UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Erythropoiesis-Stimulating Agents – Aranesp Utilization Management Medical Policy
- Aranesp® (darbepoetin alfa intravenous or subcutaneous injection − Amgen)

REVIEW DATE: 07/08/2026; selected revision 09/16/2026

OVERVIEW

Aranesp, an erythropoiesis-stimulating agent (ESA), is indicated for the following uses:[1]

- **Anemia due to chronic kidney disease** (CKD), including patients on dialysis and patients not on dialysis.
- **Anemia due to chemotherapy in patients with cancer,** in patients with non-myeloid malignancies where anemia is due to the effect of concomitant myelosuppressive chemotherapy, and upon initiation, there is a minimum of two additional months of planned chemotherapy.

Limitations of Use: Aranesp has not been shown to improve quality of life, fatigue, or patient well-being.[1] Aranesp is not indicated for the following uses:

- In patients with cancer receiving hormonal agents, biologic products, or radiotherapy unless also receiving concomitant myelosuppressive chemotherapy.
- In patients with cancer receiving myelosuppressive chemotherapy when the anticipated outcome is cure.
- In patients with cancer receiving myelosuppressive chemotherapy in whom anemia can be managed by transfusion.
- As a substitute for red blood cell (RBC) transfusions in those who require immediate correction of anemia.

The iron status should be evaluated in all patients before and during treatment with ESAs.[1] Therapy should be initiated for **adults with CKD on dialysis** when the hemoglobin (Hb) level is < 10.0 g/dL and if the Hb level approaches or exceeds 11.0 g/dL, reduce or interrupt the Aranesp dose. For **adults with CKD who are not on dialysis**, consider initiating Aranesp only when Hb is < 10.0 g/dL and other considerations apply (e.g., rate of Hb decline indicates patient is likely to need RBC transfusion and reducing the risk of alloimmunization and/or other RBC transfusion-related risks is a goal). If the Hb level exceeds 10.0 g/dL, reduce or interrupt the Aranesp dose and use the lowest dose sufficient to reduce the need for RBC transfusions. For **pediatric patients with CKD**, initiate Aranesp when the Hb < 10.0 g/dL and if the Hb level approaches 12.0 g/dL, reduce or interrupt the dose of Aranesp. Initiate Aranesp for **patients on cancer** chemotherapy only if the Hb is < 10.0 g/dL and if there is a minimum of two additional months of planned chemotherapy.

Dosing Information

Chronic Kidney Disease

In controlled trials, patients experienced greater risks for death, serious adverse cardiovascular reactions, and stroke when administered ESAs to target a hemoglobin level > 11 g/dL.[1] No trial has identified a hemoglobin target level, Aranesp dose, or dosing strategy that does not increase these risks. Individualize/titrate dosing based on Hb values. Use the lowest dose of Aranesp sufficient to reduce the need for RBC transfusions. Refer to the prescribing information regarding increasing, reducing, interrupting, or conversion dosing. For adult patients with CKD not on dialysis, the recommended starting dose is 0.45 mcg/kg body weight intravenously or subcutaneously given once at 4-week intervals as appropriate. In pivotal trial (N2) involving adults with CKD not on dialysis, the starting dose of 0.45

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mcg/kg weekly was evaluated. In pivotal trials (N3 and N4) involving adults with CKD not on dialysis, the starting dose of 0.75 mcg/kg administered once every 2 weeks was evaluated. For pediatric patients with CKD, the recommended starting dose is 0.45 mcg/kg body weight intravenously or subcutaneously given weekly; patients not receiving dialysis may be initiated at 0.75 mcg/kg once every 2 weeks.

Cancer
ESAs shortened overall survival and/or increased the risk of tumor progression or recurrence in clinical studies of patients with breast, non-small cell lung, head and neck, lymphoid, and cervical cancers.[1] To decrease these risks, as well as the risk of serious cardiovascular and thromboembolic reactions, use the lowest dose needed to avoid RBC transfusions. Recommended starting doses and schedules are: 2.25 mcg/kg every week subcutaneously or 500 mcg every 3 weeks subcutaneously. If hemoglobin increases by less than 1 g/dL and remains below 10 g/dL after 6 weeks of therapy and patient is utilizing a weekly dosing schedule, increase dose to 4.5 mcg/kg subcutaneously. Discontinue following the completion of a chemotherapy course.

