

CMS Manual System	Department of Health & Human Services (DHHS)
Pub 100-03 Medicare National Coverage Determinations	Centers for Medicare & Medicaid Services (CMS)
Transmittal 127	Date: October 8, 2010
	Change Request 7137

SUBJECT: Allogeneic Hematopoietic Stem Cell Transplantation (HSCT) for Myelodysplastic Syndrome (MDS)

I. SUMMARY OF CHANGES: Effective for claims with dates of service on and after August 4, 2010, contractors shall be aware that the use of allogeneic HSCT for treatment of MDS is only covered by Medicare if provided in the context of a Medicare-approved clinical study meeting specific criteria under the CED paradigm.

This revision [to the Medicare National Coverage Determinations Manual] is a national coverage determination (NCD). NCDs are binding on all carriers, fiscal intermediaries, [contractors with the Federal government that review and/or adjudicate claims, determinations, and/or decisions], 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.)

EFFECTIVE DATE: AUGUST 4, 2010
IMPLEMENTATION DATE: November 10, 2010

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	1/110.8.1/Stem Cell Transplantation (Various Effective Dates Below)

III. FUNDING:

For Fiscal Intermediaries (FIs), Regional Home Health Intermediaries (RHHIs) and/or Carriers:
 No additional funding will be provided by CMS; contractor activities are to be carried out within their operating budgets.

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: 127	Date: October 8, 2010	Change Request: 7137
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SUBJECT: Allogeneic Hematopoietic Stem Cell Transplantation (HSCT) for Myelodysplastic Syndrome (MDS)

EFFECTIVE DATE: AUGUST 4, 2010

IMPLEMENTATION DATE: November 10, 2010

I. GENERAL INFORMATION

A. Background: Myelodysplastic Syndrome (MDS) refers to a group of diverse blood disorders in which the bone marrow does not produce enough healthy, functioning blood cells. These disorders are varied with regard to clinical characteristics, cytologic and pathologic features, and cytogenetics. On November 10, 2009, the Centers for Medicare & Medicaid Services (CMS) accepted a formal request from several bone marrow and cancer organizations and societies. The requestors asked for national coverage of allogeneic hematopoietic stem cell transplantation (HSCT) for Medicare beneficiaries "who would either be at high risk for progression to leukemia or be at risk for MDS complications that place them at high risk for death or prevent the future possibility of a transplant."

B. Policy: On August 4, 2010, CMS issued a final decision stating that it believes the evidence does not demonstrate that the use of allogeneic HSCT improves health outcomes in Medicare beneficiaries with MDS. Therefore, allogeneic HSCT for MDS is not reasonable and necessary under §1862(a)(1)(A) of the Social Security Act (the Act). However, allogeneic HSCT for MDS is reasonable and necessary under §1862(a)(1)(E) of the Act and therefore covered by Medicare ONLY if provided pursuant to a Medicare-approved clinical study under Coverage with Evidence Development (CED).

Refer to Pub. 100-04, chapter 32, section 69, on information regarding CEDs. In addition, there are additional billing requirements specific to this NCD in the below business requirements.

II. BUSINESS REQUIREMENTS TABLE

Number	Requirement	Responsibility (place an "X" in each applicable column)								
		A / B M A C	D M E M A C	F I	C A R R I E R	R H I	Shared-System Maintainers			
						F I S S	M C S	V M S	C W F	
7137-03.1	Effective for claims with dates of service on and after August 4, 2010, contractors shall be aware that the use of allogeneic HSCT for treatment of MDS is only covered by Medicare if provided in the context of a Medicare-approved clinical study meeting specific criteria under the CED paradigm. See Pub. 100-03, chapter 1, section 110.8.1, of the NCD Manual, and Pub. 100-04, chapter 32, section 90.6 and chapter 3, section 90.3.1, of the Claims Processing Manual, for	X		X	X					

Number	Requirement	Responsibility (place an "X" in each applicable column)									
		A / B M A C	D M E M A C	F I	C A R R I E R	R H H I	Shared-System Maintainers				OTHER
							F I S S	M C S	V M S	C W F	
	further information.										

