Stem Cell Transplantation (NCD 110.8.1)

IMPORTANT NOTE ABOUT THIS REIMBURSEMENT POLICY

This policy is applicable to UnitedHealthcare Medicare Advantage Plans offered by UnitedHealthcare and its affiliates.

You are responsible for submission of accurate claims. This reimbursement policy is intended to ensure that you are reimbursed based on the code or codes that correctly describe the health care services provided. UnitedHealthcare reimbursement policies 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.

This reimbursement policy applies to all health care services billed on CMS 1500 forms and, when specified, to those billed on UB04 forms (CMS 1450). Coding methodology, industry-standard reimbursement logic, regulatory requirements, benefits design and other factors are considered in developing reimbursement policy. This information is intended to serve only as a general resource regarding UnitedHealthcare’s reimbursement policy for the services described and is not intended to address every aspect of a reimbursement situation. Accordingly, UnitedHealthcare may use reasonable discretion in interpreting and applying this policy to health care services provided in a particular case. Further, the policy does not address all issues related to reimbursement for health care services provided to UnitedHealthcare enrollees. Other factors affecting reimbursement may supplement, modify or, in some cases, supersede this policy. These factors may include, but are not limited to: legislative mandates, the physician or other provider contracts, and/or the enrollee’s benefit coverage documents. Finally, this policy may not be implemented exactly the same way on the different electronic claims processing systems used by UnitedHealthcare due to programming or other constraints; however, UnitedHealthcare strives to minimize these variations.

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Application
This reimbursement policy applies to services reported using the Health Insurance Claim Form CMS-1500 or its electronic equivalent or its successor form, and services reported using facility claim form CMS-1450 or its electronic equivalent or its successor form. This policy applies to all products, all network and non-network physicians, and other health care professionals.

The HCPCS/CPT code(s) may be subject to Correct Coding Initiative (CCI) edits. This policy does not take precedence over CCI edits. Please refer to the CCI for correct coding guidelines and specific applicable code combinations prior to billing UnitedHealthcare. It is not enough to link the procedure code to a correct, payable ICD-9-CM diagnosis code. The diagnosis must be present for the procedure to be paid. Compliance with the provisions in this policy is subject to monitoring by pre-payment review and/or post-payment data analysis and subsequent medical review. The effective date of changes/additions/deletions to this policy is the committee meeting date unless otherwise indicated. CPT codes and descriptions are copyright 2010 American Medical Association (or such other date of publication of CPT). All rights reserved. CPT is a registered trademark of the American Medical Association. Applicable FARS/DFARS restrictions apply to Government use. Fee schedules, relative value units, conversion factors, and/or related components are not assigned by the AMA, are not part of CPT, and the AMA is not recommending their use. The AMA assumes no liability for data contained or not contained herein. Current Dental Terminology (CDT), including procedure codes, nomenclature, descriptors, and other data contained therein, is copyright by the American Dental Association, 2002, 2004. All rights reserved. CDT is a registered trademark of the American Dental Association. Applicable FARS/DFARS apply.

Summary
Overview
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.

Reimbursement Guidelines
Indications and Limitations of Coverage
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.

Nationally Covered Indications
The following uses of allogeneic HSCT are covered under Medicare:
1. 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,
2. 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.
3. Effective for services performed on or after August 4, 2010, for the treatment of Myelo dysplastic 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.

Clinical Study Criteria

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:
  o Relapse-free mortality,
  o progression free survival,
  o relapse, and
  o 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:
  o Relapse-free mortality,
  o progression free survival,
  o relapse, and
  o overall survival?

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

Nationally Non-Covered Indications

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

Nationally Covered Indications

1. 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.

2. 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.

3. 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%.

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.

Other

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

CPT/HCPCS Codes

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<td>Allogeneic lymphocyte infusions</td>
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#### Modifiers (CED)

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#### Condition Codes

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#### ICP/PCS Codes

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#### Questions and Answers (CED)

**Q:** Have you verified the CPT/HCPCS code(s) on your claim may have limited coverage under CED (Coverage with Evidence Development)?

**A:** If no, clinical trial number, modifier Q0 or Q1 and diagnosis code V70.7 should not be submitted. If yes, the three requirements listed above are required. Claims without the required information will be denied.

#### References Included (but not limited to):

**CMS NCD(s)**

- NCD 110.8.1 Stem Cell Transplantation
- Reference NCD: NCD 310.1 Routine Costs in Clinical Trials

**CMS Article(s)**

- Numerous articles

**CMS Claims Processing Manual**

- Chapter 3; § 90.3 Stem Cell Transplantation
- Chapter 4; § 231.10 Billing for Autologous Stem Cell Transplants, § 231.11 Billing for Allogeneic Stem Cell Transplants
- Chapter 32; § 69 Qualifying Clinical Trials, § 90 Stem Cell Transplantation

**CMS Transmittals**

- Transmittal 2062, Change Request 7137, Dated 10/08/2010 (Allogeneic Hematopoietic Stem Cell Transplantation (HSCT) for Myelodysplastic Syndrome (MDS))

**UnitedHealthcare Medicare Advantage Coverage Summaries**

- Experimental Procedures and Items, Investigational Devices and Clinical Trials
- Genetic Testing
- Transplants – Organ and Tissue Transplants

**UnitedHealthcare Reimbursement Policies**

- Molecular Pathology/Molecular Diagnostics/Genetic Testing

**MLN Matters**

- Article MM5790, Use of an 8-Digit Registry Number on Clinical Trial Claims
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Article MM7137, Allogeneic Hematopoietic Stem Cell Transplantation (HSCT) for Myelodysplastic Syndrome (MDS)
Article MM8401, Mandatory Reporting of an 8-Digit Clinical Trial Number on Claims
Article SE1344, Further Information on Mandatory Reporting of an 8-Digit Clinical Trial Number on Claims

**Others**
CED Allogeneic Hematopoietic Stem Cell Transplantation for the treatment of Myelodysplastic Syndromes, CMS Website

### History

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