Medical Policy:

Erythropoiesis Stimulating Agents (ESAs): Aranesp® (darbepoetin alfa) (Subcutaneous/Intravenous)

POLICY NUMBER	LAST REVIEW	ORIGIN DATE
MG.MM.PH.80	May 13, 2025	January 1, 2020

The treating physician or primary care provider must submit to EmblemHealth, or ConnectiCare, as applicable (hereinafter jointly referred to as "EmblemHealth"), the clinical evidence that the member meets the criteria for the treatment or surgical procedure. Without this documentation and information, EmblemHealth will not be able to properly review the request preauthorization or post-payment review. The clinical review criteria expressed below reflects how EmblemHealth determines whether certain services or supplies are medically necessary. This clinical policy is not intended to pre-empt the judgment of the reviewing medical director or dictate to health care providers how to practice medicine. Health care providers are expected to exercise their medical judgment in rendering appropriate care. Health care providers are expected to exercise their medical judgment in rendering appropriate care.

EmblemHealth established the clinical review criteria based upon a review of currently available clinical information (including clinical outcome studies in the peer reviewed published medical literature, regulatory status of the technology, evidence-based guidelines of public health and health research agencies, evidence-based guidelines and positions of leading national health professional organizations, views of physicians practicing in relevant clinical areas, and other relevant factors). EmblemHealth expressly reserves the right to revise these conclusions as clinical information changes and welcomes further relevant information. Each benefit program defines which services are covered. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered and/or paid for by EmblemHealth, as some programs exclude coverage for services or supplies that EmblemHealth considers medically necessary.

If there is a discrepancy between this guideline and a member's benefits program, the benefits program will govern. Identification of selected brand names of devices, tests and procedures in a medical coverage policy is for reference only and is not an endorsement of any one device, test or procedure over another. In addition, coverage may be mandated by applicable legal requirements of a state, the Federal Government or the Centers for Medicare & Medicaid Services (CMS) for Medicare and Medicaid members. All coding and web site links are accurate at time of publication.

EmblemHealth may also use tools developed by third parties, such as the MCG™ Care Guidelines, to assist us in administering health benefits. The MCG™ Care Guidelines are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice. EmblemHealth Services Company, LLC, has adopted this policy in providing management, administrative and other services to EmblemHealth Plan, Inc., EmblemHealth Insurance Company, EmblemHealth Services Company, LLC, and Health Insurance Plan of Greater New York (HIP) related to health benefit plans offered by these entities. ConnectiCare, an EmblemHealth company, has also adopted this policy. All of the aforementioned entities are affiliated companies under common control of EmblemHealth Inc.

Length of Authorization

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

Dosing Limits [Medical Benefit]

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

Guideline

****For Medicare members – Aranesp-please refer to our separate LCD/NCD Medicare criteria**

I. Initial Approval Criteria

1. Lab values are obtained within 30 days of the date of administration (unless otherwise indicated); **AND**
2. 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**
3. Initiation of therapy Hemoglobin (Hb) < 10 g/dL and/or Hematocrit (Hct) < 30%; **AND**
4. Other causes of anemia (e.g. hemolysis, bleeding, vitamin deficiency, etc.) have been ruled out; **AND**
5. Patient does not have uncontrolled hypertension; **AND**

Aranesp is covered for the following indication(s):

Anemia secondary to myelodysplastic syndrome (MDS) ‡

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

Anemia secondary to Myeloproliferative Neoplasms (MPN) - Myelofibrosis ‡

1. Endogenous serum erythropoietin level of < 500 mUnits/mL

Anemia secondary to chemotherapy treatment †

1. Patient is receiving concurrent myelosuppressive chemotherapy; **AND**
2. Patient's chemotherapy is not being administered with curative intent; **AND**
3. There are a minimum of two additional months of planned chemotherapy

Anemia secondary to chronic kidney disease (non-dialysis patients) †

1. Patient at least 1 month of age

† FDA approved indications; **‡** Compendium approved indications

I.Renewal Criteria

Coverage can be renewed based upon the following criteria:

1. Last dose less than 60 days ago; **AND**
2. Disease response; **AND**
3. 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**
4. Lab values are obtained within 30 days of the date of administration (unless otherwise indicated); **AND**
5. 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**
6. Other causes of anemia (e.g., hemolysis, bleeding, vitamin deficiency, etc.) have been ruled out; **AND**

Anemia secondary to myelodysplastic syndrome (MDS):

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

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

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

Anemia secondary to chemotherapy treatment

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

Anemia secondary to chronic kidney disease:

1. *Pediatric patients*: Hemoglobin (Hb) < 12 g/dL and/or Hematocrit (Hct) < 36%
2. *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
55513-0025-xx	Aranesp 100mcg/0.5mL
5513-0057-xx	Aranesp 25mcg/0.42mL

ICD-10 Diagnoses

Code	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	Malignant neoplasm of peripheral nerves of upper limb, including shoulder
D47.4	Malignant neoplasm of peripheral nerves of abdomen
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	Secondary polycythemia
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
N18.3	Chronic kidney disease, stage 3 (moderate)
N18.31	Chronic kidney disease, stage 3b
N18.4	Chronic kidney disease, stage 4 (severe)
N18.5	Chronic kidney disease, stage 5
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 N18.5

Revision History

Company(ies)	DATE	REVISION
EmblemHealth & ConnectiCare	5/13/2025	Updated dual coding requirements. Updated Diagnosis Codes Removed references to “Non-Dialysis” in dosage limits and criteria: Anemia secondary to chronic kidney disease. Revision: Removed “*NON-DIALYSIS*” from the title of the policy
EmblemHealth & ConnectiCare	1/6/2025	Restored references to “Non-Dialysis” in dosage limits and criteria: Anemia secondary to chronic kidney disease.
EmblemHealth & ConnectiCare	12/19/2024	Removed references to “Non-Dialysis” in dosage limits and criteria: Anemia secondary to chronic kidney disease.
EmblemHealth & ConnectiCare	8/7/2024	Revision: Removed “*NON-DIALYSIS*” from the title of the policy
EmblemHealth & ConnectiCare	6/17/2024	Annual Review: Added Statement “**For Medicare members – Aranesp-please refer to our separate LCD/NCD Medicare criteria” Updated dosing limits. Anemia secondary to chronic kidney disease (non-dialysis patients) Added: “Patient at least 1 month of age” Added NDCs: 55513-0025-xx and 5513-0057-xx.

<table>
<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 May 2025
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

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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
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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.