Guidelines

The Kidney Disease Improving Global Outcomes (KDIGO) clinical practice guidelines for anemia in CKD (2026) provide recommendations for the use of ESAs.[2] Guidelines recommend addressing all correctable causes of anemia (i.e. iron deficiency, malignancy, infection, etc.) before initiating treatment with an ESA or hypoxia-inducible factor-prolyl hydroxylase inhibitor (HIF-PHI). After all correctable causes of anemia are addressed, KDIGO suggests using ESAs as first-line therapy for treating anemia in patients with CKD rather than HIF-PHIs. Although clinical trials have revealed noninferiority of HIF-PHIs versus ESAs for efficacy as treatment for anemia, some studies suggested a higher risk of major adverse cardiovascular events with HIF-PHIs compared to ESAs in at least some CKD populations. For patients with CKD on dialysis, the guidelines recommend ESA therapy should be initiated when the Hb level is ≤ 9.0 to 10.0 g/dL. For patients with CKD who are not on dialysis, the decision to initiate ESA therapy should be individualized based on many factors (e.g., rate of Hb decline, prior response to iron therapy, transfusion risk, patient symptoms). In adults with anemia and CKD who are being treated with an ESA, ESA therapy should not be used to maintain Hb concentrations above 11.5 g/dL. For pediatric patients with anemia and CKD, the selection of an Hb target for ESA maintenance therapy should be individualized considering potential benefits and harms. Baseline and periodic monitoring (e.g., iron, total iron-binding capacity, transferrin saturation, or ferritin levels) and instituting iron replacement when needed may be useful in limiting the need for ESAs, maximizing symptomatic improvement in patients, and determining the reason for inadequate response to ESAs. Iron deficiency can occur following continued ESA use. Therefore, ongoing iron supplementation is often required in most patients to maintain an optimal response.

Aranesp is recommended in guidelines from the National Comprehensive Cancer Network (NCCN):

- **Hematopoietic Growth Factors:** NCCN guidelines (version 3.2026 – December 5, 2025) indicate Aranesp and epoetin alfa with or without iron supplementation may be warranted for the long-term management of anemia in high-risk patients or in asymptomatic patients with comorbidities receiving myelosuppressive chemotherapy where are cure is not anticipated.[3]
- **Myelodysplastic Syndrome (MDS):** NCCN guidelines (version 3.2026 – January 12, 2026) list Aranesp and epoetin alfa products as having utility in anemic, symptomatic patients with MDS if serum erythropoietin levels are ≤ 500 mU/mL (category 2A recommendation).[4] Iron stores should be adequate. Due to safety issues, the guidelines suggest that ESAs be used in the management of symptomatic anemia in patients with MDS and to aim for a target Hb range of 10 to 12.0 g/dL but not to exceed 12.0 g/dL.
- **Myeloproliferative Neoplasms:** The NCCN guidelines (version 2.2026 – June 16, 2026) address Aranesp and epoetin alfa products as options for treatment of patients with anemia related to myelofibrosis having a serum erythropoietin level < 500 mU/mL (category 2B recommendation).[5]

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Iron stores should be adequate. The guidelines also advise that ESAs are generally less effective for the management of transfusion-dependent anemia.

Safety

ESAs carry a boxed warning for increased risk of death, myocardial infarction, stroke, venous thromboembolism, thrombosis of vascular access, and tumor progression or recurrence.[1] These risks are greater when targeting higher hemoglobin levels.

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of Aranesp in patients with conditions other than CKD who are on dialysis. The intent of this policy is to provide recommendations for uses other than anemia in patients with CKD who are on dialysis. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indications. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. Because of the specialized skills required for evaluation and diagnosis of patients treated with Aranesp as well as the monitoring required for adverse events and long-term efficacy, approval requires Aranesp to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Aranesp is recommended in those who meet one of the following criteria:

FDA-Approved Indications

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1. Anemia in a Patient with Chronic Kidney Disease who is on Dialysis. Approve for 3 years.

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2. Anemia in a Patient with Chronic Kidney Disease who is not on Dialysis. Approve for 1 year if the patient meets ONE of the following (A or B):

- **A)** Initial Therapy. Approve if the patient meets BOTH of the following (i and ii):
  - **i.** Patient meets ONE of the following (a or b):
    - **a)** Patient is ≥ 18 years of age with a hemoglobin < 10.0 g/dL; OR
    - **b)** Patient is < 18 years of age with a hemoglobin ≤ 11.0 g/dL; AND
  - **ii.** Patient meets ONE of the following (a or b):
    - **a)** Patient is currently receiving iron therapy; OR
    - **b)** Patient has adequate iron stores according to the prescriber; OR
- **B)** Patient is Currently Receiving an Erythropoiesis-Stimulating Agent. Approve if the patient meets BOTH of the following (i and ii):
  Note: Examples of erythropoiesis-stimulating agents include an epoetin alfa product (e.g., Epogen, Procrit, Retacrit), a darbepoetin alfa product (e.g., Aranesp), or a methoxy polyethylene glycol-epoetin beta product (e.g., Mircera).
  - **i.** Patient has a hemoglobin ≤ 12.0 g/dL; AND
  - **ii.** Patient meets ONE of the following (a or b):

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a) Patient is currently receiving iron therapy; OR
b) Patient has adequate iron stores according to the prescriber.

