Policy Key: High Dose Chemotherapy and Stem Cell Transplant

TriWest Clinical Operations – TRICARE West

SCOPE

This Policy Key provides criteria to use during medical necessity review transplantation of stem cells from blood, bone marrow, or umbilical cord blood, with or without High Dose Chemotherapy (HDC), for treatment of the indications under the coverage criteria.
There are 5 general types of stem cell 'transplantation" or "rescue" (See Definitions for full description): [1]

- Autologous Bone Marrow Transplant (ABMT)
- Autologous Peripheral Stem Cell Transplantation (PSCT)
- Allogeneic Bone Marrow Transplantation (BMT)
- Allogeneic Peripheral Stem Cell Transplantation (PSCT)
- Umbilical Cord Blood Stem Cell Transplantation (UCBT)

Note: Immunoablative and myeloablative therapy are considered identical therapies under this TRICARE policy. [1]

For Active-Duty Service Members (ADSM) and TRICARE Prime Remote (TPR) beneficiaries, reviewers must first apply guidance outlined in TRICARE Operations Manual Chapter 17, Section 3, Supplemental Health Care Program (SHCP). If a service is excluded under ADSM/TPR provisions, no further policy review is required under this or any other Policy Key. [2]

NOT COVERED [1]

- Expenses waived by the transplant center (i.e., beneficiary/sponsor not financially liable)
- Services and supplies not provided in accordance with applicable program criteria (i.e., part of a grant or research program, unproven procedure)
- Administration of an unproven immunosuppressant drug that is not United States (U.S.) Food and Drug Administration (FDA) approved
- Pre- or post-transplant nonmedical expenses (i.e., out-of-hospital living expenses, to include, hotel, meals, privately owned vehicle for the beneficiary or family members)
- Donor transportation
- Allogeneic BMT for treatment of low grade non-Hodgkin's lymphoma
- Autologous UCBT therapy
- Allogeneic BMT for neuroblastoma
- Allogeneic donor BMT (infusion) performed with or after organ transplants for the purpose of increasing tolerance of the organ transplant

- Allogeneic non-myeloablative hematopoietic stem cell transplantation for Crohn's disease
- HDC with ABMT or PSCT for treatment of breast cancer
- HDC with ABMT or autologous PSCT, allogeneic BMT or allogeneic PSCT, with or without HDC, or allogeneic UCBT, with or without HDC, if the patient has a concurrent condition (other existing illness) that would jeopardize the achievement of successful transplantation
- HDC with allogeneic BMT is not a benefit for treatment of Waldenstrom's macroglobulinemia
- HDC with Stem Cell Rescue (SCR) for the treatment of epithelial ovarian cancer
- HDC with allogeneic stem cell transplantation for the treatment of cold agglutinin disease
- Donor lymphocyte infusion if not specifically listed in the coverage criteria
- Immunoablative therapy with BMT or PSCT for rheumatoid arthritis and juvenile idiopathic arthritis treatment
- Immunoablative therapy with allogeneic BMT or allogeneic PSCT for systemic lupus erythematosus treatment
- When BMT, PSCT, or UCBT is noncovered, none of the steps are covered.
- The prophylactic harvesting, cryopreservation, and storage of bone marrow, peripheral blood stem cells, or umbilical cord blood stem cells when proposed for possible future use is not covered.

COVERAGE CRITERIA

General Coverage Information [1]

- BMT, PSCT, and UCBT is a process which includes mobilization, harvesting, and transplant of bone marrow, peripheral blood stem cell, or umbilical cord blood stem cells and the administration of HDC or radiotherapy before the actual transplant. When BMT, PSCT, or UCBT is covered, all necessary steps are included in coverage.
- The following services and supplies related to HDC and stem cell transplant are covered:
    - Cost for donor searches (fully itemized and billed by the transplant center, cost-shared in accordance with established reimbursement guidelines for outpatient diagnostic testing, billed at any time, without limit on how many searches requested from the search printout)
    - Regarding TRICARE coverage, the greatest degree of incompatibility allowed between donor or recipient (for either related or unrelated donors) is a single antigen mismatch at the A, B, or Dr. locus except for:
        - Patients with undifferentiated leukemia, CML, aplastic anemia, Acute Lymphocytic Leukemia (ALL), or Acute Myelogenous Leukemia (AML); when histocompatible related or unrelated donors are not available, a three antigen mismatch is allowed for related donors.
        - For patients under 18 years of age with a relapsed leukemia, when histocompatible related or unrelated donors are not available, parental CD34++ stem cell transplantation with two-three antigen mismatch is allowed.
    - If the patient expires before the stem cell reinfusion being completed, benefits for the harvesting may be allowed

