



Medicare Coverage Database	NCD for Erythropoiesis Stimulating Agents(ESAs) in Cancer and Related Neoplastic Conditions (110.21)
<ul style="list-style-type: none"> Overview Search Indexes Reports Downloads Basket MCD Help 	<p>Publication Number</p> <p>100-3</p> <p>Manual Section Number</p> <p>110.21</p> <p>Version Number</p> <p>1</p> <p>Effective Date of this Version</p> <p>7/30/2007</p> <p>Implementation Date</p> <p>4/7/2008</p> <p>Benefit Category</p> <p>Drugs and Biologicals</p> <p>Note: This may not be an exhaustive list of all applicable Medicare benefit categories for this item or service.</p> <p>Item/Service Description</p> <p>A. General</p> <p>The 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.</p> <p>Indications and Limitations of Coverage</p>

B. Nationally Covered Indications

The 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 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.

C. Nationally Non-Covered Indications

The 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.

D. Other

Local Medicare contractors may continue to make reasonable and necessary

determinations on all other uses of ESAs not specified in this NCD.

See the Medicare Benefit Policy Manual, chapter 11, section 90 and chapter 15, section 50.5.2 for coverage of ESAs for end-stage renal disease related anemia.

(This NCD last reviewed July 2007.)

Transmittal Number

80

Transmittal Link

<http://www.cms.hhs.gov/transmittals/downloads/R80NCD.pdf>

Revision History

01/2008 - CMS has determined that ESA treatment is reasonable and necessary for anemia secondary to myelosuppressive anticancer chemotherapy in solid tumors, multiple myeloma, lymphoma and lymphocytic leukemia under specified conditions. CMS has also determined that 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. Effective date: 07/30/2007 ([TN 80](#)) Implementation date: 04/07/2008. (CR5818)

Claims Processing Instructions

- [TN 1413 \(Medicare Claims Processing\)](#)

National Coverage Analyses (NCAs)

This NCD has been or is currently being reviewed under the National Coverage Determination process. The following are existing associations with NCAs, from the National Coverage Analyses database.

- [Original consideration for Erythropoiesis Stimulating Agents \(ESAs\) for non-renal disease indications \(CAG-00383N\)](#)

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News Flash - Test Your Medicare Claims Now! After you have submitted claims containing both National Provider Identifiers (NPIs) and legacy identifiers and those claims have been paid, Medicare urges you to send a small batch of claims now with only the NPI in the primary provider fields. If the results are positive, begin increasing the number of claims in the batch. (Reminder: For institutional claims, the primary provider fields are the Billing and Pay-to Provider fields. For professional claims, the primary provider fields are the Billing, Pay-to, and Rendering Provider fields. If the Pay-to Provider is the same as the Billing Provider, the Pay-to Provider does not need to be identified.)

MLN Matters Number: MM5818 **Revised**

Related Change Request (CR) #: 5818

Related CR Release Date: January 14, 2008

Effective Date: July 30, 2007

Related CR Transmittal #: R80NCD and R1413CP

Implementation Date: April 7, 2008

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

Note: This article was April 25, 2008, to correct the bullet on page 3 regarding the "Maintenance of ESA therapy" (See bullet in **bold**). It should have stated that 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%)." All other information remains the same.

Provider Types Affected

Providers and suppliers who bill Medicare contractors (carriers, fiscal intermediaries (FI), Regional Home Health Intermediaries (RHHI), Medicare Administrative Contractors (A/B MAC) and Durable Medical Equipment Medicare Administrative Contractors (DME MAC)) for administering or supplying Erythropoiesis Stimulating Agents (ESAs) for cancer and related neoplastic conditions to Medicare beneficiaries.

What You Need to Know

Following a National Coverage Analysis (NCA) to evaluate the uses ESAs in non-renal disease applications, the Centers for Medicare & Medicaid Services (CMS), on July 30, 2007, issued a Decision Memorandum (DM) that addressed ESA use

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in non-renal disease applications (specifically in cancer and other neoplastic conditions).