III. PROVIDER EDUCATION TABLE

Number	Requirement	Responsibility (place an "X" in each applicable column)									
		A / B M A C	D M E M A C	F I	C A R R I E R	R H H I	Shared-System Maintainers				OTHER
							F I S S	M C S	V M S	C W F	
7137-03.2	<p>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.</p> <p>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.</p>	X		X	X						

IV. SUPPORTING INFORMATION: N/A

V. CONTACTS

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Post-Implementation Contact(s): Appropriate regional office

VI. FUNDING

A. For *Fiscal Intermediaries (FIs)*, *Regional Home Health Intermediaries (RHHIs)*, and/or *Carriers*:

Section A: 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)*:

Section B: 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.

110.8.1 - Stem Cell Transplantation (Various Effective Dates Below)

(Rev. 127, Issued: 10-08-10, Effective: 08-04-10, Implementation: 11-10-10)

A. General

Stem cell transplantation is a process in which stem cells are harvested from either a patient's (*autologous*) or donor's (*allogeneic*) bone marrow or peripheral blood for intravenous infusion. Autologous stem cell transplants (AuSCT) must be used to effect hematopoietic reconstitution following severely myelotoxic doses of chemotherapy (HDCT) and/or radiotherapy used to treat various malignancies. Allogeneic stem cell transplants may be used to restore function in recipients having an inherited or acquired deficiency or defect. *Hematopoietic stem cells are multi-potent stem cells that give rise to all the blood cell types; these stem cells form blood and immune cells. A hematopoietic stem cell is a cell isolated from blood or bone marrow that can renew itself, differentiate to a variety of specialized cells, can mobilize out of the bone marrow into circulating blood, and can undergo programmed cell death, called apoptosis - a process by which cells that are unneeded or detrimental self destruct.*

The Centers for Medicare & Medicaid Services (CMS) is clarifying that bone marrow and peripheral blood stem cell transplantation is a process which includes mobilization, harvesting, and transplant of bone marrow or peripheral blood stem cells and the administration of high dose chemotherapy or radiotherapy prior to the actual transplant. When bone marrow or peripheral blood stem cell transplantation is covered, all necessary steps are included in coverage. When bone marrow or peripheral blood stem cell transplantation is non-covered, none of the steps are covered.

1. Allogeneic *Hematopoietic* Stem Cell Transplantation (*HSCT*)

Allogeneic *hematopoietic* stem cell transplantation (*HSCT*) is a procedure in which a portion of a healthy donor's stem cell or bone marrow is obtained and prepared for intravenous infusion.

a. *Nationally* Covered Indications

The following uses of allogeneic *HSCT* are covered under Medicare:

- i.* Effective for services performed on or after August 1, 1978, for the treatment of leukemia, leukemia in remission, or aplastic anemia when it is reasonable and necessary,
- ii.* Effective for services performed on or after June 3, 1985, for the treatment of severe combined immunodeficiency disease (SCID) and for the treatment of Wiskott-Aldrich syndrome.
- iii.* *Effective for services performed on or after August 4, 2010, for the treatment of Myelodysplastic Syndromes (MDS) pursuant to Coverage with Evidence Development (CED) in the context of a Medicare-approved, prospective clinical study.*

The MDS refers to a group of diverse blood disorders in which the bone marrow does not produce enough healthy, functioning blood cells. These disorders are varied with regard to clinical characteristics, cytologic and pathologic features, and cytogenetics. The abnormal production of blood cells in the bone marrow leads to low blood cell counts, referred to as cytopenias, which are a hallmark feature of MDS along with a dysplastic and hypercellular-appearing bone marrow.

Medicare payment for these beneficiaries will be restricted to patients enrolled in an approved clinical study. In accordance with the Stem Cell Therapeutic and Research Act of 2005 (US Public Law 109-129) a standard dataset is collected for all allogeneic transplant patients in the United States by the Center for International Blood and Marrow Transplant Research. The elements in this dataset, comprised of two mandatory forms plus one additional form, encompass the information we require for a study under CED.

