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# 5.85.001

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| **Section:** | Prescription Drugs | **Effective Date:** | July 1, 2024 |
| **Subsection:** | Hematological Agents | **Original Policy Date:** | December 7, 2011 |
| **Subject:** | Aranesp | **Page:** | 1 of 6 |

***Last Review Date:*** June 13, 2024

# Aranesp

## Description

### Aranesp (darbepoetin alfa)

**Background**
Aranesp (darbepoetin alfa) is an erythropoiesis stimulating agent (ESA) that binds to progenitor stem cells and stimulates the production and differentiation of red blood cells (RBC). The treatment of anemia associated with chronic kidney disease is supported by the Normal Hematocrit Study and early clinical studies that show the use of darbepoetin alfa reduced the need for RBC transfusions. The treatment of anemia secondary to chemotherapy is supported by clinical studies that demonstrated safety and efficacy in reducing the number of patients receiving RBC transfusions (1-2).

**Regulatory Status**
FDA-approved indications: Aranesp is an erythropoiesis-stimulating agent (ESA) indicated for the treatment of anemia due to: (1)

- Chronic Kidney Disease (CKD) in patients on dialysis and patients not on dialysis
- The effects of concomitant myelosuppressive chemotherapy, and upon initiation, there is a minimum of two additional months of planned chemotherapy.

Limitations of Use: (1)
Aranesp has not been shown to improve quality of life, fatigue, or patient well-being.
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 the anemia can be managed by transfusion
- As a substitute for RBC transfusions in patients who require immediate correction of anemia

The FDA has recommended conservative dosing guidelines for darbepoetin alfa when used to treat anemia in patients with chronic kidney disease (CKD) due to the increased risk of cardiovascular events. Clinical trials have shown that when darbepoetin alfa is dosed to achieve a normal or near normal blood hemoglobin (Hgb) level, there is an increased risk for cardiovascular events, such as heart attack or stroke. Physicians and their patients with CKD should weigh the possible benefits of using darbepoetin alfa to decrease the need for red blood cell transfusions against the increased risks for serious adverse cardiovascular events. Treatment should be individualized to assure the lowest dose of darbepoetin alfa is used to reduce the need for transfusion. These recommendations for dosing darbepoetin alfa in CKD patients are based on clinical trials including TREAT (Trial to Reduce Cardiovascular Events with Aranesp Therapy) (1-3).

Transferrin saturation should be at least 20% and serum ferritin at least 100 ng/mL prior to treatment with erythropoietin stimulating agents, to ensure adequate iron stores. Supplemental iron therapy should be administered to reach these levels before initiating darbepoetin alfa. However, there are upper limits for both transferrin saturation and serum ferritin. Supplemental iron is no longer a safe option if either the transferrin saturation exceeds 50% or the serum ferritin exceeds 500 ng/ml. Erythropoietin stimulating agents are indicated in these clinical situations (1-3).

Myelodysplastic syndromes (MDS) encompass a series of hematological conditions characterized by chronic cytopenias, including anemia, accompanied by abnormal cellular maturation. As a result, patients with MDS are at risk for symptomatic anemia. At least 80 percent of patients are anemic at the time of diagnosis, while about 50 percent have a hemoglobin level less than 10 g/dL. The use of darbepoetin alfa for the treatment of symptomatic anemia in patients with MDS is an unlabeled use that is supported by the American Society of Hematology (ASH), the American Society of Clinical Oncology (ASCO), and the National Comprehensive Cancer Network (NCCN) (5-8).

Anemia associated with Hepatitis C therapy is a frequent cause of dose reduction or discontinuation of therapy. Clinical recommendation is to reduce the dosage if anemia developed. This reduction increases the likelihood of treatment failure. Addition of an ESA agent allows the optimal probability of treatment success (9).

A boxed warning suggests that ESAs increase the risk of death, myocardial infarction, stroke, and venous thromboembolism, thrombosis of vascular access and tumor progression or recurrence (1).

**Related policies**

Epoetin alfa agents

## Policy

*This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.*

Aranesp may be considered **medically necessary** if the conditions indicated below are met

Aranesp may be considered **investigational** for all other indications.

## Prior-Approval Requirements

### Diagnoses

Patient must have **ONE** of the following:

1. Anemia associated with chronic renal failure
   a. Serum ferritin ≥ 100 ng/ml (labs must have been taken within the last 3 months)

   **AND ONE** of the following:

   1. ***If patient is NOT on dialysis***
      a. Initial treatment: Hemoglobin < 10 g/dl*
      b. Continuing treatment: Hemoglobin ≤ 10 g/dl*

   2. ***If patient is ON dialysis***
      a. Initial treatment: Hemoglobin < 10 g/dl*
      b. Continuing treatment: Hemoglobin ≤ 11 g/dl*

* if the hemoglobin level exceeds this level then the prescribing physician must confirm that the dose will be held or reduced until the hemoglobin level returns to the required level.

2. Anemia secondary to chemotherapy
   a. Concomitant myelosuppressive therapy and the anticipated outcome of therapy is NOT cure of cancer
   b. There is a minimum of two additional months of planned chemotherapy
   c. Must discontinue use of agent upon completion of the chemotherapy
   d. Patient's anemia cannot be managed by transfusions

3. Myelodysplastic syndrome (MDS)

4. Anemia associated with Hepatitis C (HCV) treatment

**AND** the following
   a. **NOT** used in combination with another erythropoiesis stimulating agent

## Prior – Approval *Renewal* Requirements

Same as above

## Policy Guidelines

### Pre - PA Allowance

None

### Prior - Approval Limits

**Duration** 6 months

## Prior – Approval *Renewal* Limits

Same as above

## Rationale

**Summary**

Aranesp (darbepoetin alfa) is an erythropoiesis stimulating agent (ESA) that binds to progenitor stem cells and stimulates the production and differentiation of red blood cells (RBC) (1). The treatment of anemia associated with chronic kidney disease is supported by the Normal

Hematocrit Study and early clinical studies that show the use of darbepoetin alfa reduced the need for RBC transfusions (2).

The FDA has recommended conservative dosing guidelines for darbepoetin alfa when used to treat anemia in patients with chronic kidney disease (CKD) due to the increased risk of cardiovascular events. Clinical trials have shown that when darbepoetin alfa is dosed to achieve a normal or near normal blood hemoglobin (Hgb) level, there is an increased risk for cardiovascular events, such as heart attack or stroke (1-9).

Prior authorization is required to ensure the safe, clinically appropriate, and cost-effective use of Aranesp while maintaining optimal therapeutic outcomes.

**References**

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## Policy History

| Date | Action |
|---|---|
| December 2011 | New policy |
| December 2012 | Annual editorial review and reference update |
| March 2014 | Annual editorial review and reference update.<br>Removal of TSAT level requirement.<br>Modified use with chemotherapy to reflect package insert. |
| March 2015 | Annual editorial review and reference update<br>Addition of not used in combination with another erythropoiesis stimulating agent |
| December 2016 | Annual editorial review and reference update<br>Policy code changed from 5.10.01 to 5.85.01 |
| September 2017 | Annual editorial review and reference update<br>Addition of requirement to anemia secondary to chemotherapy: Patient's anemia cannot be managed by transfusions |
| September 2018 | Annual editorial review and reference update |
| September 2019 | Annual review and reference update |
| September 2020 | Annual review |
| March 2021 | Annual review |
| June 2021 | Annual review |
| March 2022 | Annual review |
| March 2023 | Annual review. Changed policy number to 5.85.001 |
| June 2023 | Annual review |
| March 2024 | Annual review and reference update |
| June 2024 | Annual review |

## Keywords

**This policy was approved by the FEP® Pharmacy and Medical Policy Committee on June 13, 2024 and is effective on July 1, 2024.**