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Darbepoetin alfa

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INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Overview

This policy supports medical necessity review for darbepoetin alfa intravenous or subcutaneous injection (Aranesp®).

Receipt of sample product does not satisfy any criteria requirements for coverage.

Medical Necessity Criteria

Darbepoetin alfa (Aranesp®) is considered medically necessary when ONE of the following is met:

1. **Anemia in an Individual with Chronic Kidney Disease who is on Dialysis.**

2. **Anemia in an Individual with Chronic Kidney Disease who is <u>not</u> on Dialysis.** Individual meets **BOTH** of the following criteria:
   A. **ONE** of the following:

i. Age 18 years or older with a hemoglobin less than 10.0 g/dL
ii. Less than age 18 years with a hemoglobin less than 11.0 g/dL

B. **ONE** of the following:
i. Currently receiving iron therapy
ii. Has adequate iron stores according to the prescriber

3. **Anemia in an Individual with Cancer due to Cancer Chemotherapy.** Individual meets **ALL** of the criteria:
A. Hemoglobin less than 10.0 g/dL
B. Currently receiving myelosuppressive chemotherapy
C. **ONE** of the following:
i. Currently receiving iron therapy
ii. Has adequate iron stores according to the prescriber

4. **Anemia Associated with Myelodysplastic Syndrome.** Individual meets **ALL** of the following criteria:
A. Age 18 years or older
B. **ONE** of the following:
i. Hemoglobin less than 10.0 g/dL
ii. Serum erythropoietin level less than or equal to 500 mU/mL
C. **ONE** of the following:
i. Currently receiving iron therapy
ii. Has adequate iron stores according to the prescriber
D. Medication is prescribed by or in consultation with a hematologist or oncologist

5. **Anemia Associated with Myelofibrosis.** Individual meets **ALL** of the following criteria:
A. **ONE** of the following:
i. Hemoglobin less than 10.0 g/dL
ii. Serum erythropoietin level less than or equal to 500 mU/mL
B. **ONE** of the following:
i. Currently receiving iron therapy
ii. Has adequate iron stores according to the prescriber
C. Medication is prescribed by or in consultation with a hematologist or oncologist

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Reauthorization Criteria

Continuation of darbepoetin alfa (Aranesp) is considered medically necessary when **ONE** of the following is met:

1. **Anemia in an Individual with Chronic Kidney Disease who is on Dialysis.** Individual meets the following criteria:
A. Above medical necessity criteria are met AND there is documentation of beneficial response

2. **Anemia in an Individual with Chronic Kidney Disease who is <u>not</u> on Dialysis.** Individual meets the following criteria:
A. **ONE** of the following:
i. 18 years of age or older with a hemoglobin less than 11.5 g/dL
ii. Less than 18 years of age with a hemoglobin less than or equal to 12.0 g/dL

3. **Anemia in an Individual with Cancer due to Cancer Chemotherapy.** Individual meets the following criteria:
A. Hemoglobin less than or equal to 12.0 g/dL

4. **Anemia Associated with Myelodysplastic Syndrome.** Individual meets the following criteria:
    A. Hemoglobin less than or equal to 12.0 g/dL

5. **Anemia Associated with Myelofibrosis.** Individual meets **BOTH** of the following criteria:
    A. Hemoglobin less than or equal to 12.0 g/dL
    B. According to the prescriber, individual has responded to therapy defined as hemoglobin greater than or equal to 10 g/dL or a hemoglobin increase of greater than or equal to 2 g/dL

Authorization Duration

Initial approval duration:

1. **Anemia in an Individual with Chronic Kidney Disease who is on Dialysis:** Up to 3 years.
2. **Anemia in an Individual with Chronic Kidney Disease who is not on Dialysis:** Up to 12 months.
3. **Anemia in an Individual with Cancer due to Cancer Chemotherapy:** Up to 6 months.
4. **Anemia Associated with Myelodysplastic Syndrome:** Up to 12 months.
5. **Anemia Associated with Myelofibrosis:** Up to 3 months.

Reauthorization approval duration:

1. **Anemia in an Individual with Chronic Kidney Disease who is on Dialysis:** Up to 3 years.
2. **Anemia in an Individual with Chronic Kidney Disease who is not on Dialysis:** Up to 12 months.
3. **Anemia in an Individual with Cancer due to Cancer Chemotherapy:** Up to 6 months.
4. **Anemia Associated with Myelodysplastic Syndrome:** Up to 12 months.
5. **Anemia Associated with Myelofibrosis:** Up to 12 months.

Conditions Not Covered

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive):

1. **Anemia Associated with Cancer in an Individual not Receiving Myelosuppressive Cancer Chemotherapy.** Aranesp is not indicated in individuals 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 individuals with cancer who are given only radiation therapy.[1]

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

5. **Use in Individuals Receiving Myelosuppressive Chemotherapy with a Curative Intent.** Erythropoiesis-stimulating agents (ESAs) are not indicated for use in individuals with cancer receiving myelosuppressive chemotherapy when the anticipated outcome is cure.[1]

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

Coding Information

1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

HCPCS Codes	Description
J0881	Injection, darbepoetin alfa, 1 microgram (non-ESRD use)
J0882	Injection, darbepoetin alfa, 1 microgram (for ESRD on dialysis)

Background

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.

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.

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 several guidelines from the National Comprehensive Cancer Network (NCCN):

- **Myelodysplastic Syndrome (MDS):** NCCN guidelines (version 3.2021 – January 15, 2021) 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 ≤ 12.0 g/dL.
- **Myeloproliferative Neoplasms:** The NCCN guidelines (version 1.2021 – April 13, 2021) 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.

References

1. Aranesp intravenous or subcutaneous injection [prescribing information]. Thousand Oaks, CA: Amgen; 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 3.2021 – January 15, 2021). © 2021 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on July 8, 2021.
4. The NCCN Myeloproliferative Neoplasms Clinical Practice Guidelines in Oncology (version 1.2021 – April 13, 2021). © 2021 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on July 8, 2021.