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# Clinical Coverage Guideline



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## Erythropoiesis Stimulating Agents in Cancer and Related Neoplastic Conditions

**Guideline Number: HS-059**

**Original Effective Date: 11/20/2008**

**Revision Date: 11/24/2009**

The Clinical Coverage Guideline is intended to supplement certain standard WellCare benefit plans. The terms of a member's particular Benefit Plan, Evidence of Coverage, Certificate of Coverage, etc., may differ significantly from this Coverage Position. For example, a member's benefit plan may contain specific exclusions related to the topic addressed in this Clinical Coverage Guideline. When a conflict exists between the two documents, the Member's Benefit Plan always supersedes the information contained in the Clinical Coverage Guideline. Additionally, Clinical Coverage Guidelines relate exclusively to the administration of health benefit plans and are NOT recommendations for treatment, nor should they be used as treatment guidelines. The application of the Clinical Coverage Guideline is subject to the benefit determinations set forth by the Centers for Medicare and Medicaid Services (CMS) National and Local Coverage Determinations and state-specific Medicaid mandates, if any.

# Clinical Coverage Guideline HS-059

## Erythropoiesis Stimulating Agents (ESAs) in Cancer and Related Neoplastic Conditions

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### DISCLAIMER

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### APPLICATION STATEMENT

The application of the Clinical Coverage Guideline is subject to the benefit determinations set forth by the Centers for Medicare and Medicaid Services (CMS) National and Local Coverage Determinations and state-specific Medicaid mandates, if any.

### CLINICAL COVERAGE GUIDELINE

**Erythropoiesis Stimulating Agent (ESA) treatment for anemia secondary to myelosuppressive anticancer chemotherapy in solid tumors, multiple myeloma, lymphoma, and lymphocytic leukemia is considered medically necessary under the following specified conditions:**

- The hemoglobin level immediately prior to initiation or maintenance of ESA treatment is <10 g/dL (or the hematocrit is <30%).
- The starting dose for ESA treatment is the recommended FDA label starting dose, no more than 150 U/kg/3 times weekly for epoetin and 2.25 mcg/kg/1 time weekly for darbepoetin alpha. Equivalent doses may be given over other approved time periods.
- Maintenance of ESA therapy is the starting dose if the hemoglobin level remains below 10 g/dL (or hematocrit is <30%) 4 weeks after initiation of therapy and the rise in hemoglobin is  $\geq$  1g/dL (hematocrit  $\geq$  3%).
- For patients whose hemoglobin rises <1 g/dl (hematocrit rise <3%) compared to pretreatment baseline over 4 weeks of treatment and whose hemoglobin level remains <10 g/dL after the 4 weeks of treatment (or the hematocrit is <30%), the recommended FDA label starting dose may be increased once by 25%. Continued use of the drug is not reasonable and necessary if the hemoglobin rises <1 g/dl (hematocrit rise <3 %) compared to pretreatment baseline by 8 weeks of treatment.
- Continued administration of the drug is not reasonable and necessary if there is a rapid rise in hemoglobin >1 g/dl (hematocrit >3%) over 2 weeks of treatment unless the hemoglobin remains below or subsequently falls to <10 g/dL (or the hematocrit is <30%). Continuation and reinstatement of ESA therapy must include a dose reduction of 25% from the previously administered dose.
- ESA treatment duration for each course of chemotherapy includes the 8 weeks following the final dose of myelosuppressive chemotherapy in a chemotherapy regimen.

**ESA treatment is contraindicated in members with certain clinical conditions, either because of:**

- 1) A deleterious effect of the ESA on their underlying disease; **OR,**
- 2) Because the underlying disease increases their risk of adverse effects related to ESA use.

Such underlying disease states may include:

- Any anemia in cancer or cancer treatment patients due to folate deficiency, B-12 deficiency, iron deficiency, hemolysis, bleeding, or bone marrow fibrosis;
- The anemia associated with the treatment of acute and chronic myelogenous leukemias (CML, AML), or erythroid cancers;
- The anemia of cancer not related to cancer treatment;
- Any anemia associated only with radiotherapy;
- Prophylactic use to prevent chemotherapy-induced anemia;
- Prophylactic use to reduce tumor hypoxia;
- Patients with erythropoietin-type resistance due to neutralizing antibodies; and
- Anemia due to cancer treatment if patients have uncontrolled hypertension.

**BACKGROUND**

Erythropoietin is an endogenous hormone that stimulates the production, maturation, and release of red blood cells. Erythropoietin is produced primarily by the kidneys and is secreted when the kidneys detect changes in oxygen delivery. Low levels of erythropoietin can lead to significant anemia.

Two hematopoietic growth factors are currently available in the United States: epoetin alfa and darbepoetin alfa. Epoetin alfa (Epogen®, Procrit®) is a recombinant form of erythropoietin that is administered intravenously or subcutaneously from one to three times per week. Darbepoetin alfa is a long-acting erythropoiesis-stimulating protein. Like epoetin alfa, it can be administered either intravenously or subcutaneously.

