VENTURA COUNTY
HEALTH CARE PLAN

UTILIZATION REVIEW MEDICAL POLICY

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

REVIEW DATE: 07/22/2020

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 use:

- 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.

Therapy should be initiated for adult patients 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.[1] For adult patients with CKD not on dialysis, Aranesp should be initiated when Hb is < 10.0 g/dL and other considerations apply (e.g., patient is likely to need transfusions). 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. Initiate Aranesp for patients on cancer chemotherapy only if the Hb is < 10.0 g/dL. Use the lowest dose of Aranesp to avoid 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.

Dosing Information

Doses of Aranesp are titratable 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 failure to adequately respond to ESAs. Iron deficiency can occur following continued ESA use and, therefore, iron supplementation is required in most patients to maintain an optimal response.

Clinical practice guidelines from the National Comprehensive Cancer Network (NCCN) for myelodysplastic syndrome (MDS) [version 2.2020 – February 28, 2020] list Aranesp as having utility ni 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 ≤ 12.0 g/dL. The NCCN guidelines for myeloproliferative neoplasms (version 1.2020 – May 21, 2020) 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 not 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 indication(s). 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.

RECOMMENDED AUTHORIZATION CRITERIA

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

FDA-Approved Indications

1. **Anemia in Patients with Chronic Kidney Disease who are on Dialysis.** Approve for 3 years.

2. **Anemia in Patients with Chronic Kidney Disease who are not on Dialysis.** Approve for 1 year if the patient meets the following criteria (A or B):
   A) Initial Therapy. Approve if the patient meets the following criteria (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 (ESA). Approve if the patient meets the following criteria (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 meets one of the following (a or b):
  a) Patient is ≥ 18 years of age with a hemoglobin < 11.5 g/dL; OR
  b) Patient is < 18 years of age with 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 the following dosing regimens (A or B):
A) Patients ≥ 18 years of age. Approve if the dose meets 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) Patients < 18 years of age. Approve if the dose meets 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.

---

3. Anemia in Patients with Cancer due to Cancer Chemotherapy. Approve for 6 months if the patient meets the following criteria (A or B):
A) Initial Therapy. Approve if the patient meets the following criteria (i, ii, and iii):
i. Patient has a hemoglobin < 10.0 g/dL; AND
ii. Patient is currently receiving myelosuppressive chemotherapy; 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 (ESA). Approve if the patient meets the following criteria (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 is currently receiving myelosuppressive chemotherapy; 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 the following dosing regimens (A or B):
A) Patients ≥ 18 years of age. Approve if the dose meets 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) Patients < 18 years of age. Approve if the dose meets 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

---

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

A) Initial Therapy. Approve if the patient meets the following criteria (i, ii, iii, and iv):
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 is ≥ 18 years of age; AND
iii. Aranesp is prescribed by or in consultation with a hematologist or oncologist; AND
iv. 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 (ESA). Approve if the patient meets the following criteria (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 is ≥ 18 years of age; AND
iii. Aranesp is prescribed by or in consultation with a hematologist or oncologist; AND
iv. 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 if the dose meets 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. Approve for the duration noted below if the patient meets the following criteria (A or B):

A) Initial Therapy. Approve for 3 months if the patient meets the following criteria (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. The agent is prescribed by or in consultation with a hematologist or oncologist; 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 (ESA) therapy. Approve for 1 year if the patient meets the following criteria (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.** The ESA therapy is prescribed by or in consultation with a hematologist or oncologist; 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.** According to the prescriber, patient has responded to therapy defined as hemoglobin ≥ 10 g/dL or a hemoglobin increase of ≥ 2 g/dL.

