemia in Patients With End-Stage Renal Disease Being Switched From Recombinant Human Erythropoietin: Results of a Phase IIIb, 27-Week, Multicenter, Open-Label Study in Greek Patients," Curr Ther Res, 2005, 66(3):195-211.
11. Gabrilove J, Paquette R, Lyons RM, et al. Phase 2, single-arm trial to evaluate the effectiveness of darbepoetin alfa for correcting anaemia in patients with myelodysplastic syndromes. Br J Haematol. 2008;142(3):379-393.
12. Park S, Fenaux P, Greenberg P, et al. Efficacy and safety of darbepoetin alpha in patients with myelodysplastic syndromes: a systematic review and meta-analysis. Br J Haematol 2016;174(5):730-747. Doi: 10.1111/bjh.14116
13. Park S, Greenberg P, Yucel A, et al. Clinical effectiveness and safety of erythropoietin-stimulating agents for the treatment of low- and intermediate-1-risk myelodysplastic syndrome: a systematic literature review. Br J Haematol. 2019;184(2):134-160. doi: 10.1111/bjh.15707
14. Toto RD, Pichette V, Brenner R, et al, "Darbepoetin Alfa Effectively Treats Anemia in Patients With Chronic Kidney Disease With de novo Every-Other-Week Administration," Am J Nephrol, 2004, 24(4):453-60.
15. Warady BA, Arar MY, Lerner G, et al, "Darbepoetin Alfa for the Treatment of Anemia in Pediatric Patients With Chronic Kidney Disease," Pediatr Nephrol, 2006, 21(8):1144-52.
16. Kidney Disease: Improving Global Outcomes (KDIGO) Anemia Work Group. KDIGO clinical practice guideline for anemia in chronic kidney disease. Kidney Int Suppl. 2012;2(suppl):279-335. https://kdigo.org/guidelines/anemia-in-ckd/ . Published August 2012.
17. Pfeffer MA, Burdmann EA, Chen CY, et al; TREAT Investigators. A trial of darbepoetin alfa in type 2 diabetes and chronic kidney disease. N Engl J Med. 2009 Nov 19;361(21):2019-32. doi: 10.1056/NEJMoa0907845.
18. Mikhail A, Brown C, Williams JA, et al. Renal association clinical practice guideline on Anaemia of Chronic Kidney Disease. BMC Nephrol. 2017 Nov 30;18(1):345. doi: 10.1186/s12882-017-0688-1.
19. Lexi-Comp Online. (2021, February). AHFS DI. *Darbepoetin alfa*. Retrieved April 30, 2021 from Lexi-Comp Online with AHFS.
20. MICROMEDEX Health Care Series. Drugdex Drug Evaluation. (2020, April) *Darbepoetin alfa*. Retrieved April 30, 2021 from MICROMEDEX Healthcare Series.

EFFECTIVE DATE 8/31/2021

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