

Medical Policy

Healthcare Services Department

<p>Policy Name</p> <p>Stem Cell Transplantation Autologous/Allogenic</p> <p>Bone Marrow</p>	<p>Policy Number</p> <p>MP-SCT-FP-03-23</p>	<p>Scope</p> <p><input checked="" type="checkbox"/> MMM MA <input type="checkbox"/> MMM Multihealth</p>										
<p>Service Category</p> <table border="0"> <tr> <td><input type="checkbox"/> Anesthesia</td> <td><input type="checkbox"/> Medicine Services and Procedures</td> </tr> <tr> <td><input type="checkbox"/> Surgery</td> <td><input type="checkbox"/> Evaluation and Management Services</td> </tr> <tr> <td><input type="checkbox"/> Radiology Procedures</td> <td><input type="checkbox"/> DME/Prosthetics or Supplies</td> </tr> <tr> <td><input type="checkbox"/> Pathology and Laboratory Procedures</td> <td><input checked="" type="checkbox"/> <u>Other Transplant</u></td> </tr> <tr> <td></td> <td><u>Stem Cell Transplantation Autologous/Allogenic</u></td> </tr> </table>			<input type="checkbox"/> Anesthesia	<input type="checkbox"/> Medicine Services and Procedures	<input type="checkbox"/> Surgery	<input type="checkbox"/> Evaluation and Management Services	<input type="checkbox"/> Radiology Procedures	<input type="checkbox"/> DME/Prosthetics or Supplies	<input type="checkbox"/> Pathology and Laboratory Procedures	<input checked="" type="checkbox"/> <u>Other Transplant</u>		<u>Stem Cell Transplantation Autologous/Allogenic</u>
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Service Description

NCD 110.23

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 transplantation (AuSCT) is a technique for restoring stem cells using the patient's own previously stored cells. AuSCT must be used to effect hematopoietic reconstitution following severely myelotoxic doses of chemotherapy (HDCT) and/or radiotherapy used to treat various malignancies. 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.

Allogeneic HSCT 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 will 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.

Please note that all services described in this policy require prior authorization.

- Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.
- Providers should report all services using the most up-to-date industry-standard procedure, revenue, and diagnosis codes, including modifiers where applicable.
- Providers must submit all required and requested documentation for case evaluation and determination.
- The plan may request additional documentation and information not received and or provided initially related to condition and diagnosis for case evaluation and determination.
- Any additional documentation submitted specifying medical necessity criteria and considered important for case evaluation and determination will be reviewed by Clinical Team utilizing guidelines and regulation criteria.

Medical Necessity Guidelines**Indications and Limitations of Coverage****B. Nationally Covered Indications****I. Allogeneic Hematopoietic Stem Cell Transplantation (HSCT)**

- a) 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,
- b) 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.
- c) 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.

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 cytopenia's, 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:

1. 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?

2. Prospectively, in Medicare beneficiaries with MDS who receive HSCT, how do International Prognostic Scoring System (IPSS) scores, patient age, cytopenias, and comorbidities predict the following outcomes:

- Relapse-free mortality,
- progression free survival,
- relapse, and

-overall survival?

3. 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. If a study is regulated by the Food and Drug Administration (FDA), it must be in compliance with 21 CFR parts 50 and 56.
- 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

Facilities must submit the required transplant essential data to the Stem Cell Therapeutics Outcomes Database.

d) Effective for claims with dates of service on or after January 27, 2016, allogeneic HSCT for multiple myeloma is covered by Medicare only for beneficiaries with Durie-Salmon Stage II or III multiple myeloma, or International Staging System (ISS) Stage II or Stage III multiple myeloma, and participating in an approved prospective clinical study that meets the criteria below. There must be appropriate statistical techniques to control for selection bias and confounding by age, duration of diagnosis, disease classification, International Myeloma Working Group (IMWG) classification, ISS stage, comorbid conditions, type of preparative/conditioning regimen, graft vs. host disease (GVHD) prophylaxis, donor type and cell source.

A prospective clinical study seeking Medicare coverage for allogeneic HSCT for multiple myeloma pursuant to CED must address the following question:

Compared to patients who do not receive allogeneic HSCT, do Medicare beneficiaries with multiple myeloma who receive allogeneic HSCT have improved outcomes as indicated by:

Graft vs. host disease (acute and chronic);
 Other transplant-related adverse events;
 Overall survival; and
 (optional) Quality of life?

All CMS-approved clinical studies and registries must adhere to the below listed standards of scientific integrity and relevance to the Medicare population as listed in section g.

e) Effective for claims with dates of service on or after January 27, 2016, allogeneic HSCT for myelofibrosis (MF) is covered by Medicare only for beneficiaries with Dynamic International Prognostic Scoring System (DIPSSplus) intermediate-2 or High primary or secondary MF and participating in an approved prospective clinical study. All Medicare approved studies must use appropriate statistical techniques in the analysis to control for selection bias and potential confounding by age, duration of diagnosis, disease classification, DIPSSplus score, comorbid conditions, type of preparative/conditioning regimen, graft vs. host disease (GVHD) prophylaxis, donor type and cell source.

A prospective clinical study seeking Medicare coverage for allogeneic HSCT for myelofibrosis pursuant to Coverage with Evidence Development (CED) must address the following question:

Compared to patients who do not receive allogeneic HSCT, do Medicare beneficiaries with MF who receive allogeneic HSCT transplantation have improved outcomes as indicated by:

Graft vs. host disease (acute and chronic);
 Other transplant-related adverse events;
 Overall survival; and
 (optional) Quality of life?