CR 5818 communicates the NCA findings and the coverage policy in the National Coverage Determination (NCD). Specifically, CMS determines that ESA treatment is reasonable and necessary for anemia secondary to myelosuppressive anticancer chemotherapy in solid tumors, multiple myeloma, lymphoma, and lymphocytic leukemia under specified conditions; and not reasonable and necessary for beneficiaries with certain other clinical conditions, as listed below.

The HCPCS codes specific to non-end-stage renal disease (ESRD) ESA use are J0881 and J0885. Claims processed with dates of service July 30, 2007, through December 31, 2007, do not have to include the ESA modifiers as the modifiers are not effective until January 1, 2008. However, providers are to begin using the modifiers as of January 1, 2008, even though full implementation of related system edits are not effective until April 7, 2008.

Make sure that your billing staffs are aware of this guidance regarding ESA use.

Background

Emerging safety concerns (thrombosis, cardiovascular events, tumor progression, and reduced survival) derived from clinical trials in several cancer and non-cancer populations prompted CMS to review its coverage of ESAs. In so doing, on March 14, 2007, CMS opened an NCA to evaluate the uses of ESAs in non-renal disease applications, and on July 30, 2007, issued a DM specifically narrowed to the use of ESAs in cancer and other neoplastic conditions.

Reasonable and Necessary ESA Use

CMS has determined that ESA treatment for the anemia secondary to a regimen of myelosuppressive anticancer chemotherapy in solid tumors, multiple myeloma, lymphoma, and lymphocytic leukemia is reasonable and necessary only under the following specified conditions:

- The hemoglobin level immediately prior to the first administration is < 10 g/dL (or the hematocrit is < 30%) and the hemoglobin level prior to any maintenance administration is < 10g/dL (or the hematocrit is < 30%);
- The starting dose for ESA treatment is up to either of the recommended Food and Drug Administration (FDA) approved label starting doses for cancer patients receiving chemotherapy, which includes the 150 U/kg/3 times weekly or the 40,000 U weekly doses for epoetin alfa and the 2.25 mcg/kg/weekly or the 500 mcg once every three week dose for darbepoetin alpha;

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- **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 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 any 2 week period 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; and
- ESA treatment duration for each course of chemotherapy includes the 8 weeks following the final dose of myelosuppressive chemotherapy in a chemotherapy regimen.

Not Reasonable and Necessary ESA Use

Either because of a deleterious effect of ESAs on the underlying disease, or because the underlying disease increases the risk of adverse effects related to ESA use, CMS has also determined that ESA treatment is not reasonable and necessary for beneficiaries with the following clinical conditions:

- Any anemia in cancer or cancer treatment patients due to folate deficiency (diagnosis code 281.2), B-12 deficiency (281.1 or 281.3), iron deficiency (280.0-280.9), hemolysis (282.0, 282.2, 282.9, 283.0, 283.2, 283.9, 283.10, 283.19), bleeding (280.0 or 285.1), or bone marrow fibrosis;
- Anemia associated with the treatment of acute and chronic myelogenous leukemias (CML, AML) (205.00-205.21, 205.80-205.91), or erythroid cancers (207.00-207.81);
- 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;

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- Erythropoietin-type resistance due to neutralizing antibodies; and
- Anemia due to cancer treatment if patients have uncontrolled hypertension.

