CMS Manual System	Department of Health & Human Services (DHHS)
Pub 100-03 Medicare National Coverage Determinations	Centers for Medicare & Medicaid Services (CMS)
Transmittal 80	Date: JANUARY 14, 2008
	Change Request 5818

NOTE: Transmittal 80 dated, January 14, 2008, is being reissued because of a typographical error that is being corrected to align with the language both in the corresponding final decision memo and the MedLearn Matters Article. The 3rd bullet under B in the NCD Manual should read as follows: 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 ≥ 1g/dL (hematocrit ≥ 3%). The transmittal number, dates and all other information remains the same.

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

I. SUMMARY OF CHANGES: 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.

This addition/revision of section 110.21 of Pub.100-03 is a national coverage determination (NCD). NCDs are binding on all carriers, fiscal intermediaries, 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.)

NEW / REVISED MATERIAL
EFFECTIVE DATE: JULY 30, 2007
Modifiers: January 1, 2008
IMPLEMENTATION DATE: APRIL 7, 2008

Disclaimer for manual changes only: The revision date and transmittal number apply only to red italicized material. Any other material was previously published and remains unchanged. However, if this revision contains a table of contents, you will receive the new/revised information only, and not the entire table of contents.

II. CHANGES IN MANUAL INSTRUCTIONS: (N/A if manual is not updated)
R=REVISED, N=NEW, D=DELETED

R/N/D	CHAPTER / SECTION / SUBSECTION / TITLE
R	1/Table of Contents
N	1/110.21/Erythropoiesis Stimulating Agents (ESAs) in Cancer and Related Neoplastic Conditions

III. FUNDING:

SECTION A: For Fiscal Intermediaries and Carriers:
No additional funding will be provided by CMS; contractor activities are to be carried out within their operating budgets.

SECTION B: For Medicare Administrative Contractors (MACs):
The Medicare administrative contractor is hereby advised that this constitutes technical direction as defined in your contract. CMS does not construe this as a change to the MAC Statement of Work. The contractor is not obligated to incur costs in excess of the amounts allotted in your contract unless and until specifically authorized by the contracting officer. If the contractor considers anything provided, as described above, to be outside the current scope of work, the contractor shall withhold performance on the part(s) in question and immediately notify the contracting officer, in writing or by e-mail, and request formal directions regarding continued performance requirements.

IV. ATTACHMENTS:

Business Requirements
Manual Instruction

Unless otherwise specified, the effective date is the date of service.

Attachment – Business Requirements

Pub. 100-03	Transmittal: 80	Date: January 14, 2008	Change Request: 5818

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

Effective Date: NCD: July 30, 2007
Modifiers: January 1, 2008
Implementation Date: April 7, 2008

I. GENERAL INFORMATION

A. Background: The United States Food and Drug Administration (FDA) recently issued alerts and warnings for ESAs administered for a number of clinical conditions, including cancer and renal disease. Recently published studies report a higher risk of serious and life-threatening events associated with the use of ESAs in various clinical applications. As a result, on March 14, 2007, CMS opened a National Coverage Analysis (NCA) to evaluate the uses of ESAs in non-renal disease applications. On July 30, 2007, CMS issued a Decision Memorandum for the uses of ESAs in non-renal disease applications, specifically narrowed to the use of ESAs in cancer and other neoplastic conditions. This change request (CR) communicates the findings resulting from the NCA and the coverage policy listed in the National Coverage Determination (NCD).

In addition, the Tax Relief and Health Care Act of 2006 requires providers to report a recent hemoglobin or hematocrit level on claims for anti-anemia drugs administered in connection with the treatment of cancer beginning January 1, 2008. To implement this requirement, CMS issued CR 5699, transmittal 1412, dated January 11, 2008, that instructs providers to report a hematocrit or hemoglobin for all non-ESRD anti-anemia claims, inclusive of ESAs. CR 5699 instructs providers to report one of three modifiers (EA, EB or EC). The definitions of the modifiers are: EA: ESA, anemia, chemo-induced; EB: ESA, anemia, radio-induced and EC: ESA, anemia, non-chemo/radio. Refer to CR 5699 for further reporting requirement details.

