UTILIZATION MANAGEMENT MEDICAL POLICY

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

REVIEW DATE: 07/17/2024

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.

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.[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. Use the lowest dose of Aranesp to avoid RBC transfusions.

Dosing Information

Doses of Aranesp are titrated based on Hb values. Refer to the prescribing information regarding increasing, reducing, interrupting, or conversion dosing. Use the lowest dose sufficient to reduce the need for RBC transfusions.

Guidelines

The Kidney Disease Improving Global Outcomes (KDIGO) clinical practice guidelines for anemia in CKD (2012) state that for adults with CKD on dialysis, ESA therapy should be used to avoid having the Hb concentration fall below 9.0 g/dL by initiating ESA therapy when the Hb is between 9.0 and 10.0 g/dL.[2] The guidelines recommend against ESA therapy for adult patients with CKD who are not on dialysis when

Hb levels are ≥ 10.0 g/dL. For adult patients with CKD who are not on dialysis with Hb levels < 10.0 g/dL, the decision whether to initiate ESA therapy should be individualized based on many factors (e.g., prior response to iron therapy, the risk of needing a transfusion, presence of symptoms). In general, ESAs should not be used to maintain Hb concentrations above 11.5 g/dL in adult patients with CKD. For pediatric patients with CKD, the Hb concentration in which ESAs should be initiated in the individual patient should be considered while being aware of the potential benefits and potential harms. In all pediatric patients with CKD receiving ESA therapy, the selected Hb concentration should be in the range of 11.0 to 12.0 g/dL. Iron supplementation can improve response to ESA therapy. 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, iron supplementation is required in most patients to maintain an optimal response.

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

- **Myelodysplastic Syndrome (MDS):** NCCN guidelines (version 2.2024 – May 22, 2024) list Aranesp and epoetin alfa products as having utility in anemic, symptomatic patients with MDS if serum erythropoietin levels are ≤ 500 mU/mL.[3] 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 1.2024 – December 21, 2023) 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.[4] Iron stores should be adequate. The guidelines also advise that ESAs are generally less effective for the management of transfusion-dependent anemia.

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. Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. 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.

*Indications and/or approval conditions noted with **[EviCore]** are managed by EviCore healthcare for those clients who use EviCore for oncology and/or oncology-related reviews. For these conditions, a prior authorization review should be directed to EviCore at www.EviCore.com.*

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, or 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):
  - **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) Patient is ≥ 18 years of age. Approve if the dose meets BOTH of the following (i and ii):
- **i.** Each dose is ≤ 0.45 mcg/kg; AND
- **ii.** Each dose is given no more frequently than once every 4 weeks; OR

B) Patient is < 18 years of age. Approve if the dose meets BOTH of the following (i and ii):
- **i.** Each dose is ≤ 0.75 mcg/kg; 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. ***[EviCore]*** 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, or 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) Patient is ≥ 18 years of age. 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) Patient is < 18 years of age. Approve if the dose meets BOTH of the following (i and ii):
  i. Each dose is ≤ 2.25 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. ***[EviCore]*** 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, or 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.

5. **Anemia Associated with Myelofibrosis.** *[EviCore]* 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, or 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.

   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.

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.** *[EviCore]* 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.** *[EviCore]* 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.** *[EviCore]* 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; April 2024.
2. Kidney Disease: Improving Global Outcomes (KDIGO) Anemia Work Group. KDIGO Clinical Practice Guideline for Anemia in Chronic Kidney Disease. *Kidney Int*. 2012; 2(Suppl):279-335.
3. The NCCN Myelodysplastic Syndromes Clinical Practice Guidelines in Oncology (version 2.2024 – May 22, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on July 8, 2024.
4. The NCCN Myeloproliferative Neoplasms Clinical Practice Guidelines in Oncology (version 1.2024 – December 21, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on July 8, 2024.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	07/19/2023
Annual Revision	No criteria changes	07/17/2024