| CMS Manual System | Department of Health & Human Services (DHHS) |
|---|---|
| Pub 100-03 Medicare National Coverage Determinations | Centers for Medicare & Medicaid Services (CMS) |
| **Transmittal 12948** | **Date: November 6, 2024** |
| | **Change Request 13604** |

**Transmittal 12868 issued October 07, 2024, is being rescinded and replaced by Transmittal 12948, dated November 6, 2024, to revise BR 04.4.2 and messaging and add new BR 04.4.2.1 and to update the ICD-10 spreadsheet and IOM for publication 100-04. All other information remains the same.**

**SUBJECT: Allogeneic Hematopoietic Stem Cell Transplantation (HSCT) for Myelodysplastic Syndromes (MDS) National Coverage Determination (NCD) 110.23**

**I. SUMMARY OF CHANGES:** The purpose of this Change Request (CR) is to inform contractors that CMS is expanding Medicare coverage for allogeneic hematopoietic stem cell transplant using bone marrow, peripheral blood or umbilical cord blood stem cell products for Medicare patients with MDS who meet specific criteria.

The Federal government creates NCDs that are binding on the MACs who review and/or adjudicate claims, make coverage determinations, and/or payment decisions, and also binds quality improvement organizations, qualified independent contractors, the Medicare appeals council, and Administrative Law Judges (ALJs) (see 42 Code of Federal Regulations (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: March 6, 2024**
**Unless otherwise specified, the effective date is the date of service.*
**IMPLEMENTATION DATE: October 7, 2024**

***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-*Only One Per Row.*

| R/N/D | CHAPTER / SECTION / SUBSECTION / TITLE |
|---|---|
| R | 1/110/23/Stem Cell Transplantation (Formerly 110.8.1) (Various Effective Dates Below) |

**III. FUNDING:**

**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**

# Attachment - Business Requirements

| Pub. 100-03 | Transmittal:12948 | Date: November 6, 2024 | Change Request: 13604 |
|---|---|---|---|

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**I. SUMMARY OF CHANGES:** The purpose of this Change Request (CR) is to inform contractors that CMS is expanding Medicare coverage for allogeneic hematopoietic stem cell transplant using bone marrow, peripheral blood or umbilical cord blood stem cell products for Medicare patients with MDS who meet specific criteria.

## II. GENERAL INFORMATION

**A. Background:** The purpose of this Change Request (CR) is to inform contractors that CMS is expanding Medicare coverage for allogeneic hematopoietic stem cell transplant using bone marrow, peripheral blood or umbilical cord blood stem cell products for Medicare patients with MDS who meet specific criteria.

Hematopoietic stem cell transplantation (HSCT) is a process that includes mobilization, harvesting, and transplant of stem cells and the administration of high dose chemotherapy and/or radiotherapy prior to the actual transplant. During the process stem cells are harvested from either the patient (autologous) or a donor (allogeneic) and subsequently administered by intravenous infusion to the patient.

Myelodysplastic Syndromes **(**MDS) are a heterogeneous group of hematologic disorders characterized by (1) cytopenia (decreased number of red blood cells, white blood cells and platelets) due to bone marrow failure and (2) the potential development of acute myeloid leukemia (AML). The bone marrow does not produce enough healthy, functioning blood cells. For treatment purposes, patients with MDS are often stratified into risk groups based on the potential development of AML, which varies widely across MDS subtypes.

**B. Policy:** On March 6, 2024, CMS issued a final decision under National Coverage Determination (NCD) 110.23 to expand Medicare coverage for allogeneic hematopoietic stem cell transplant using bone marrow, peripheral blood or umbilical cord blood stem cell products for Medicare patients with MDS who have prognostic risk scores of:

- ≥ 1.5 (Intermediate-2 or high) using the International Prognostic Scoring System (IPSS), or
- ≥ 4.5 (high or very high) using the International Prognostic Scoring System - Revised (IPSS-R), or
- ≥ 0.5 (high or very high) using the Molecular International Prognostic Scoring System (IPSS-M).

For these patients, the evidence demonstrates that the treatment is reasonable and necessary under section 1862(a)(1)(A) of the Social Security Act (the Act).

In addition, coverage of all other indications for stem cell transplantation not otherwise specified will be made by local Medicare Administrative Contractors (MACs) under section 1862(a)(1)(A) of the Act.

Refer to Publication (Pub) 100-03, NCD Manual, chapter 1, section 110.23, for information regarding this NCD and Pub. 100-04, Claims Processing Manual (CPM), chapter 3, section 90.3.1 for further billing instructions.