B. NCD Policy: The Centers for Medicare & Medicaid Services (CMS) reviewed the evidence and determined that ESA treatment is reasonable and necessary under §1862(a)(1)(A) of the Social Security Act for anemia secondary to myelosuppressive anticancer chemotherapy in solid tumors, multiple myeloma, lymphoma, and lymphocytic leukemia under specified conditions. 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. The complete NCD can be accessed at section 110.21 of Publication (Pub.) 100-03, NCD Manual, and claims processing instructions can be accessed at Pub. 100-04, Claims Processing Manual, chapter 17, sections 80.8-80.12. The HCPCS codes specific to non-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 they are not effective until January 1, 2008.

II. BUSINESS REQUIREMENTS TABLE

Use"Shall" to denote a mandatory requirement

Number	Requirement	Responsibility (place an "X" in each applicable column)									
		A/B MAC	DME MAC	FI	CARRIER	RHHI	Shared-System Maintainers				OTHER
							FISS	MCS	VMS	CWF	
5818.1	Effective with dates of service on and after July 30, 2007, contractors shall process claims for covered and non-covered indications as specified in Pub.100-03, section 110.21.B. and Pub. 100-04, chapter 17, sections 80.8-80.12. See Pub. 100-04 accompanying business requirements for further information.	X		X	X	X					

III. PROVIDER EDUCATION TABLE

Number	Requirement	Responsibility (place an "X" in each applicable column)									
		A/B MAC	DME MAC	FI	CARRIER	RHHI	Shared-System Maintainers				OTHER
							FISS	MCS	VMS	CWF	
5818.2	A provider education article related to this instruction will be available at http://www.cms.hhs.gov/MLNMattersArticles shortly after the CR is released. You will receive notification of the article release via the established "MLN Matters" listserv. Contractors shall post this article, or a direct link to this article, on their Web site and include information about it in a listserv message within one week of the availability of the provider education article. In addition, the provider education article shall be included in your next regularly scheduled bulletin. Contractors are free to supplement MLN Matters articles with localized information that would benefit their provider community in billing and administering the Medicare program correctly.	X		X	X	X					

IV. SUPPORTING INFORMATION

A. For any recommendations and supporting information associated with listed requirements, use the box below:

Use "Should" to denote a recommendation.

X-Ref Requirement Number	Recommendations or other supporting information:

B. For all other recommendations and supporting information, use this space:

V. CONTACTS

Pre-Implementation Contact(s):
National Coverage Determination: Maria Ciccanti, maria.ciccanti@cms.hhs.gov, 410-786-3107 or
Kim Long, kimberly.long@cms.hhs.gov, 410-786-5702
Institutional Claims Processing: Sherry Murray, sherry.murray@cms.hhs.gov, 410-786-6145
Practitioner Claims Processing: Melvia Page-Lasowski, melvia.pagelasowski@cms.hhs.gov, 410-786-4727

Post-Implementation Contact(s): Appropriate RO

VI. FUNDING

A. ***For Fiscal Intermediaries, Carriers, and the Durable Medical Equipment Regional Carrier (DMERC):***
No additional funding will be provided by CMS; contractor activities are to be carried out within their operating budgets.

B. ***For Medicare Administrative Contractors (MACs):***
The contractor is hereby advised that this constitutes technical direction as defined in your contract. CMS does not construe this as a change to the Statement of Work (SOW). The contractor is not obligated to incur costs in excess of the amounts allotted in your contract unless and until specifically authorized by the contracting officer. If the contractor considers anything provided, as described above, to be outside the current scope of work, the contractor shall withhold performance on the part(s) in question and immediately notify the contracting officer, in writing or by e-mail, and request formal directions regarding continued performance requirements.

Medicare National Coverage Determinations Manual

Chapter 1, Part 2 (Sections 90 – 160.26)

Coverage Determinations

Table of Contents

(Rev. 80, 01-14-08)

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

(Rev. 80; Issued: 01-14-08; Effective: 07-30-07; Implementation: 04-07-08)

A. General

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.

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 reinstitution 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.)