Aranesp® (darbepoetin alfa)
(Subcutaneous/Intravenous)

NON-DIALYSIS

Document Number: SHP-0242

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I. Length of Authorization

- Coverage will be provided for 60 days and may be renewed.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC unit]:

- Aranesp 10 mcg prefilled syringe: 1 syringe up to every 7 days
- Aranesp 25 mcg vial or prefilled syringe: 1 vial or syringe up to every 7 days
- Aranesp 40 mcg vial or prefilled syringe: 1 vial or syringe up to every 7 days
- Aranesp 60 mcg vial or prefilled syringe: 1 vial or syringe up to every 7 days
- Aranesp 100 mcg vial or prefilled syringe: 1 vial or syringe up to every 7 days
- Aranesp 150 mcg prefilled syringe: 1 syringe up to every 7 days
- Aranesp 200 mcg vial or prefilled syringe: 1 vial or syringe up to every 7 days
- Aranesp 300 mcg vial or prefilled syringe: 1 vial or syringe up to every 14 days (MPN may be as frequent as every 7 days)
- Aranesp 500 mcg prefilled syringe: 1 syringe up to every 14 days

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

- MDS (J0881 only): 500 billable units every 14 days
- MPN (J0881 only): 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

III. Initial Approval Criteria [1,4,5]

Coverage is provided in the following conditions:

- 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 [1,3,16,18]

- 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 4 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 Due to Myelodysplastic Syndrome (MDS) ‡ [2,4]

- Patient has symptomatic anemia; **AND**
  - Patient has lower risk disease (defined as IPSS [Low/Intermediate-1]); **AND**
    - Used as a single agent for del(5q) mutation *(excluding use in patients with cytogenetic abnormality involving chromosome 7)*; **OR**
  - Patient has lower risk disease (defined as IPSS-R [Very Low, Low, Intermediate]); **AND**
    - Patient does not have del(5q) mutation; **AND**
      - Patient has a serum erythropoietin (EPO) ≤ 500 mU/mL; **AND**
        - Patient has ring sideroblasts < 15% (or <5% with an SF3B1 mutation); **AND**
          - Used as a single agent; **OR**
          - Used in combination with either lenalidomide or a granulocyte-colony stimulating factor (G-CSF) following no response (despite adequate iron stores) or erythroid response followed by loss of response to an erythropoiesis-stimulating agent (ESA) alone; **OR**
        - Patient has ring sideroblasts ≥15% (or ring sideroblasts ≥5% with an SF3B1 mutation); **AND**
          - Used as a single agent; **OR**
          - Used in combination with a G-CSF

Anemia Due to Myeloproliferative Neoplasms (MPN) - Myelofibrosis ‡ [2,5]

- Endogenous serum erythropoietin level of < 500 mUnits/mL

Anemia Due to Chemotherapy Treatment † [1-3]

- Patient is receiving concomitant myelosuppressive chemotherapy for a non-myeloid malignancy; **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 Due to Chronic Kidney Disease (Non-Dialysis Patients) † [1,16,18]

- Patient at least 1 month of age

† FDA Approved Indications; ‡ Compendia Recommended Indication(s); Φ Orphan Drug

IV. Renewal Criteria [1,4,5]

Coverage can be renewed based upon the following criteria:

- Patient continues to meet universal and other indication-specific relevant criteria identified in section III; **AND**
- Previous dose was administered within the past 120 days; **AND**
- Disease response with treatment as defined by improvement in anemia 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 Due to Myelodysplastic Syndrome (MDS):

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

Anemia Due to Myeloproliferative Neoplasms (MPN) – Myelofibrosis:

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

Anemia Due to Chemotherapy Treatment:

- *Refer to Section III for criteria*

Anemia Due to Chronic Kidney Disease (Non-Dialysis Patients):

- **Pediatric patients:** Hemoglobin (Hb) < 12 g/dL and/or Hematocrit (Hct) < 36%
- **Adult patients:** Hemoglobin (Hb) < 11 g/dL and/or Hematocrit (Hct) < 33%

** Intravenous iron supplementation may be considered 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.

V. Dosage/Administration [1,3-5,7,17]

Indication	Dose
Anemia due to chemotherapy §	**Initial Dose:** Administer 2.25 mcg/kg subcutaneously every 7 days **-OR-** Administer 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 Chronic Kidney Disease – Non-dialysis §	**Initial Dose in Adult and Pediatric Patients:** Administer 0.45 mcg/kg intravenously or subcutaneously every 28 days **-OR-** Administer 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:** Administer 150 to 300 mcg subcutaneously every 14 days **Maximum Dose:** May increase up to 500 mcg every 14 days
Anemia due to MPN §	**Initial Dose:** Administer 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 still required or following completion of a chemotherapy course discontinue therapy.

VI. Billing Code/Availability Information

HCPCS code:

- J0881 – Injection, darbepoetin alfa, 1 microgram (non-ESRD use); 1 billable unit = 1 mcg

NDC:

Single-dose Vial		Single-dose Prefilled Syringe	
1 Vial/Pack, 4 Packs/Case		*1 Syringe/Pack, 4 Packs/Case*	
200 mcg/1 mL	55513-0006-xx	200 mcg/0.4 mL	55513-0028-xx
300 mcg/1 mL	55513-0110-xx	300 mcg/0.6 mL	55513-0111-xx
		500 mcg/1 mL	55513-0032-xx
4 Vials/Pack, 10 Packs/Case		*4 Syringes/Pack, 10 Packs/Case*	
25 mcg/1 mL	55513-0002-xx	10 mcg/0.4 mL	55513-0098-xx
40 mcg/1 mL	55513-0003-xx	25 mcg/0.42 mL	55513-0057-xx
60 mcg/1 mL	55513-0004-xx	40 mcg/0.4 mL	55513-0021-xx
100 mcg/1 mL	55513-0005-xx	60 mcg/0.3 mL	55513-0023-xx
		100 mcg/0.5 mL	55513-0025-xx
		150 mcg/0.3 mL	55513-0027-xx