A prospective clinical study seeking Medicare payment for treating a beneficiary with allogeneic HSCT for MDS pursuant to CED must meet one or more aspects of the following questions:

- *Prospectively, compared to Medicare beneficiaries with MDS who do not receive HSCT, do Medicare beneficiaries with MDS who receive HSCT have improved outcomes as indicated by:
 - *Relapse-free mortality,*
 - *progression free survival,*
 - *relapse, and*
 - *overall survival?**

- *Prospectively, in Medicare beneficiaries with MDS who receive HSCT, how do International Prognostic Scoring System (IPSS) score, patient age, cytopenias and comorbidities predict the following outcomes:
 - *Relapse-free mortality,*
 - *progression free survival,*
 - *relapse, and*
 - *overall survival?**

- *Prospectively, in Medicare beneficiaries with MDS who receive HSCT, what treatment facility characteristics predict meaningful clinical improvement in the following outcomes:
 - *Relapse-free mortality,*
 - *progression free survival,*
 - *relapse, and*
 - *overall survival?**

In addition, the clinical study must adhere to the following standards of scientific integrity and relevance to the Medicare population:

- a. *The principal purpose of the research study is to test whether a particular intervention potentially improves the participants' health outcomes.*
- b. *The research study is well supported by available scientific and medical information or it is intended to clarify or establish the health outcomes of interventions already in common clinical use.*
- c. *The research study does not unjustifiably duplicate existing studies.*
- d. *The research study design is appropriate to answer the research question being asked in the study.*
- e. *The research study is sponsored by an organization or individual capable of executing the proposed study successfully.*
- f. *The research study is in compliance with all applicable Federal regulations concerning the protection of human subjects found at 45 CFR Part 46.*
- g. *All aspects of the research study are conducted according to appropriate standards of scientific integrity (see <http://www.icmje.org>).*
- h. *The research study has a written protocol that clearly addresses, or incorporates by reference, the standards listed here as Medicare requirements for CED coverage.*
- i. *The clinical research study is not designed to exclusively test toxicity or disease pathophysiology in healthy individuals. Trials of all medical technologies measuring therapeutic outcomes as one of the objectives meet this standard only if the disease or condition being studied is life threatening as defined in 21 CFR §312.81(a) and the patient has no other viable treatment options.*
- j. *The clinical research study is registered on the ClinicalTrials.gov Web site by the principal sponsor/investigator prior to the enrollment of the first study subject.*
- k. *The research study protocol specifies the method and timing of public release of all pre-specified outcomes to be measured including release of outcomes if outcomes are negative or study is terminated early. The results must be made public within 24 months of the end of data collection. If a report is planned to be published in a peer-reviewed journal, then that initial release may be an abstract that meets the requirements of the International Committee of Medical Journal Editors (<http://www.icmje.org>). However a full report of the outcomes must be made public no later than 3 years after the end of data collection.*
- l. *The research study protocol must explicitly discuss subpopulations affected by the treatment under investigation, particularly traditionally underrepresented groups in clinical studies, how the inclusion and exclusion criteria effect enrollment of these populations, and a plan for the retention and reporting of said populations on the trial. If the inclusion and exclusion*

criteria are expected to have a negative effect on the recruitment or retention of underrepresented populations, the protocol must discuss why these criteria are necessary.

- m. The research study protocol explicitly discusses how the results are or are not expected to be generalizable to the Medicare population to infer whether Medicare patients may benefit from the intervention. Separate discussions in the protocol may be necessary for populations eligible for Medicare due to age, disability or Medicaid eligibility.*

Consistent with section 1142 of the Social Security Act, the Agency for Health Research and Quality (AHRQ) supports clinical research studies that CMS determines meet the above-listed standards and address the above-listed research questions.