All CMS-approved clinical studies and registries must adhere to the below listed standards of scientific integrity and relevance to the Medicare population as listed in section g.

f) Effective for claims with dates of service on or after January 27, 2016, allogeneic HSCT for sickle cell disease (SCD) is covered by Medicare only for beneficiaries with severe, symptomatic SCD who participate in an approved prospective clinical study.

A prospective clinical study seeking Medicare coverage for allogeneic HSCT for sickle cell disease pursuant to Coverage with Evidence Development (CED) must address the following question:

Compared to patients who do not receive allogeneic HSCT, do Medicare beneficiaries with SCD who receive allogeneic HSCT have improved outcomes as indicated by:

Graft vs. host disease (acute and chronic),
 Other transplant-related adverse events;
 Overall survival; and

(optional) Quality of life?

All CMS-approved clinical studies and registries must adhere to the below listed standards of scientific integrity and relevance to the Medicare population listed in section g:

g) All CMS-approved clinical studies and registries in sections d, e and f must adhere to the below listed standards of scientific integrity and relevance to the Medicare population:

- The principal purpose of the study is to test whether the item or service meaningfully improves health outcomes of affected beneficiaries who are represented by the enrolled subjects.
- The rationale for the study is well supported by available scientific and medical evidence.
- The study results are not anticipated to unjustifiably duplicate existing knowledge.
- The study design is methodologically appropriate and the anticipated number of enrolled subjects is sufficient to answer the research question(s) being asked in the National Coverage Determination.
- The study is sponsored by an organization or individual capable of completing it successfully.
- The research study is in compliance with all applicable Federal regulations concerning the protection of human subjects found in the Code of Federal Regulations (CFR) at 45 CFR Part 46. If a study is regulated by the Food and Drug Administration (FDA), it is also in compliance with 21 CFR Parts 50 and 56. In addition, to further enhance the protection of human subjects in studies conducted under CED, the study must provide and obtain meaningful informed consent from patients regarding the risks associated with the study items and/or services, and the use and eventual disposition of the collected data.
- All aspects of the study are conducted according to appropriate standards of scientific integrity.
- The study has a written protocol that clearly demonstrates adherence to the standards listed here as Medicare requirements.
- The study is not designed to exclusively test toxicity or disease pathophysiology in healthy individuals. Such studies may meet this requirement 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.
- The clinical research studies and registries are registered on the www.ClinicalTrials.gov website by the principal sponsor/investigator prior to the enrollment of the first study subject. Registries are also registered in the Agency for Healthcare Quality (AHRQ) Registry of Patient Registries (RoPR).
- The research study protocol specifies the method and timing of public release of all prespecified outcomes to be measured including release of outcomes if outcomes are negative or study is terminated early. The results must be made public within 12 months of the study's primary completion date, which is the date the final subject had final data collection for the primary endpoint, even if the trial does not achieve its primary aim. -
- The results must include number started/completed, summary results for primary and secondary outcome measures, statistical analyses, and adverse events. Final results must be reported in a publicly accessible manner; either in a peer-reviewed scientific journal (in print or on-line), in an on-line publicly accessible registry dedicated to the dissemination of clinical trial information such as ClinicalTrials.gov , or in journals willing to publish in abbreviated format (e.g., for studies with negative or incomplete results).
- The study protocol must explicitly discuss beneficiary subpopulations affected by the item or service 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 in 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.

-The study protocol explicitly discusses how the results are or are not expected to be generalizable to affected beneficiary subpopulations. 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 Act, the Agency for Healthcare Research and Quality (AHRQ) supports clinical research studies that CMS determines meet the above-listed standards and address the above-listed research questions.

II. Autologous Stem Cell Transplantation (AuSCT)

a) Effective for services performed on or after April 28, 1989, AuSCT is considered reasonable and necessary under §1862(a)(1)(A) of 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.

b) 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.

c) 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%.

C. Nationally Non-Covered Indications

I. Allogeneic Hematopoietic Stem Cell Transplantation (HSCT)

-Effective for claims with dates of service on or after May 24, 1996, through January 26, 2016, allogeneic HSCT is not covered as treatment for multiple myeloma.

II. Autologous Stem Cell Transplantation (AuSCT)

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

- a) Acute leukemia not in remission;
- b) Chronic granulocytic leukemia;
- c) Solid tumors (other than neuroblastoma);
- d) Up to October 1, 2000, multiple myeloma;
- e) Tandem transplantation (multiple rounds of AuSCT) for patients with multiple myeloma;
- f) Effective October 1, 2000, non primary AL amyloidosis; and,
- g) Effective October 1, 2000, through 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.

Limits or Restrictions

D. Other

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

(This NCD last reviewed January 2016.)

Reference Information

NCD 110.23
Stem Cell Transplantation (Formerly 110.8.1)

Medicare Coverage Database (MCD)

Link: <https://www.cms.gov/medicare-coverage-database/search.aspx>

Cross Reference

NCD 110.23

CED page - Allogeneic Hematopoietic Stem Cell Transplant for MDS

Link: <https://www.cms.gov/medicare/coverage/evidence/stem-cell-transplant-mds>

CED page - Allogeneic Hematopoietic Stem Cell Transplant for Multiple Myeloma

Link: <https://www.cms.gov/medicare/coverage/evidence/stem-cell-transplant-multiple-myelomas>

CED page - Allogeneic Hematopoietic Stem Cell Transplant for Myelofibrosis

Link: <https://www.cms.gov/medicare/coverage/evidence/stem-cell-transplant-myelofibrosis>

CED page - Allogeneic Hematopoietic Stem Cell Transplant for Sickle Cell Disease

<https://www.cms.gov/medicare/coverage/evidence/stem-cell-transplant-sickle-cell>

Policy History

Date	Version	Comments
12/07/2023	Draft	New Medical Policy
12/15/2023	Final	Approved by Medical Policy Committee