Claims Processing

Effective for claims with dates of service on or after January 1, 2008, Medicare will deny non-ESRD ESA services for J0881 or J0885 when:

- Billed with modifier EC (ESA, anemia, non-chemo/radio) when a diagnosis on the claim is present for any anemia in cancer or cancer treatment patients due to folate deficiency (diagnosis code 281.2), B-12 deficiency (281.1 or 281.3), iron deficiency (280.0-280.9), hemolysis (282.0, 282.2, 282.9, 283.0, 283.2, 283.9, 283.10, 283.19), bleeding (280.0 or 285.1), anemia associated with the treatment of acute and chronic myelogenous leukemias (CML, AML) (205.00-205.21, 205.80-205.91), or erythroid cancers (207.00-207.81).
- Billed with modifier EC for any anemia in cancer or cancer treatment patients due to bone marrow fibrosis, anemia of cancer not related to cancer treatment, prophylactic use to prevent cancer-induced anemia, prophylactic use to reduce tumor hypoxia, erythropoietin-type resistance due to neutralizing antibodies, and anemia due to cancer treatment if patients have uncontrolled hypertension.
- Billed with modifier EA (ESA, anemia, chemo-induced) for anemia secondary to myelosuppressive anticancer chemotherapy in solid tumors, multiple myeloma, lymphoma, and lymphocytic leukemia when a hemoglobin 10.0g/dL or greater or hematocrit 30.0% or greater is reported.
- Billed with modifier EB (ESA, anemia, radio-induced).

Note: Denial of claims for non-ESRD ESAs for cancer and related neoplastic indications as outlined in NCD 110.21 are based on reasonable and necessary determinations. A provider may have the beneficiary sign an Advance Beneficiary Notice (ABN), making the beneficiary liable for services not covered by Medicare. When denying ESA claims, contractors will use Medicare Summary Notice 15.20, *The following policies [NCD 110.21] were used when we made this decision*, and remittance reason code 50, *These are non-covered services because this is not deemed a 'medical necessity' by the payer*. However, standard systems shall assign liability for the denied charges to the provider unless documentation of the ABN is present on the claim. Denials are subject to appeal and standard

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systems shall allow for medical review override of denials. Contractors may reverse the denial if the review results in a determination of clinical necessity.

Medicare contractors have discretion to establish local coverage policies for those indications not included in NCD 110.21

Medicare contractors will not search files to retract payment for claims paid prior to April 7, 2008. However, contractors shall adjust claims brought to their attention.

Additional Information

If you have any questions, please contact your Medicare contractor at their toll-free number, which may be found at

<http://www.cms.hhs.gov/MLNProducts/downloads/CallCenterTollNumDirectory.zip> on the CMS website.

This addition/revision of section 110.21 of Pub.100-03 is an NCD. NCDs are binding on all carriers, FIs, quality improvement organizations, qualified independent contractors, the Medicare Appeals Council, and administrative law judges (ALJs) (see 42 CFR section 405.1060(a)(4) (2005)). An NCD that expands coverage is also binding on a Medicare advantage organization. In addition, an ALJ may not review an NCD. (See section 1869(f)(1)(A)(i) of the Social Security Act.)

The official instruction, CR5818, was issued to your contractor in two transmittals. The first is the NCD transmittal and that is available at

<http://www.cms.hhs.gov/Transmittals/downloads/R80NCD.pdf> on the CMS website. The second transmittal revises the Medicare Claims Processing Manual and it is at <http://www.cms.hhs.gov/Transmittals/downloads/R1413CP.pdf> on the same site.

News Flash - It's Not Too Late to Get the Flu Shot. We are in the midst of flu season and a flu vaccine is still the best way to prevent infection and the complications associated with the flu. But re-vaccination is necessary each year because flu viruses change each year. Please encourage your Medicare patients who haven't already done so to get their annual flu shot. – And don't forget to immunize yourself and your staff. Protect yourself, your patients, and your family and friends. Get Your Flu Shot – Not the Flu! Remember - Influenza vaccination is a covered Part B benefit. Note that influenza vaccine is NOT a Part D covered drug. Health care professionals and their staff can learn more about Medicare's coverage of adult immunizations and related provider education resources, by reviewing Special Edition MLN Matters article SE0748 at <http://www.cms.hhs.gov/MLNMattersArticles/downloads/SE0748.pdf> on the CMS website.

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