Medical Policy:
Erythropoiesis Stimulating Agents (ESAs): Aranesp® (darbepoetin alfa) (Subcutaneous/Intravenous) *NON-DIALYSIS*

POLICY NUMBER	LAST REVIEW	ORIGIN DATE
MG.MM.PH.80	September 22, 2023	January 1, 2020

Length of Authorization

Coverage will be provided for 90 days and may be renewed.

Dosing Limits [Medical Benefit]

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

Guideline

I. Initial

- 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**
- Patient does not have uncontrolled hypertension; **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 chemotherapy treatment †

- Patient is receiving concurrent myelosuppressive chemotherapy; **AND**
- Patient's chemotherapy is not being administered with curative intent; **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

I.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%

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

Applicable Procedure Codes

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

Applicable NDCs

Code	Description
55513-0032-xx	Aranesp 0.5mg/1mL
55513-0098-xx	Aranesp 0.01mg/0.4mL
55513-0027-xx	Aranesp 0.15/0.3mL
55513-0006-xx	Aranesp 0.2mg/1 mL
55513-0005-xx	Aranesp 0.1mg/1mL
55513-0004-xx	Aranesp 0.06mg/1mL
55513-0003-xx	Aranesp 0.04mg/1mL
55513-0002-xx	Aranesp 0.025mg/1mL
55513-0021-xx	Aranesp 0.04/0.4mL
55513-0111-xx	Aranesp 0.3mg/0.6mL
55513-0057-xx	Aranesp 0.025mg/0.42mL
55513-0028-xx	Aranesp 0.2mg/0.4mL
55513-0023-xx	Aranesp 0.06/0.3mL

ICD-10 Diagnoses

Code	Description
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
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

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

Revision History

<table>
<tr><th>Company(ies)</th><th>DATE</th><th>REVISION</th></tr>
<tr><td>EmblemHealth & ConnectiCare</td><td>9/22/2023</td><td>Annual Review: Transferred to new co-branded template, updated NDC chart

Initial Criteria: added “Patient does not have uncontrolled hypertension; AND”

Removed “Anemia secondary to Hepatitis C treatment ‡
o Patient must be receiving interferon AND ribavirin”
Removed “Anemia secondary to Hepatitis C treatment:
Hemoglobin (Hb) < 11 g/dL and/or Hematocrit (Hct) < 33%; AND
o Patient must be receiving interferon AND ribavirin”
Removed Codes:
<table><tr><td>B18.2</td><td>Chronic viral hepatitis C</td></tr><tr><td>B19.20</td><td>Unspecified viral hepatitis C without hepatic coma</td></tr><tr><td>B18.2</td><td>Chronic viral hepatitis C</td></tr><tr><td>B19.20</td><td>Unspecified viral hepatitis C without hepatic coma</td></tr></table></td></tr>
<tr><td>EmblemHealth & ConnectiCare</td><td>4/21/2021</td><td>Removed the following verbiage:
“Limitations/Exclusions
Aranesp is not considered medically necessary for indications other than those listed above due to insufficient evidence of therapeutic value.”</td></tr>
<tr><td>EmblemHealth & ConnectiCare</td><td>1/1/2021</td><td>Extended coverage duration from 60 days to 90 days</td></tr>
</table>

References

1. Aranesp [package insert] Thousand Oaks, CA; Amgen Inc; January 2019. Accessed December 2019.
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
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 Hematology, 134: 184–186. doi:10.1111/j.1365-2141.2006.06142.x
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.