Dosing. Approve if the dose meets 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 Patients 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® injection for intravenous or subcutaneous use [prescribing information]. Thousand Oaks, CA: Amgen, Inc.; January 2019.
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 2.2020 – February 28, 2020). © 2020 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on June 29, 2020.
4. The NCCN Myeloproliferative Neoplasms Clinical Practice Guidelines in Oncology (version 1.2020 – May 21, 2020). © 2020 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on June 29, 2020.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual revision	Criteria that previously stated Epogen/Procrit were changed to cite epoetin alfa to address the approval of Retacrit. For patients with anemia due to CKD who are on dialysis, the criteria were changed to reflect approval of Mircera in pediatric patients who are on hemodialysis. For patients requesting to use Aranesp who are currently receiving Mircera, the target Hb of ≤ 12.0 g/dL was added for children, similar to other ESAs. Previously the criteria only addressed the Hb threshold in adults (≤ 11.5 g/dL) who were receiving Mircera and requesting to transition to Aranesp. For children with CKD not on dialysis the starting dose of 0.45 mcg/kg body weight given as a single SC or IV injection once weekly was added as an option. The Aranesp dose of 500 mcg SC once every 3 weeks for MDS was added as a treatment option.	06/20/2018
Annual revision	The following changes were made: 1. **Anemia in CKD for Patients Who are on Dialysis:** The approval duration was changed from 6 months to 1 year. For the criteria that requires the patient have a specified Hb value, changed the wording of "adults" to "patients ≥ 18 years of age". For the criteria that requires children to have a specified Hb value, changed the wording of "children" to "patients < 18 years of age". For the criteria that addresses patients who are currently receiving an ESA, changed from citing examples of the ESA products in criteria to providing a list of ESAs in a note. The example cited that the "Aranesp prescribing information recommends supplemental iron therapy when serum ferritin is < 100 mcg/L or when serum transferrin saturation is < 20%" was deleted. Initial approval and extended approval was removed, including criteria that required a response to therapy in for extended approval. Dosing was revised to reflect maximum doses and intervals; the route of administration was removed (see policy). The "Duration of Therapy" and "Labs/Diagnostics" sections were also deleted. 2. **Anemia in CKD for Patients Who are Not on Dialysis:** The approval duration was changed from 6 months to 1 year. For the criteria that requires the patient have a specified Hb value, changed the wording of "adults" to "patients ≥ 18 years of age". For the criteria that requires children to have a specified Hb value, changed the wording of "children" to "patients < 18 years of age". For the criteria that addresses patients who are currently receiving an ESA, changed from citing examples of the ESA products in criteria to providing a list of ESAs in a note. The example cited that the "Aranesp prescribing information recommends supplemental iron therapy when serum ferritin is < 100 mcg/L or when serum transferrin saturation is < 20%" was deleted. Initial approval and extended approval was removed as a separate section, including criteria that required a response to therapy in for extended approval. Dosing was revised to reflect maximum doses and intervals; the route of administration was removed (see policy). The "Duration of Therapy" and "Labs/Diagnostics" sections were also deleted. 3. **Anemia in Patients with Cancer Due to Cancer Chemotherapy:** The approval duration was changed from 4 months to 6 months. For the criteria that addresses patients who are currently receiving an ESA, changed from citing examples of the ESA products in criteria to providing a list of ESAs in a note. The example cited that the "Aranesp prescribing information recommends supplemental iron therapy when serum ferritin is < 100 mcg/L or when serum transferrin saturation is < 20%" was deleted. Initial approval and extended approval as a separate section was removed. Dosing was revised to reflect maximum doses and intervals; the route of administration was removed (see policy).	07/24/2019

	Removed "until completion of a chemotherapy course" from dosing regimens. The "Duration of Therapy" and "Labs/Diagnostics" sections were also deleted. 4. **Anemia Associated with MDS:** The approval duration was changed from 6 months to 1 year. For the criteria that addresses patients who are currently receiving an ESA, changed from citing examples of the ESA products in criteria to providing a list of ESAs in a note. Initial approval and extended approval as a separate section was removed, including the criteria that defined response. The example cited that the "Aranesp prescribing information recommends supplemental iron therapy when serum ferritin is < 100 mcg/L or when serum transferrin saturation is < 20%" was deleted. 5. **Anemia Associated with Myelofibrosis:** New criteria were approved, along with recommended dosing. See policy. 6. **Waste Management for All Indications:** This section was removed from the policy.	
Selected revision	**Anemia in CKD for Patients Who are on Dialysis.** Existing criteria and dosing were removed. This indication is no longer a targeted indication for this policy. All requests for anemia in CKD for patients who are on dialysis changed to approve for 1 year.	9/11/2019
Selected revision	For **Anemia in Patients with Chronic Kidney Disease who are on Dialysis,** the approval duration was changed from 1 year to 3 years.	11/06/2019
Annual Revision	No criteria changes.	07/22/2020