- Benefits are allowed for Hepatitis B and pneumococcal vaccines for patients undergoing transplantation.
- Benefits may be allowed for Deoxyribonucleic Acid-Human Leucocyte Antigen (DNA-HLA) tissue typing in determining histocompatibility.
- Patient transportation by air ambulance may be cost-shared when determined to be medically necessary
- Benefits for advanced life support air ambulance (to include attendant) may be preauthorized by the appropriate preauthorizing authority on an individual case basis in conjunction with the preauthorization for the services themselves

Note: The list of indications in the following sections is not all inclusive. Other indications are covered when documented by reliable evidence as safe, effective and comparable or superior to standard care. [1]

Autologous Hematopoietic Stem Cell Transplant for Multiple Sclerosis [3, 4]

- Initial Level of Review may approve if **ALL** the following criteria are met:
  - Adults age 50 or younger; and
  - Disease duration of 10 years or less; and
  - Specifically indicated for Relapsing-Remitting MS (RRMS) with "highly active" or "aggressive" disease; and
  - Expanded Disability Status Scale (EDSS) score between 3.0 and 6.0; and
  - Evidence of substantial breakthrough disease activity, defined as:
    - New inflammatory central nervous system lesions on MR;
    - Clinical relapses despite treatment with high-efficacy disease-modifying therapies (DMTs).

  Note: Myeloablative and non-myeloablative therapy with BMT or PSCT for multiple sclerosis treatment is **currently approved** as a medical benefit, but has not been updated in the TOM as of yet.

HDC with ABMT or autologous PSCT [1]

Non-Hodgkin's lymphoma, follicular, intermediate (mantle cell lymphomas), or high-grade

- **Initial Level of Review** may approve for **ANY** of the following:
  - Conventional dose chemotherapy has failed.
  - Relapse following a course of radiation therapy
  - The beneficiary is in first complete remission with risk factors for relapse.

Hodgkin's Disease

- **Initial Level of Review** may approve for **ANY** of the following:

- Conventional dose chemotherapy has failed.
- The beneficiary has relapsed following a course of radiation therapy, **and** has also failed at least one course of conventional dose chemotherapy subsequent to the failed radiation therapy.
- The beneficiary is in second or third complete remission.

Neuroblastoma

- **Initial Level of Review** may approve for **ANY** of the following:
  - Stage III or IV, when the patient is one for whom further treatment with a conventional dose therapy is not likely to achieve a durable remission
  - Tandem autologous PSCT for high-risk neuroblastoma (INSS Stage III with either N-MYC gene amplification or unfavorable Shimada histology or INSS Stage IV)

Other

- **Initial Level of Review** may approve for **ANY** of the following:
  - Acute lymphocytic or nonlymphocytic leukemias (e.g., myelocytic, myelogenous, myeloblastic, or myelomonoblastic)
  - Primitive Neuroectodermal Tumors (PNET)/Ewing's Sarcoma
  - Gliofibromas (also known as desmoplastic astrocytoma; desmoplastic glioblastoma)
  - Glioblastoma multiforme
  - Posterior fossa teratoid brain tumors
  - Rhabdomyosarcoma and undifferentiated sarcomas
  - Multiple myeloma
    - Tandem autologous stem cell transplantation is covered for the treatment of multiple myeloma.
  - Chronic myelogenous leukemia
  - Waldenstrom's macroglobulinemia
  - AL (Amyloid Light-Chain) Amyloidosis
  - Wilms' tumor
  - Trilateral retinoblastoma/pineoblastoma
  - Osteosarcoma (osteogenic sarcoma)
  - Germ cell tumors in a second or subsequent relapse
  - HDC with ABMT or PSCT for the treatment of desmoplastic small round cell tumor may be considered on a case-by-case basis under the TRICARE provisions for treatment of rare diseases
  - Immunoablative therapy with ABMT or autologous PSCT for the treatment of severe systemic lupus erythematosus refractory to conventional treatment

Allogeneic BMT or allogeneic PSCT, with or without HDC, is covered in the treatment of the following disease processes when either a related or unrelated donor is used.

