

Erythropoiesis Stimulating Agents (ESAs) in Cancer and Related Neoplastic Conditions (NCD 110.21)

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[↪ Terms and Conditions](#)

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Related Medicare Advantage Policy Guidelines
<ul style="list-style-type: none"> Coverage of Drugs and Biologicals for Label and Off-Label Uses Erythropoietin Stimulating Agent (ESA)
Related Medicare Advantage Coverage Summary
<ul style="list-style-type: none"> Medications/Drugs (Outpatient Part B)

Policy Summary

[↪ See Purpose](#)

Overview

Erythropoiesis stimulating agents (ESAs) stimulate the bone marrow to make more red blood cells and are United States Food and Drug Administration (FDA) approved for use in reducing the need for blood transfusion in patients with specific clinical indications. The FDA has issued alerts and warnings for ESAs administered for a number of clinical conditions, including cancer. Published studies report a higher risk of serious and life-threatening events associated with oncologic uses of ESAs.

Guidelines

Nationally Covered Indications

ESA treatment for the anemia secondary to myelosuppressive anticancer chemotherapy in solid tumors, multiple myeloma, lymphoma, and lymphocytic leukemia is only reasonable and 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 10g/dL (or hematocrit is < 30%) 4 weeks after initiation of therapy and the rise in hemoglobin is ≥ 1g/dL (hematocrit ≥ 3%).
- For patients whose hemoglobin rises < 1g/dl (hematocrit rise < 3%) compared to pretreatment baseline over 4 weeks of treatment and whose hemoglobin level remains < 10g/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 < 1g/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 > 1g/dl (hematocrit > 3%) over 2 weeks of treatment unless the hemoglobin remains below or subsequently falls to < 10g/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.

Nationally Non-Covered Indications

ESA treatment is not reasonable and necessary for beneficiaries with certain clinical conditions, either because of a deleterious effect of the ESA on their underlying disease or because the underlying disease increases their risk of adverse effects related to ESA use. These conditions 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.

Other

Local Medicare Administrative Contractors may continue to make reasonable and necessary determinations on all other uses of ESAs not specified in this National Coverage Determination.

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this guideline does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

HCPCS Code	Description
J0881	Injection, darbepoetin alfa, 1 microgram (Non-ESRD use) (refer to the Medicare Advantage Policy Guideline titled Erythropoietin Stimulating Agent (ESA))
J0885	Injection, epoetin alfa, (for Non-ESRD use), 1000 units (refer to the Medicare Advantage Policy Guideline titled Erythropoietin Stimulating Agent (ESA))
Q5106	Injection, epoetin alfa, biosimilar, (Retacrit) (for non-ESRD use), 1000 units (refer to the Medicare Advantage Policy Guideline titled Erythropoietin Stimulating Agent (ESA))

Modifier	Description
EA	Erythropoetic stimulating agent (ESA) administered to treat anemia due to anticancer chemotherapy
EB	Erythropoetic stimulating agent (ESA) administered to treat anemia due to anticancer radiotherapy
EC	Erythropoetic stimulating agent (ESA) administered to treat anemia not due to anticancer radiotherapy or anticancer chemotherapy

References

CMS National Coverage Determinations (NCDs)

[NCD 110.21 Erythropoiesis Stimulating Agents \(ESAs\) in Cancer and Related Neoplastic Conditions](#)

CMS Local Coverage Determinations (LCDs) and Articles

LCD	Article	Contractor	Medicare Part A	Medicare Part B
L34356 Erythropoiesis Stimulating Agents ESA	A56462 Billing and Coding: Erythropoiesis Stimulating Agents ESA	CGS	KY, OH	KY, OH
L36276 Erythropoiesis Stimulating Agents	A57628 Billing and Coding: Erythropoiesis Stimulating Agents	First Coast	FL, PR, VI	FL, PR, VI
L34633 Erythropoiesis Stimulating Agents	A56795 Billing and Coding: Erythropoiesis Stimulating Agents ESAs	WPS	AK, AL, AR, AZ, CO, CT, DE, FL, GA, HI, IA, ID, IL, IN, KS, KY, LA, MA, MD, ME, MI, MO, MS, MT, NC, ND, NE, NH, NJ, NM, NV, OH, OK, OR, PA, RI, SC, SD, TN, TX, UT, VA, VT, WA, WI, WV, WY	IA, KS, MO, NE, IN, MI

CMS Benefit Policy Manual

[Chapter 1 Inpatient Hospital Services Covered Under Part A](#)

[Chapter 6: § 30 Drugs and Biologicals](#)

[Chapter 15: § 50 Drugs and Biologicals](#)

CMS Claims Processing Manual

[Chapter 17: § 80.9 Required Modifiers for ESAs Administered to Non-ESRD Patients, § 80.12 Claims Processing Rules for ESAs Administered to Cancer Patients](#)

CMS Transmittal(s)

[Transmittal 2202, Change Request 11005, dated 11/09/2018 \(International Classification of Diseases, 10th Revision \(ICD-10\) and Other Coding Revisions to National Coverage Determination \(NCDs\)\)](#)

[Transmittal 2243, Change Request 11134, dated 02/01/2019 \(International Classification of Diseases, 10th Revision \(ICD-10\) and Other Coding Revisions to National Coverage Determination \(NCDs\)\)](#)

[Transmittal 4048, Change Request 10624, dated 06/26/2018 \(Quarterly Healthcare Common Procedure Coding System \(HCPCS\) Drug/Biological Code Changes - July 2018 Update\)](#)