Anemia in patients with cancer may be related to the cancer chemotherapy, infiltration of the bone marrow by cancer cells, or nonspecific processes like iron deficiency, low endogenous erythropoietin levels, or the inhibitory effect of tumor necrosis factor. Prior to the development of epoetin alfa, the management of anemia in cancer patients primarily consisted of blood transfusions. The American Society of Clinical Oncology (ASCO) and the American Society of Hematology (ASH) have developed guidelines for the use of epoetin alfa in anemic patients with cancer. Darbepoetin alfa was not marketed at the time the guidelines were written in 2002. The ASCO/ASH guidelines are based on an evidence review from the Agency for Healthcare Research and Quality (AHRQ). The National Cancer Institute (NCI) and the World Health Organization (WHO) have different rating scales for anemia. The NCI has a more conservative definition of grades 0, 1, and 2 anemia. The National Comprehensive Cancer Network (NCCN) uses a different scale and defines mild anemia as Hgb 10–11 g/dL, moderate anemia as Hgb 8–10 g/dL, and severe anemia as Hgb < 8 g/dL. The NCCN guidelines recommend erythropoietin therapy if patients are symptomatic and Hgb level is 10–11 g/dL and to strongly consider therapy if Hgb is < 10 g/dL.

**CODING**

**Covered CPT®\* Code**

Not applicable

**Covered ICD-9-CM Procedure Codes**

99.28 Injection or infusion of biological response modifier (BRM) as an antineoplastic agent

**Covered HCPCS Codes**

J0881 Injection, darbepoetin alfa, 1 mcg (non-ESRD use)

J0885 Injection, epoetin alfa, (for non-ESRD use), 1,000 units

### Covered ICD-9-CM Diagnosis Codes

140.0 - 149.9	Malignant Neoplasm of Lip, Oral Cavity and Pharynx
150.0 - 159.9	Malignant neoplasm of Digestive Organs and Peritoneum
160.0 - 165.9	Malignant Neoplasm of Respiratory and Intrathoracic Organs
170.0 - 176.9	Malignant Neoplasm of Bone, Connective Tissue, Skin and Breast
179 - 189.9	Malignant Neoplasm of Genitourinary Organs (Male and Female)
190.0 - 199.2	Malignant Neoplasm of Other and Unspecified Sites
200.00 - 200.88	Malignant Neoplasm of Lymphatic and Hematopoietic Tissue
201.00 - 201.98	Hodgkin's Disease
202.00 - 202.98	Other Malignant neoplasm of Lymphoid and Histiocytic tissue
203.00 - 203.82	Multiple Myeloma, without mention of having achieved remission and other immunoproliferative neoplasm, in relapse
204.00 - 204.92	Lymphoid Leukemia, without mention of having achieved remission and unspecified Lymphoid leukemia, in relapse
209.00 - 209.03	Malignant Neuroendocrine Tumors
209.10 - 209.17	Malignant Carcinoid Tumor of the Appendix, Large Intestine and Rectum
209.20 - 209.29	Malignant Carcinoid Tumor of Other and Unspecified Sites
209.30	Malignant Poorly Differentiated Neuroendocrine Tumors
230.0 - 234.9	Carcinoma in Situ of Digestive Organs, Respiratory System, Skin, Breast & Genitourinary and Unspecified Sites.
235.0 - 235.9	Neoplasm of Uncertain Behavior of Digestive and Respiratory System
236.0 - 236.99	Neoplasm of Uncertain Behavior of Genitourinary Organs
237.0 - 237.9	Neoplasm of Uncertain Behavior of Endocrine Glands and Nervous System
238.0 - 238.6	Neoplasm of Uncertain behavior of Other and Unspecified sites and tissues
238.71 - 238.9	Other Lymphatic and Hematopoietic Tissues
239.0 - 239.9	Neoplasm of Unspecified Nature
273.3	Macroglobulinemia
285.22	Anemia in neoplastic disease
283.5	Anemia due to antineoplastic chemotherapy

\*Current Procedural Terminology (CPT®) ©2010 American Medical Association: Chicago, IL.

### REFERENCES

1. Centers for Medicare and Medicaid Services (CMS), National Coverage Determination (NCD) for Erythropoiesis Stimulating Agents (ESAs) in Cancer and Related Neoplastic Conditions (110.21).
2. American Society of Clinical Oncology/American Society of Hematology clinical practice guideline update. Use of epoetin and darbepoetin in patients with cancer: 2007.
3. UnitedHealthcare Drug Guideline, Anemia Drugs: darbepoetin alfa and epoetin alfa. March 5, 2007.
4. American Society of Hematology. Practice Update: ODAC Recommends ESAs Continue to be Indicated for Treatment of Chemotherapy-Induced Anemia But with New Restrictions. March 14, 2008.
5. NCCN. Clinical Practice Guidelines in Oncology: Cancer and treatment-related anemia. 2007.
6. American Society of Clinical Oncology and the American Society of Hematology. Use of epoetin in patients with cancer: evidence-based clinical practice guidelines. 2002.