Erythropoiesis Stimulating Agents (ESAs): Aranesp® (darbepoetin alfa)

(Subcutaneous/Intravenous)

NON-DIALYSIS

Document Number: IC-0242

Last Review Date: 05/01/2018

Date of Origin: 10/17/2008

Dates Reviewed: 11/2008, 06/2009, 12/2009, 09/2010, 12/2010, 02/2011, 03/2011, 06/2011, 08/2011, 09/2011, 12/2011, 03/2012, 06/2012, 09/2012, 10/2012, 12/2012, 03/2013, 05/2013, 06/2013, 09/2013, 12/2013, 03/2014, 06/2014, 09/2014, 12/2014, 03/2015, 05/2015, 08/2015, 11/2015, 02/2016, 05/2016, 08/2016, 11/2016, 02/2017, 04/2017, 8/2017, 11/2017, 02/2018, 05/2018

I. Length of Authorization

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

II. Dosing Limits

A. Quantity Limit (max daily dose) [Pharmacy Benefit]:

- 10 mcg; 25 mcg; 40 mcg; 60 mcg; 100 mcg; 150 mcg; 200 mcg: 1 vial or prefilled syringe up to every 7 days
- 300 mcg: 1 vial or prefilled syringe up to every 14 days (MDS may be as frequent as every 7 days)
- 500 mcg: 1 vial or prefilled syringe up to every 21 days

B. Max Units (per dose and over time) [Medical Benefit]:

- MDS or MPN (J0881 only): 900 billable units every 21 days
- All other indications: 600 billable units every 21 days

III. Initial Approval Criteria

- Lab values are obtained within 30 days of the date of administration (unless otherwise indicated); **AND**
- Prior to initiation of therapy, patient should have adequate iron stores as demonstrated by serum ferritin ≥ 100 ng/mL (mcg/L) and transferrin saturation (TSAT) ≥ 20%*****; **AND**
- Initiation of therapy Hemoglobin (Hb) < 10 g/dL and/or Hematocrit (Hct) < 30%; **AND**
- Other causes of anemia (e.g. hemolysis, bleeding, vitamin deficiency, etc.) have been ruled out; **AND**

Aranesp is covered for the following indication(s):

Anemia secondary to myelodysplastic syndrome (MDS) ‡

- Treatment of lower risk disease associated with symptomatic anemia; **AND**
- Endogenous serum erythropoietin level of ≤ 500 mUnits/mL

Anemia secondary to Myeloproliferative Neoplasms (MPN) - Myelofibrosis ‡

- Endogenous serum erythropoietin level of < 500 mUnits/mL

Anemia secondary to Hepatitis C treatment ‡

- Patient must be receiving interferon AND ribavirin

Anemia secondary to chemotherapy treatment †

- Patient is receiving concurrent 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) †

† FDA approved indications; ‡ Compendium approved indications

IV. Renewal Criteria

Coverage can be renewed based upon the following criteria:

- Last dose less than 60 days ago; **AND**
- Disease response; **AND**
- Absence of unacceptable toxicity from the drug. Examples include pure red cell aplasia, severe allergic reactions (anaphylaxis, angioedema, bronchospasm, etc), severe cardiovascular events (stroke, myocardial infarction, congestive heart failure, thromboembolism, uncontrolled hypertension), seizures, increased risk of tumor progression/recurrence in patients with cancer, etc.; **AND**
- Lab values are obtained within 30 days of the date of administration (unless otherwise indicated); **AND**
- Adequate iron stores as demonstrated by serum ferritin ≥ 100 ng/mL (mcg/L) and transferrin saturation (TSAT) ≥ 20% measured within the previous 3 months*; **AND**
- Other causes of anemia (e.g., hemolysis, bleeding, vitamin deficiency, etc.) have been ruled out; **AND**

Anemia secondary to myelodysplastic syndrome (MDS):

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

Anemia secondary to myeloproliferative neoplasms (MF, post-PV myelofibrosis, post-ET myelofibrosis)

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

Anemia secondary to chemotherapy treatment

- Hemoglobin (Hb) < 10 g/dL and/or Hematocrit (Hct) < 30%; **AND**
- Patient is receiving concurrent myelosuppressive chemotherapy; **AND**
- There are a minimum of two additional months of planned chemotherapy

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%

Anemia secondary to Hepatitis C treatment:

- Hemoglobin (Hb) < 11 g/dL and/or Hematocrit (Hct) < 33%; **AND**
- Patient must be receiving interferon AND ribavirin

***** Intravenous iron supplementation may be taken into account when evaluating iron status

V. Dosage/Administration

Indication	Dose
Anemia due to myelosuppressive chemotherapy§	• Initiate at 2.25 mcg/kg subcutaneously every 7 days; may increase up to 4.5 mcg/kg every 7 days for insufficient response • Initiate at 500 mcg subcutaneously every 21 days
Anemia due to CKD-Not on dialysis§	Adults • Initiate at 0.45 mcg/kg intravenously or subcutaneously every 28 days Pediatric patients • Initiate at 0.45 mcg/kg intravenously or subcutaneously every 7 days or 0.75 mcg/kg every 14 days
Anemia due to ribavirin/Interferon therapy for HCV	Up to 3 mcg/kg subcutaneously every 14 days
Anemia due to MDS and myeloproliferative neoplasms	• Up to 300 mcg subcutaneously every 7 days • Initiate at 500 mcg subcutaneously every 21 days
Most common weekly dose	Up to 200 mcg
Most common every 2 week dose	Up to 300 mcg
Most common every 3 week dose	Up to 500 mcg

§
– 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.
– For patients with CKD,
  - 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 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

Jcode:

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

NDC:

Single-dose Vial		Single-dose Prefilled Syringe	
1 Vial/Pack, 4 Packs/Case		*1 Syringe/Pack, 4 Packs/Case*	
200 mcg/1 mL	55513-0006-01	200 mcg/0.4 mL	55513-0028-01
300 mcg/1 mL	55513-0110-01	300 mcg/0.6 mL	55513-0111-01
		500 mcg/1 mL	55513-0032-01
4 Vials/Pack, 10 Packs/Case		*4 Syringes/Pack, 10 Packs/Case*	
25 mcg/1 mL	55513-0002-04	10 mcg/0.4 mL	55513-0098-04
40 mcg/1 mL	55513-0003-04	25 mcg/0.42 mL	55513-0057-04
60 mcg/1 mL	55513-0004-04	40 mcg/0.4 mL	55513-0021-04
100 mcg/1 mL	55513-0005-04	60 mcg/0.3 mL	55513-0023-04
150 mcg/0.75 mL	55513-0053-04	100 mcg/0.5 mL	55513-0025-04
		150 mcg/0.3 mL	55513-0027-04

VII. References

1. Aranesp [package insert] Thousand Oaks, CA; Amgen Inc; January 2018. Accessed March 2018.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) darbepoetin alfa. National Comprehensive Cancer Network, 2018. 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 March 2018.

3. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Cancer-and Chemotherapy-Induced Anemia Version 1.2018. National Comprehensive Cancer Network, 2017. 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 March 2018.
4. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Myelodysplastic Syndrome Version 1.2018. National Comprehensive Cancer Network, 2017. 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 March 2018.
5. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Myeloproliferative Neoplasms Version 2.2018. National Comprehensive Cancer Network, 2018. 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 March 2018
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8. Wisconsin Physicians Service Insurance Corporation. Local Coverage Determination (LCD): Erythropoiesis Stimulating Agents (ESAs) (L34633). Centers for Medicare & Medicaid Services, Inc. Updated on 09/20/2017 with effective dates 10/1/2017. Accessed March 2018.
9. CGS Administrators, Inc. Local Coverage Determination (LCD): Erythropoiesis Stimulating Agents (ESAs) (L34356). Centers for Medicare & Medicare Services. Updated on 02/26/2018 with effective dates 10/01/2017. Accessed March 2018.
10. First Coast Service Options, Inc. Local Coverage Determination (LCD): Erythropoiesis Stimulating Agents (ESAs) (L36276). Centers for Medicare & Medicare Services. Updated on 02/22/2018 with effective dates 02/08/2018. Accessed March 2018.
11. National Coverage Determination (NCD); Erythropoiesis Stimulating Agents (ESAs) in Cancer and Related Neoplastic Conditions (110.21). Centers for Medicare & Medicaid Services, Inc. Updated on 12/3/2015 with effective dates 10/01/2015. Accessed March 2018.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
B18.2	Chronic viral hepatitis C
B19.20	Unspecified viral hepatitis C without hepatic coma
C92.10	Chronic myeloid leukemia, BCR/ABL-positive, not having achieved remission
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	Malignant neoplasm of peripheral nerves of upper limb, including shoulder
D47.4	Malignant neoplasm of peripheral nerves of abdomen
D61.1	Drug-induced aplastic anemia
D61.2	Aplastic anemia due to other external agent
D63.0	Anemia in neoplastic disease
D63.1	Anemia in chronic kidney disease
D63.8	Anemia in other chronic diseases classified elsewhere
D64.81	Anemia due to antineoplastic chemotherapy
D64.9	Anemia unspecified
D75.81	Secondary polycythemia
I12.0	Hypertensive chronic kidney disease with stage 5 chronic kidney disease or end stage renal disease
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
I13.11	Hypertensive heart and chronic kidney disease without heart failure, with stage 5 chronic kidney disease, or end stage renal disease
I13.2	Hypertensive heart and chronic kidney disease with heart failure and with stage 5 chronic kidney disease, or end stage renal disease
N18.1	Chronic kidney disease, stage 1
N18.2	Chronic kidney disease, stage 2 (mild)

N18.3	Chronic kidney disease, stage 3 (moderate)
N18.4	Chronic kidney disease, stage 4 (severe)
N18.5	Chronic kidney disease, stage 5
N18.6	End stage renal disease
N18.9	Chronic kidney disease, unspecified
Z51.11	Encounter for antineoplastic chemotherapy
Z51.89	Encounter for other specified aftercare

Dual coding requirements:

- J0881 must be billed in conjunction with BOTH D63.1 AND one of the I or N series of codes for CKD not on dialysis
- J0881 must be billed in conjunction with BOTH D63.8 OR D64.9 AND one of the B series of codes for anemia due to HCV

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) and Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. They can be found at: http://www.cms.gov/medicare-coverage-database/search/advanced-search.aspx. Additional indications may be covered at the discretion of the health plan.

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

Jurisdiction(s): ALL	**NCD/LCD Document (s):** 110.21
https://www.cms.gov/medicare-coverage-database/search/document-id-search-results.aspx?DocID=110.21&bc=gAAAAAAAAAAAAA%3d%3d&	

Jurisdiction(s): 5, 8	**NCD/LCD Document (s):** L34633
https://www.cms.gov/medicare-coverage-database/search/lcd-date-search.aspx?DocID=L34633&bc=gAAAAAAAAAAAAA==	

Jurisdiction(s): 15	**NCD/LCD Document (s):** L34356
https://www.cms.gov/medicare-coverage-database/search/lcd-date-search.aspx?DocID=L34356&bc=gAAAAAAAAAAAAA==	

Jurisdiction(s): N	**NCD/LCD Document (s):** L36276
https://www.cms.gov/medicare-coverage-database/search/lcd-date-search.aspx?DocID=L36276&bc=gAAAAAAAAAAAAA==	

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
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
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