## III. BUSINESS REQUIREMENTS TABLE

*"Shall" denotes a mandatory requirement, and "should" denotes an optional requirement.*

| Number | Requirement | Responsibility | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | A/B MAC | | | DME | Shared-System Maintainers | | | | Other |
| | | A | B | HHH | MAC | FISS | MCS | VMS | CWF | |
| 13604 - 03.1 | Effective for claims with dates of service on and after March 6, 2024, contractors shall be aware that Medicare is expanding coverage for allogeneic hematopoietic stem cell transplant using bone marrow, peripheral blood or umbilical cord blood stem cell products for Medicare patients with myelodysplastic syndromes who have prognostic risk scores of:<br>• ≥ 1.5 (Intermediate-2 or high) using the International Prognostic Scoring System (IPSS), or<br>• ≥ 4.5 (high or very high) using the International Prognostic Scoring System - Revised (IPSS-R), or<br>• ≥ 0.5 (high or very high) using the Molecular International Prognostic Scoring System (IPSS-M).<br><br>In addition, coverage of all other indications for stem cell transplantation not otherwise specified will be made by local Medicare Administrative Contractors under section 1862(a)(1)(A) of the Act. Please see Pub. 100-03, chapter 1, section 110.23, of the NCD Manual, and Pub. 100-04, | X | X | | | | | | | |

| Number | Requirement | Responsibility | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | A/B MAC | | | DME | Shared-System Maintainers | | | | Other |
| | | A | B | HHH | MAC | FISS | MCS | VMS | CWF | |
| | chapter 3, section 90.3.1, of the Claims Processing Manual, for further instructions. | | | | | | | | | |

## IV. PROVIDER EDUCATION

Medicare Learning Network® (MLN): CMS will develop and release national provider education content and market it through the MLN Connects® newsletter shortly after we issue the CR. MACs shall link to relevant information on your website and follow IOM Pub. No. 100-09 Chapter 6, Section 50.2.4.1 for distributing the newsletter to providers. When you follow this manual section, you don't need to separately track and report MLN content releases. You may supplement with your local educational content after we release the newsletter.

**Impacted Contractors:** A/B MAC Part B, A/B MAC Part A

## V. SUPPORTING INFORMATION

**Section A: Recommendations and supporting information associated with listed requirements:** N/A

*"Should" denotes a recommendation.*

| X-Ref Requirement Number | Recommendations or other supporting information: |
|---|---|

**Section B: All other recommendations and supporting information:**N/A

## VI. CONTACTS

**Post-Implementation Contact(s):** Contact your Contracting Officer's Representative (COR).

## VII. FUNDING

**Section A: 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.

**ATTACHMENTS: 0**

# Medicare National Coverage Determinations Manual

## Chapter 1, Part 2 (Sections 90 – 160.26)

## Coverage Determinations

**Table of Contents**

*(Rev. 12948; Issued 11-06-24)*

## 110.23 - Stem Cell Transplantation (Formerly 110.8.1) (Various Effective Dates Below)

***(Rev. 12948; Issued: 11-06-24; Effective:03-06-24; Implementation:10-07-24)***

**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.

**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 March 6, 2024, allogeneic hematopoietic stem cell transplant using bone marrow, peripheral blood or umbilical cord blood stem cell products for Medicare patients with myelodysplastic syndromes who have prognostic risk scores of:*

- *≥ 1.5 (Intermediate-2 or high) using the International Prognostic Scoring System (IPSS), or*
- *≥ 4.5 (high or very high) using the International Prognostic Scoring System - Revised (IPSS-R), or*
- *≥ 0.5 (high or very high) using the Molecular International Prognostic Scoring System (IPSS-M).*

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.

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:

a. 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.
b. The rationale for the study is well supported by available scientific and medical evidence.
c. The study results are not anticipated to unjustifiably duplicate existing knowledge.
d. 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.
e. The study is sponsored by an organization or individual capable of completing it successfully.
f. 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.
g. All aspects of the study are conducted according to appropriate standards of scientific integrity.
h. The study has a written protocol that clearly demonstrates adherence to the standards listed here as Medicare requirements.
i. 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.
j. 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).
k. 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 accessibly 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).
l. 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.

m. 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 §l862(a)(1)(A) of the Act for the following conditions and is covered under Medicare for patients with:

1. Acute leukemia in remission who have a high probability of relapse and who have no human leucocyte antigens (HLA)-matched;
2. Resistant non-Hodgkin's lymphomas or those presenting with poor prognostic features following an initial response;
3. Recurrent or refractory neuroblastoma; or,
4. 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 §l862(a)(1)(A) of the Act and is not covered under Medicare.

**D. Other**

*Coverage of all other indications for stem cell transplantation not otherwise specified above as covered or non-covered will be made by local Medicare Administrative Contractors under section 1862(a)(1)(A).*

**(This NCD last reviewed *March 2024*.)**