Dosing. Approve ONE of the following dosing regimens (A or B):
Note: Subsequent doses are titratable based on patient-specific hemoglobin response. Refer to the prescribing information regarding dose increases, dose reductions, treatment interruption, and ESA conversion dosing. Use the lowest dose sufficient to reduce the need for red blood cell transfusions.
A) Approve if the dose meets BOTH of the following (i and ii):
i. The starting dose is ≤ 0.45 mcg/kg and then may be titrated; AND
ii. Each dose is given no more frequently than once every week; OR
B) Approve if the dose meets BOTH of the following (i and ii):
i. The starting dose is ≤ 0.75 mcg/kg and then may be titrated; AND
ii. Each dose is given no more frequently than once every 2 weeks.

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3. Anemia in a Patient with Cancer due to Cancer Chemotherapy. Approve for 6 months if the patient meets ONE of the following (A or B):
A) Initial Therapy. Approve if the patient meets ALL of the following (i, ii, and iii):
i. Patient has a hemoglobin < 10.0 g/dL; AND
ii. Patient meets BOTH of the following (a and b):
a) Patient is currently receiving myelosuppressive chemotherapy; AND
b) According to the prescriber, myelosuppressive chemotherapy is considered non-curative; AND
iii. Patient meets ONE of the following (a or b):
a) Patient is currently receiving iron therapy; OR
b) Patient has adequate iron stores according to the prescriber; OR
B) Patient is Currently Receiving an Erythropoiesis-Stimulating Agent. Approve if the patient meets ALL of the following (i, ii, and iii):
Note: Examples of erythropoiesis-stimulating agents include an epoetin alfa product (e.g., Epogen, Procrit, Retacrit) or a darbepoetin alfa product (e.g., Aranesp).
i. Patient has a hemoglobin ≤ 12.0 g/dL; AND
ii. Patient meets BOTH of the following (a and b):
a) Patient is currently receiving myelosuppressive chemotherapy; AND
b) According to the prescriber, myelosuppressive chemotherapy is considered non-curative; AND
iii. Patient meets ONE of the following (a or b):
a) Patient is currently receiving iron therapy; OR
b) Patient has adequate iron stores according to the prescriber.

Dosing. Approve ONE of the following dosing regimens (A or B):
A) Approve if the dose meets BOTH of the following (i and ii):
i. Each dose is ≤ 500 mcg; AND
ii. Each dose is given no more frequently than once every week; OR
B) Approve if the dose meets BOTH of the following (i and ii):
i. Each dose is ≤ 4.5 mcg/kg; AND
ii. Each dose is given no more frequently than once every week.

Other Uses with Supportive Evidence

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4. Anemia Associated with Myelodysplastic Syndrome. Approve for 1 year if the patient meets ONE of the following (A or B):

A) Initial Therapy. Approve if the patient meets ALL of the following (i, ii, iii, and iv):
- **i.** Patient is ≥ 18 years of age; AND
- **ii.** Patient meets ONE of the following (a or b):
  - **a)** Patient has a hemoglobin < 10.0 g/dL; OR
  - **b)** Patient has a serum erythropoietin level ≤ 500 mU/mL; AND
- **iii.** Patient meets ONE of the following (a or b):
  - **a)** Patient is currently receiving iron therapy; OR
  - **b)** Patient has adequate iron stores according to the prescriber; AND
- **iv.** The medication is prescribed by or in consultation with a hematologist or oncologist.

B) Patient is Currently Receiving an Erythropoiesis-Stimulating Agent. Approve if the patient meets ALL of the following (i, ii, iii, and iv):
Note: Examples of erythropoiesis-stimulating agents include an epoetin alfa product (e.g., Epogen, Procrit, Retacrit) or a darbepoetin alfa product (e.g., Aranesp).
- **i.** Patient is ≥ 18 years of age; AND
- **ii.** Patient has a hemoglobin ≤ 12.0 g/dL; AND
- **iii.** Patient meets ONE of the following (a or b):
  - **a)** Patient is currently receiving iron therapy; OR
  - **b)** Patient has adequate iron stores according to the prescriber; AND
- **iv.** The medication is prescribed by or in consultation with a hematologist or oncologist.

Dosing. Approve if the dose meets BOTH of the following (A and B):
A) Each dose is ≤ 500 mcg; AND
B) Each dose is given no more frequently than once every 2 weeks.