[Transmittal 10432, Change Request 12027, dated 10/01/2020 \(International Classification of Diseases, 10th Revision \(ICD-10\) and Other Coding Revisions to National Coverage Determination \(NCDs\)–April 2021\)](#)

MLN Matters

[Article MM5818, Erythropoiesis Stimulating Agents \(ESAs\) in Cancer and Related Neoplastic Conditions](#)

[Article MM10624, Quarterly Healthcare Common Procedure Coding System \(HCPCS\) Drug/Biological Code Changes – July 2018 Update](#)

[Article MM11005, International Classification of Diseases, 10th Revision \(ICD-10\) and Other Coding Revisions to National Coverage Determinations \(NCDs\), April 1, 2019](#)

[Article MM11134, International Classification of Diseases, 10th Revision \(ICD-10\) and Other Coding Revisions to National Coverage Determination \(NCDs\), July 1, 2019](#)

[Article MM12027, International Classification of Diseases, 10th Revision \(ICD-10\) and Other Coding Revisions to National Coverage Determination \(NCDs\)–April 2021](#)

UnitedHealthcare Commercial Policy

[Erythropoiesis-Stimulating Agents](#)

Other(s)

[CMS Medicare Part B ASP Drug Pricing Files](#)

[FDA label for Retacrit \(epoetin alfa-epbx\) injection](#)

[Medicare Prescription Drug Benefit Manual, Chapter 6, Appendix C - Medicare Part B versus Part D Coverage Issues](#)

[UnitedHealthcare Medicare Advantage Medical Benefit Injectable Policy: Medicare Part B Step Therapy Programs](#)

Guideline History/Revision Information

Revisions to this summary document do not in any way modify the requirement that services be provided and documented in accordance with the Medicare guidelines in effect on the date of service in question.

Date	Summary of Changes
04/01/2021	Template Update <ul style="list-style-type: none">Reformatted policy; transferred content to new template
11/11/2020	Applicable Codes <i>HCPCS Codes</i> <ul style="list-style-type: none">Added reference link to the Medicare Advantage Policy Guideline titled <i>Erythropoietin Stimulating Agent (ESA)</i> for HCPCS codes J0881, J0885, and Q5106 Modifiers <ul style="list-style-type: none">Revised description for Modifier codes EA, EB, and EC Supporting Information <ul style="list-style-type: none">Updated <i>References</i> section to reflect the most current informationArchived previous policy version MPG102.05

Purpose

The Medicare Advantage Policy Guideline documents are generally used to support UnitedHealthcare Medicare Advantage claims processing activities and facilitate providers' submission of accurate claims for the specified services. The document can be used as a guide to help determine applicable:

- Medicare coding or billing requirements, and/or
- Medical necessity coverage guidelines; including documentation requirements.

UnitedHealthcare follows Medicare guidelines such as NCDs, LCDs, LGAs, and other Medicare manuals for the purposes of determining coverage. It is expected providers retain or have access to appropriate documentation when requested to support coverage. Please utilize the links in the [References](#) section below to view the Medicare source materials used to develop this resource document. This document is not a replacement for the Medicare source materials that outline Medicare coverage requirements. Where there is a conflict between this document and Medicare source materials, the Medicare source materials will apply.

Terms and Conditions

The Medicare Advantage Policy Guidelines are applicable to UnitedHealthcare Medicare Advantage Plans offered by UnitedHealthcare and its affiliates.

These Policy Guidelines are provided for informational purposes, and do not constitute medical advice. Treating physicians and healthcare providers are solely responsible for determining what care to provide to their patients. Members should always consult their physician before making any decisions about medical care.

Benefit coverage for health services is determined by the member specific benefit plan document* and applicable laws that may require coverage for a specific service. The member specific benefit plan document identifies which services are covered, which are excluded, and which are subject to limitations. In the event of a conflict, the member specific benefit plan document supersedes the Medicare Advantage Policy Guidelines.

Medicare Advantage Policy Guidelines are developed as needed, are regularly reviewed and updated, and are subject to change. They represent a portion of the resources used to support UnitedHealthcare coverage decision making. UnitedHealthcare may modify these Policy Guidelines at any time by publishing a new version of the policy on this website. Medicare source materials used to develop these guidelines include, but are not limited to, CMS National Coverage Determinations (NCDs), Local Coverage Determinations (LCDs), Medicare Benefit Policy Manual, Medicare Claims Processing Manual, Medicare Program Integrity Manual, Medicare Managed Care Manual, etc. The information presented in the Medicare Advantage Policy Guidelines is believed to be accurate and current as of the date of publication and is provided on an "AS IS" basis. Where there is a conflict between this document and Medicare source materials, the Medicare source materials will apply.

You are responsible for submission of accurate claims. Medicare Advantage Policy Guidelines are intended to ensure that coverage decisions are made accurately based on the code or codes that correctly describe the health care services provided. UnitedHealthcare Medicare Advantage Policy Guidelines use Current Procedural Terminology (CPT®), Centers for Medicare and Medicaid Services (CMS), or other coding guidelines. References to CPT® or other sources are for definitional purposes only and do not imply any right to reimbursement or guarantee claims payment.

Medicare Advantage Policy Guidelines are the property of UnitedHealthcare. Unauthorized copying, use, and distribution of this information are strictly prohibited.

*For more information on a specific member's benefit coverage, please call the customer service number on the back of the member ID card or refer to the [Administrative Guide](#).