- **Initial Level of Review** may approve for **ANY** of the following:

- Aplastic anemia
- Acute lymphocytic or nonlymphocytic leukemias (e.g., myelocytic, myelogenous, myeloblastic, myelomonoblastic); Chronic Myelogenous Leukemia (CML); or preleukemic syndrome
- Severe combined immunodeficiency, e.g., adenosine deaminase deficiency and idiopathic deficiencies
    - Partially matched-related donor stem cell transportation (without regard for the number of mismatched antigens in determining histocompatibility) in the treatment of Bare Lymphocyte Syndrome
    - Unrelated donor and/or related donor (without regard for mismatched antigens) with or without T cell lymphocyte depletion in the treatment of Familial Erythrophagocytic Lymphohistiocytosis, (FEL; generalized lymphohistiocytic infiltration; familial lymphohistiocytosis; familial reticuloendotheliosis; Familial Hemophagocytic Lymphohistiocytosis; FHL) for patients whose medical records document failure of conventional therapy (etoposide; corticosteroids; intrathecal methotrexate; and cranial irradiation)
    - Partially matched-related donor stem cell transplantation (without regard for the number of mismatched antigens) in the treatment of X-linked Severe Combined Immunodeficiency Syndrome (X-Linked SCID)
- Wiskott-Aldrich syndrome
- Infantile malignant osteopetrosis (Albers-Schonberg syndrome or marble bone disease)
- Thalassemia major
- Intermediate and high grade non-Hodgkin's lymphoma
- Myeloproliferative/dysplastic syndrome
- Congenital mucopolysaccharidoses
- Congenital amegakaryocytic thrombocytopenia
- Metachromatic leukodystrophy
- Sickle cell disease
- Chronic Lymphocytic Leukemia (CLL) when previous therapy has failed or when the CLL is refractory to conventional therapy
- Hyperesinophilic Syndrome
- Multiple myeloma when HCD with ABMT or PSCT has failed
- X-linked hyper-IgM Syndrome
- Chediak-Higashi Syndrome
- Langerhans Cell Histiocytosis, refractory to conventional treatment
- Hodgkin's disease
- Primary Plasma Cell Leukemia

Unirradiated Donor Lymphocyte Infusion (donor buffy coat infusion, donor leukocyte infusion or donor mononuclear cell infusion)

Covered for patients with CML or Acute Myelogenous/Myeloid Leukemia (AML) who relapse following their first or subsequent course of HDC with allogeneic stem cell transplantation.

- **Initial Level of Review** may approve if the medical record contains the following documentation:
    - The beneficiary is in relapse following an adequate trial of HDC with allogeneic stem cell transplantation of CML or AML, **AND**
    - The beneficiary qualified (or would have qualified) for authorization for HDC with allogeneic stem cell transplantation according to the provisions set forth in this policy.

Allogeneic UCBT, with or without HDC, is covered in the treatment of the following disease processes when either a related or unrelated donor is used.

- **Initial Level of Review** may approve **ANY** of the following:
    - Aplastic anemia
    - Acute lymphocytic or non-lymphocytic leukemias
    - Chronic myelogenous leukemia
    - Severe combined immunodeficiency
    - Wiskott-Aldrich syndrome
    - Infantile malignant osteopetrosis
    - Blackfan-Diamond anemia
    - Fanconi anemia
    - Neuroblastoma
    - X-linked lymphoproliferative syndrome
    - Hunter syndrome
    - Hurler syndrome
    - Congenital amegakaryocytic thrombocytopenia
    - Sickle cell anemia
    - Globoid cell leukodystrophy
    - Adrenoleukodystrophy
    - Kostmann's Syndrome
    - Lesch-Nyhan disease
    - Intermediate and high grade non-Hodgkin's lymphoma
    - Thalassemia major
    - Myelodysplastic Syndrome
    - X-linked hyper-IgM Syndrome
    - Langerhans Cell Histiocytosis, refractory to conventional treatment

Syngeneic (identical twin donor)

- Medical Director may approve stem cell transplantation is covered for the treatment of Hodgkin's disease.

Policy Consideration/Medical Claims Review [1]

- If the patient expires before the stem cell reinfusion being completed, benefits for the harvesting may be allowed.

