

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 |

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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.

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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 \geq 100 ng/mL (mcg/L) and transferrin saturation (TSAT) \geq 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) $\geq 20\%$ 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

| Company(ies) | DATE | REVISION | | | | | | | | |
|-----------------------------|--|--|-------|---------------------------|--------|--|-------|---------------------------|--------|--|
| EmblemHealth & ConnectiCare | 9/22/2023 | <p>Annual Review: Transferred to new co-branded template, updated NDC chart</p> <p>Initial Criteria: added "Patient does not have uncontrolled hypertension; AND"</p> <p>Removed "Anemia secondary to Hepatitis C treatment ‡</p> <ul style="list-style-type: none"> ○ Patient must be receiving interferon <u>AND</u> ribavirin" <p>Removed "Anemia secondary to Hepatitis C treatment: Hemoglobin (Hb) < 11 g/dL and/or Hematocrit (Hct) < 33%; AND</p> <ul style="list-style-type: none"> ○ Patient must be receiving interferon AND ribavirin" <p>Removed Codes:</p> <table border="1"> <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> | B18.2 | Chronic viral hepatitis C | B19.20 | Unspecified viral hepatitis C without hepatic coma | B18.2 | Chronic viral hepatitis C | B19.20 | Unspecified viral hepatitis C without hepatic coma |
| B18.2 | Chronic viral hepatitis C | | | | | | | | | |
| B19.20 | Unspecified viral hepatitis C without hepatic coma | | | | | | | | | |
| B18.2 | Chronic viral hepatitis C | | | | | | | | | |
| B19.20 | Unspecified viral hepatitis C without hepatic coma | | | | | | | | | |
| EmblemHealth & ConnectiCare | 4/21/2021 | <p>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."</p> | | | | | | | | |
| EmblemHealth & ConnectiCare | 1/1/2021 | Extended coverage duration from 60 days to 90 days | | | | | | | | |

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
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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.