The clinical research study should also have the following features:

- It should be a prospective, longitudinal study with clinical information from the period before HSCT and short- and long-term follow-up information.*
- Outcomes should be measured and compared among pre-specified subgroups within the cohort.*
- The study should be powered to make inferences in subgroup analyses.*
- Risk stratification methods should be used to control for selection bias. Data elements to be used in risk stratification models should include:*

Patient selection:

- Patient Age at diagnosis of MDS and at transplantation*
- Date of onset of MDS*
- Disease classification (specific MDS subtype at diagnosis prior to preparative/conditioning regimen using World Health Organization (WHO) classifications). Include presence/absence of refractory cytopenias*
- Comorbid conditions*
- IPSS score (and WHO-adapted Prognostic Scoring System (WPSS) score, if applicable) at diagnosis and prior to transplantation*
- Score immediately prior to transplantation and one year post-transplantation*
- Disease assessment at diagnosis at start of preparative regimen and last assessment prior to preparative regimen Subtype of MDS (refractory anemia with or without blasts, degree of blasts, etc.)*

- *Type of preparative/conditioning regimen administered (myeloablative, non-myeloablative, reduced-intensity conditioning)*
 - *Donor type*
 - *Cell Source*
 - *IPSS Score at diagnosis*
- Facilities must submit the required transplant essential data to the Stem Cell Therapeutics Outcomes Database.*

b. *Nationally* Non-Covered Indications

Effective for services performed on or after May 24, 1996, allogeneic HSCT is not covered as treatment for multiple myeloma.

2. Autologous Stem Cell Transplantation (AuSCT)

Autologous stem cell transplantation (AuSCT) is a technique for restoring stem cells using the patient's own previously stored cells.

a. *Nationally* Covered Indications

- i. Effective for services performed on or after April 28, 1989, AuSCT is considered reasonable and necessary under §1862(a)(1)(A) of the Social Security Act (the Act) for the following conditions and is covered under Medicare for patients with:
 - Acute leukemia in remission who have a high probability of relapse and who have no human leucocyte antigens (HLA)-matched;
 - Resistant non-Hodgkin's lymphomas or those presenting with poor prognostic features following an initial response;
 - Recurrent or refractory neuroblastoma; or
 - Advanced Hodgkin's disease who have failed conventional therapy and have no HLA-matched donor.
- ii. Effective October 1, 2000, single AuSCT is only covered for Durie-Salmon Stage II or III patients that fit the following requirements:
 - Newly diagnosed or responsive multiple myeloma. This includes those patients with previously untreated disease, those with at least a partial response to prior chemotherapy (defined as a 50% decrease either in measurable paraprotein [serum and/or urine] or in bone marrow infiltration, sustained for at least 1 month), and those in responsive relapse; and,
 - Adequate cardiac, renal, pulmonary, and hepatic function.

- iii. Effective for services performed on or after March 15, 2005, when recognized clinical risk factors are employed to select patients for transplantation, high dose melphalan (HDM) together with AuSCT is reasonable and necessary for Medicare beneficiaries of any age group with primary amyloid light chain (AL) amyloidosis who meet the following criteria:
- Amyloid deposition in 2 or fewer organs; and,
 - Cardiac left ventricular ejection fraction (EF) greater than 45%.

b. *Nationally* Non-Covered Indications

Insufficient data exist to establish definite conclusions regarding the efficacy of AuSCT for the following conditions:

- Acute leukemia not in remission;
- Chronic granulocytic leukemia;
- Solid tumors (other than neuroblastoma);
- Up to October 1, 2000, multiple myeloma;
- Tandem transplantation (multiple rounds of AuSCT) for patients with multiple myeloma;
- Effective October 1, 2000, non primary AL amyloidosis; and,
- Effective October 1, 2000, thru March 14, 2005, primary AL amyloidosis for Medicare beneficiaries age 64 or older.

In these cases, AuSCT is not considered reasonable and necessary within the meaning of §1862(a)(1)(A) of the Act and is not covered under Medicare.

B. Other

All other indications for stem cell transplantation not otherwise noted above as covered or non-covered nationally remain at local contractor discretion.

(This NCD last reviewed *August 2010*.)