- TRICARE Prime enrollee must have a referral from his/her Primary Care Manager (PCM) and an authorization from TriWest before obtaining transplant-related services. If network providers furnish transplant-related services without prior PCM referral and contractor authorization, penalties will be administered according to TRICARE network provider agreements.
- TriWest shall reimburse charges for the services on a Point of Services (POS) basis if Prime enrollees receive transplant-related services from non-network civilian reporters without the required PCM referral and contractor authorization. Special cost-sharing requirements apply to POS claims.
- Charges for donor searches must be fully itemized and billed by the transplant center.
- Costs for donor searches will be cost-shared in accordance with established reimbursement guidelines for outpatient diagnostic testing.
- Donor search costs may be billed at any time. There is no limit on how many searches a transplant center may request from the search printout.
- Charges for stem cell and umbilical cord blood preparation and storage shall be billed through the transplantation facility in the name of the TRICARE patient.
- Charges for the umbilical cord blood bank may be allowed only for patients who have undergone a covered transplant.
- Claims for services and supplies related to the HDC and transplant for beneficiaries under the age of 18 will be reimbursed based on billed charges. Claims for HDC and transplant for adult patients, 18 years and older, will be reimbursed under the Diagnosis Related Group (DRG) payment system. Outpatient institutional facility charges will be paid as billed. Professional services are reimbursed under the CHAMPUS Maximum Allowable Charge (CMAC) methodology.
- In those cases where the beneficiary fails to obtain preauthorization, benefits may be extended if the services or supplies otherwise would qualify for benefits but for the failure to obtain preauthorization. If preauthorization is not received, the appropriate preauthorizing authority is responsible for determining if the patient meets the coverage criteria. Charges for transplant and transplant-related services provided to TRICARE Prime enrollees who failed to obtain PCM referral and contractor authorization for HDC with ABMT or PSCT will be reimbursed only under POS rules.

DEFINITIONS

Allogeneic Bone Marrow Transplantation (BMT), where stem cells from a histocompatible donor (other than the patient) are harvested from the bone marrow, then later infused into the bloodstream of the patient. With BMT, the patient may have either a related or unrelated donor who has the same or closely matched Human Leukocyte Antigen (HLA) typing necessary for successful transplantation. [1]

Allogeneic Peripheral Stem Cell Transplantation (PSCT), where stem cells are harvested from the bloodstream of a histocompatible donor (other than the patient) then later infused into the bloodstream of the patient. [1]

Autologous Bone Marrow Transplant (ABMT), where the patient is both donor and recipient of stem cells harvested from the bone marrow. [1]

Autologous Peripheral Stem Cell Transplantation (PSCT), where the patient is both donor and recipient of stem cells harvested from the bloodstream using the apheresis process. [1]

High Dose Chemotherapy (HDC) is defined as the use of cytotoxic therapeutic agents (that are otherwise approved by the United States (US) Food and Drug Administration (FDA) for general use in humans) in dosages and/or frequencies of dosage that exceed the FDA labeling for the agent. HDC is generally considered when conventional regimens of chemotherapeutic agents have failed to arrest disease progression. One major adverse effect of HDC is that of bone marrow suppression, itself a potentially lethal process. [1]

Stem cell "transplantation" or "rescue" is defined as a technique for collecting stem cells from a donor (either from the bone marrow or from the bloodstream), preparing and storing the collected stem cells, then reinfusing the prepared stem cells into the bloodstream of a patient in the treatment of oncologic, hematologic or lymphoproliferative disease with curative potential. The goal of stem cell "transplantation" or "rescue" is to reverse the bone marrow suppression caused by either HDC or by a primary bone marrow disease process (e.g., aplastic anemia). There are five general types of stem cell "transplantation" or "rescue" [1]

Umbilical Cord Blood Stem Cell Transplantation (UCBT), where stem cells are harvested from the umbilical cord and placenta, then later infused into the bloodstream of the patient. [1]

CODES

CPT 38221, 38240, 38241,

REFERENCES

[1] TRICARE Policy Manual 6010.63-M, April 2021, Change 17 (September, 2024), Chapter 4, Section 23.1, High Dose Chemotherapy (HDC) and Stem Cell Transplantation, https://manuals.health.mil/pages/DisplayManualHtmlFile/2024-09-20/AsOf/TPT5/C4S23_1.html

[2] TRICARE Operations Manual (TOM) 6010.62-M, Chapter 17, Section 3 — Supplemental Health Care Program (SHCP) Contractor Responsibilities, Retrieved 01/02/2026 https://manuals.health.mil/pages/DisplayManualHtmlFile/2025-12-19/AsOf/TOT5/C17S3.html

[3] Boffa G, et al. "Long-term Clinical Outcomes of Hematopoietic Stem Cell Transplantation in Multiple Sclerosis." Neurology. 2021;96:e1215-e1226.

[4] Hayes Knowledge Center. "Autologous Hematopoietic Stem Cell Transplantation for Treatment of Multiple Sclerosis." Hayes, November 14, 2024.