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5. Anemia Associated with Myelofibrosis. Approve for the duration noted below if the patient meets ONE of the following (A or B):

A) Initial Therapy. Approve for 3 months if the patient meets ALL of the following (i, ii, and iii):
- **i.** Patient meets ONE of the following (a or b):
  - **a)** Patient has a hemoglobin < 10.0 g/dL; OR
  - **b)** Patient has a serum erythropoietin level ≤ 500 mU/mL; AND
- **ii.** Patient meets ONE of the following (a or b):
  - **a)** Patient is currently receiving iron therapy; OR
  - **b)** Patient has adequate iron stores according to the prescriber; AND
- **iii.** The medication is prescribed by or in consultation with a hematologist or oncologist.

B) Patient is Currently Receiving an Erythropoiesis-Stimulating Agent. Approve for 1 year if the patient meets ALL of the following (i, ii, iii, and iv):
Note: Examples of erythropoiesis-stimulating agents include an epoetin alfa product (e.g., Epogen, Procrit, Retacrit) or a darbepoetin alfa product (e.g., Aranesp).
- **i.** Patient has a hemoglobin ≤ 12.0 g/dL; AND
- **ii.** Patient meets ONE of the following (a or b):
  - **a)** Patient is currently receiving iron therapy; OR
  - **b)** Patient has adequate iron stores according to the prescriber; AND
- **iii.** According to the prescriber, patient has responded to therapy defined as hemoglobin ≥ 10 g/dL or a hemoglobin increase of ≥ 2 g/dL; AND
- **iv.** The medication is prescribed by or in consultation with a hematologist or oncologist.

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Dosing. Approve ONE of the following dosing regimens (A or B):

A) Approve if the dose meets BOTH of the following (i and ii):
- **i.** Each dose is ≤ 500 mcg; AND
- **ii.** Each dose is given no more frequently than once every week; OR

B) Approve if the dose meets BOTH of the following (i and ii):
- **i.** Each dose is ≤ 4.5 mcg/kg; AND
- **ii.** Each dose is given no more frequently than once every week.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Aranesp is not recommended in the following situations:

1. **Anemia Associated with Cancer in a Patient not Receiving Myelosuppressive Cancer Chemotherapy.** Aranesp is not indicated in patients with cancer who are not receiving cancer chemotherapy.[1]

2. **Anemia Associated with Acute Myelogenous Leukemias (AML), Chronic Myelogenous Leukemias (CML), or other Myeloid Cancers.** Aranesp is indicated for use in non-myeloid cancers. AML and CML are examples of myeloid cancers.[1]

3. **Anemia Associated with Radiotherapy in Cancer.** Aranesp is not indicated for use in patients with cancer who are given only radiation therapy.[1]

4. **To Enhance Athletic Performance.** Aranesp is not recommended for approval because this indication is excluded from coverage in a typical pharmacy benefit.

5. **Anemia due to Acute Blood Loss.** Use of Aranesp is not appropriate in these types of situations.

6. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Aranesp® intravenous or subcutaneous injection [prescribing information]. Thousand Oaks, CA: Amgen; March 2026.
2. Kidney Disease: Improving Global Outcomes (KDIGO) Anemia Work Group. KDIGO 2026 Clinical Practice Guideline for the Management of Anemia in Chronic Kidney Disease (CKD). *Kidney Int*. 2026;109(1S):S1-S99.
3. The NCCN Hematopoietic Growth Factors Clinical Practice Guidelines in Oncology (version 3.2026 – December 5, 2025). © 2026 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on June 22, 2026.
4. The NCCN Myelodysplastic Syndromes Clinical Practice Guidelines in Oncology (version 3.2026 – January 12, 2026). © 2026 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on August 20, 2026.
5. The NCCN Myeloproliferative Neoplasms Clinical Practice Guidelines in Oncology (version 2.2026 – June 16, 2026). © 2026 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on August 20, 2026.

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HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	07/17/2024
Annual Revision	No criteria changes.	07/16/2025
Annual Revision	No criteria changes.	07/08/2026
Selected Revision	**Anemia in a Patient with Chronic Kidney Disease who is not on Dialysis**: Dosing requirements were revised to remove age-based branching and clarify that the dose limitations apply to starting doses and then may be titrated. The frequency limitation for the ≤ 0.45 mcg/kg starting dose was updated from once every 4 weeks to once weekly. A note was added to clarify that subsequent doses are titratable based on patient-specific hemoglobin response and to refer to the prescribing information for dose increases, dose reductions, treatment interruption, and erythropoiesis-stimulating agent conversion dosing. **Anemia in a Patient with Cancer due to Cancer Chemotherapy**: Dosing requirements were revised to remove age-based branching. The weight-based dose limitation was updated from ≤ 2.25 mcg/kg to ≤ 4.5 mcg/kg. **Anemia Associated with Myelofibrosis**: The frequency limitation for doses ≤ 500 mcg was updated from once every 2 weeks to once every week. Additional weight-based dose option of ≤ 4.5 mcg/kg given no more frequently than once weekly was added.	09/16/2026

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