VII. References

1. Aranesp [package insert] Thousand Oaks, CA; Amgen Inc; January 2019. Accessed April 2023.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) darbepoetin alfa. National Comprehensive Cancer Network, 2023. The

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3. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Hematopoietic Growth Factors – Management of Cancer-and Chemotherapy-Induced Anemia Version 2.2023. National Comprehensive Cancer Network, 2023. 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 2023.
4. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Myelodysplastic Syndrome Version 1.2023. National Comprehensive Cancer Network, 2023. 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 2023.
5. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Myeloproliferative Neoplasms Version 3.2022. National Comprehensive Cancer Network, 2023. 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 2023.
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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.

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Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C93.10	Chronic myelomonocytic leukemia, not having achieved remission
C94.40	Acute panmyelosis with myelofibrosis not having achieved remission
C94.41	Acute panmyelosis with myelofibrosis in remission
C94.42	Acute panmyelosis with myelofibrosis in relapse
C94.6	Myelodysplastic disease, not classified
D46.0	Refractory anemia without ring sideroblasts, so stated
D46.1	Refractory anemia with ring sideroblasts
D46.20	Refractory anemia with excess of blasts, unspecified
D46.21	Refractory anemia with excess of blasts 1
D46.4	Refractory anemia, unspecified
D46.9	Myelodysplastic syndrome, unspecified
D46.A	Refractory cytopenia with multilineage dysplasia
D46.B	Refractory cytopenia with multilineage dysplasia and ring sideroblasts
D46.C	Myelodysplastic syndrome with isolated del(5q) chromosomal abnormality
D46.Z	Other myelodysplastic syndromes
D47.1	Chronic myeloproliferative disease
D47.4	Osteomyelofibrosis
D63.0	Anemia in neoplastic disease
D63.1	Anemia in chronic kidney disease
D64.81	Anemia due to antineoplastic chemotherapy
D64.9	Anemia unspecified
D75.81	Myelofibrosis
I12.9	Hypertensive chronic kidney disease with stage 1 through stage 4 chronic kidney disease, or unspecified chronic kidney disease
I13.0	Hypertensive heart and chronic kidney disease with heart failure and stage 1 through stage 4 chronic kidney disease, or unspecified chronic kidney disease
I13.10	Hypertensive heart and chronic kidney disease without heart failure, with stage 1 through stage 4 chronic kidney disease, or unspecified chronic kidney disease
N18.30	Chronic kidney disease, stage 3 (moderate), unspecified
N18.31	Chronic kidney disease, stage 3a
N18.32	Chronic kidney disease, stage 3b
N18.4	Chronic kidney disease, stage 4 (severe)
N18.9	Chronic kidney disease, unspecified

Z51.11	Encounter for antineoplastic chemotherapy
Z51.89	Encounter for other specified aftercare

Dual coding requirements:

- Anemia due to CKD (not on dialysis): must bill D63.1 AND I12.9, I13.0, I13.10, N18.30, N18.31, N18.32, N18.4, or N18.9
- Anemia due to Chemotherapy: must bill D64.81 or D61.810 AND C-series, D-series or Q-series coding for NON-myeloid malignancies
- Anemia due to MDS: must bill D47.3 AND D75.81

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD), Local Coverage Articles (LCAs), and Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. They can be found at: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCA/LCD):

Jurisdiction(s): ALL	**NCD/LCD/LCA Document (s):** 110.21
https://www.cms.gov/medicare-coverage-database/new-search/search-results.aspx?keyword=110.21&areaId=all&docType=NCA%2CCAL%2CNCD%2CMEDCAC%2CTA%2CMCD%2C6%2C3%2C5%2C1%2CF%2CP	

Jurisdiction(s): 5, 8	**NCD/LCD/LCA Document (s):** L34633
https://www.cms.gov/medicare-coverage-database/new-search/search-results.aspx?keyword=l34633&areaId=all&docType=NCA%2CCAL%2CNCD%2CMEDCAC%2CTA%2CMCD%2C6%2C3%2C5%2C1%2CF%2CP	

Jurisdiction(s): 15	**NCD/LCD/LCA Document (s):** L34356
https://www.cms.gov/medicare-coverage-database/new-search/search-results.aspx?keyword=l34356&areaId=all&docType=NCA%2CCAL%2CNCD%2CMEDCAC%2CTA%2CMCD%2C6%2C3%2C5%2C1%2CF%2CP	

Jurisdiction(s): 5, 8	**NCD/LCD/LCA Document (s):** A56795
https://www.cms.gov/medicare-coverage-database/new-search/search-results.aspx?keyword=a56795&areaId=all&docType=NCA%2CCAL%2CNCD%2CMEDCAC%2CTA%2CMCD%2C6%2C3%2C5%2C1%2CF%2CP	

Jurisdiction(s): 15	**NCD/LCD/LCA Document (s):** A56462
https://www.cms.gov/medicare-coverage-database/new-search/search-results.aspx?keyword=a56462&areaId=all&docType=NCA%2CCAL%2CNCD%2CMEDCAC%2CTA%2CMCD%2C6%2C3%2C5%2C1%2CF%2CP	

Jurisdiction(s): J,M	NCD/LCD/LCA Document (s): A58982
https://www.cms.gov/medicare-coverage-database/search-results.aspx?keyword=a58982&areaId=all&docType=NCA%2CCAL%2CNCD%2CMEDCAC%2CTA%2CMCD%2C6%2C3%2C5%2C1%2CF%2CP.	

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC