

---

# 5.85.001

---

<b>Section:</b>	Prescription Drugs	<b>Effective Date:</b>	January 1, 2025
<b>Subsection:</b>	Hematological Agents	<b>Original Policy Date:</b>	December 7, 2011
<b>Subject:</b>	Aranesp	<b>Page:</b>	1 of 6

---

**Last Review Date:** December 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

# 5.85.001

---

<b>Section:</b>	Prescription Drugs	<b>Effective Date:</b>	January 1, 2025
<b>Subsection:</b>	Hematological Agents	<b>Original Policy Date:</b>	December 7, 2011
<b>Subject:</b>	Aranesp	<b>Page:</b>	2 of 6

---

- 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).

---

<b>Section:</b>	Prescription Drugs	<b>Effective Date:</b>	January 1, 2025
<b>Subsection:</b>	Hematological Agents	<b>Original Policy Date:</b>	December 7, 2011
<b>Subject:</b>	Aranesp	<b>Page:</b>	3 of 6

---

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  $\geq$  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  $\leq$  10 g/dl\*
2. ***If patient is ON dialysis***
  - a. Initial treatment: Hemoglobin < 10 g/dl\*
  - b. Continuing treatment: Hemoglobin  $\leq$  11 g/dl\*

<b>Section:</b>	Prescription Drugs	<b>Effective Date:</b>	January 1, 2025
<b>Subsection:</b>	Hematological Agents	<b>Original Policy Date:</b>	December 7, 2011
<b>Subject:</b>	Aranesp	<b>Page:</b>	4 of 6

---

\* 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

# 5.85.001

---

<b>Section:</b>	Prescription Drugs	<b>Effective Date:</b>	January 1, 2025
<b>Subsection:</b>	Hematological Agents	<b>Original Policy Date:</b>	December 7, 2011
<b>Subject:</b>	Aranesp	<b>Page:</b>	5 of 6

---

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

1. Aranesp [package insert]. Thousand Oaks, CA: Amgen Inc.; April 2024.
2. Berns JS. Are there implications from the Trial to Reduce Cardiovascular Events with Aranesp Therapy study for anemia management in dialysis patients? *Curr Opin Nephrol Hypertens*. 2010 Nov; 19(6):567-72.
3. KDOQI US Commentary on the 2012 KDIGO Clinical Practice Guideline for Anemia in CKD. Klinger, Alan S. et al. *American Journal of Kidney Diseases*, Volume 62, Issue 5, 849 -859. [http://www.kidney.org/professionals/kdoqi/guideline\\_updates/doqiupan\\_iii.html](http://www.kidney.org/professionals/kdoqi/guideline_updates/doqiupan_iii.html)
4. Fishbane S, Magner J. Sodium ferric gluconate complex in the treatment of iron deficiency for patients on dialysis. *Am J Kid Dis* 2001; 37:870-83.
5. Steensma DP, Bennett JM. The Myelodysplastic syndromes: diagnosis and treatment. *Mayo Clin Proc* 2006; 81:104.nt. *Mayo Clin Proc* 2006; 81:104.
6. Rizzo JD, Brouwers M, Herley P, et al. American Society of Hematology / American Society of Clinical Oncology clinical practice guideline update on the use of epoetin and darbepoetin in adult patients with cancer. *Blood* 2010; 116:4045.
7. Rizzo JD, Brouwers M, Herley P, et al. American Society of Hematology / American Society of Clinical Oncology clinical practice guideline update on the use of epoetin and darbepoetin in adult patients with cancer. *J Clin Oncol* 2010; 28:4996.
8. NCCN Clinical Practice Guidelines in Oncology® Myelodysplastic Syndromes (Version 3.2023). National Comprehensive Cancer Network, Inc. November 2023. Accessed on January 8, 2024.
9. Erythropoietin and hepatitis C therapy: Useful adjuvant therapy but remember to treat the patient and not just a number, Eric M Yoshida, Anne Dar Santos, Nilufar Partovi, Jo-Ann E Ford. *Can J Gastroenterol*. 2006 Aug; 20(8): 519–520. Accessed May 2018. <<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2659933/>>

# 5.85.001

---

<b>Section:</b>	Prescription Drugs	<b>Effective Date:</b>	January 1, 2025
<b>Subsection:</b>	Hematological Agents	<b>Original Policy Date:</b>	December 7, 2011
<b>Subject:</b>	Aranesp	<b>Page:</b>	6 of 6

---

## Policy History

Date	Action
December 2011	New policy
December 2012	Annual editorial review and reference update
March 2014	Annual editorial review and reference update. Removal of TSAT level requirement. Modified use with chemotherapy to reflect package insert.
March 2015	Annual editorial review and reference update Addition of not used in combination with another erythropoiesis stimulating agent
December 2016	Annual editorial review and reference update Policy code changed from 5.10.01 to 5.85.01
September 2017	Annual editorial review and reference update 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
December 2024	Annual review and reference update

## Keywords

---

**This policy was approved by the FEP® Pharmacy and Medical Policy Committee on December 13, 2024 and is effective on January 1, 2025.**