

HIGH DOSE CHEMOTHERAPY AND STEM CELL TRANSPLANTATION

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I. CPT¹ PROCEDURE CODES

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II. DESCRIPTION

A. High dose chemotherapy (HDC) is defined as the use of cytotoxic therapeutic agents (that are otherwise approved by the FDA for general use in humans) in dosages and/or frequencies of dosage that exceed the FDA labelling for the agent. HDC is generally considered when conventional regimens of chemotherapeutic agents have failed to arrest disease progression. One of the major adverse effects of HDC is that of bone marrow suppression, itself a potentially lethal process.

B. 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. Autologous bone marrow transplant (ABMT), where the patient is both donor and recipient of stem cells harvested from the bone marrow.
2. 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.
3. 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

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related or unrelated donor who has the same or closely matched human leukocyte antigen (HLA) typing necessary for successful transplantation.

4. Allogeneic **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.

5. 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.

III. POLICY

A. Benefits are allowed for HDC with ABMT or autologous PSCT, allogeneic **BMT** or Allogeneic **PSCT**, with or without HDC, and allogeneic **UCBT**, with or without HDC.

1. TRICARE Prime enrollee must have a referral from his/her Primary Care Manager (PCM) and an authorization from the contractor before obtaining transplant-related services. If network providers furnish transplant-related services without prior PCM referral and contractor authorization, penalties will be administered according TRICARE network provider agreements. If Prime enrollees receive transplant-related services from non-network civilian reporters without the required PCM referral and contractor authorization, Managed Care Support (MCS) contractors shall reimburse charges for the services on a Point of Services basis. Special cost-sharing requirements apply to Point of Service claims.

2. For Standard and Extra patients residing in a Managed Care Support (MCS) region, preauthorization authority is the responsibility of the MCS Medical Director or other designated utilization staff.

B. HDC with ABMT or autologous PSCT is covered in the treatment of the following malignancies. The list of indications is not all inclusive. Other indications are covered when documented by reliable evidence as safe, effective and comparable or superior to standard care (proven).

1. Non-Hodgkin's lymphoma, follicular, intermediate, or high-grade; when:

- a. Conventional dose chemotherapy has failed; or
- b. The patient has relapsed following a course of radiation therapy; or
- c. The patient is in first complete remission with risk factors for relapse.

NOTE: For purposes of coverage, mantle cell lymphomas will be considered as intermediate grade, non-Hodgkin's lymphomas.

2. Hodgkin's disease when:

- a. Conventional dose chemotherapy has failed; or

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b. The patient 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; and

c. The patient is in second or third complete remission.

3. Neuroblastoma.

a. 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.

b. Tandem autologous **PSCT** for high-risk neuroblastoma (INSS Stage III with either N-MYC gene amplification or unfavorable Shimada histology or INSS Stage IV).

4. Acute lymphocytic or nonlymphocytic leukemias (e.g., myelocytic, myelogenous, myeloblastic, or myelomonoblastic);

5. Primitive Neuroectodermal Tumors (PNET)/Ewing's Sarcoma.

6. Gliofibromas (also known as desmoplastic astrocytoma; desmoplastic glioblastoma).

7. Glioblastoma multiforme.

8. Posterior fossa teratoid brain tumors.

9. Rhabdomyosarcoma and undifferentiated sarcomas.

10. Multiple myeloma. Tandem autologous stem cell transplantation is covered for the treatment of multiple myeloma.

11. Chronic myelogenous leukemia.

12. Waldenstrom's macroglobulinemia.

13. AL (Amyloid Light-Chain) Amyloidosis.

14. Wilms'tumor.

15. Trilateral retinoblastoma/pineoblastoma.

16. Osteosarcoma (osteogenic sarcoma).

17. Germ cell tumors in a second or subsequent relapse.

18. 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.

19. Immunoablative therapy with ABMT or autologous PSCT for the treatment of severe systemic lupus erythematosus refractory to conventional treatment.

C. 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. The list of indications is not all inclusive. Other indications are covered when documented by reliable evidence as safe, effective and comparable or superior to standard care (proven).

1. Aplastic anemia.
2. Acute lymphocytic or nonlymphocytic leukemias (e.g., myelocytic, myelogenous, myeloblastic, myelomonoblastic); Chronic Myelogenous Leukemia (CML); or preleukemic syndromes.
3. Severe combined immunodeficiency; e.g., adenosine deaminase deficiency and idiopathic deficiencies.
 - a. 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.
 - b. 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).
 - c. 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).
4. Wiskott-Aldrich Syndrome.
5. Infantile malignant osteopetrosis (Albers-Schonberg syndrome or marble bone disease).
6. Thalassemia major.
7. Intermediate and high grade lymphoma.
8. Myeloproliferative/dysplastic syndromes.
9. Congenital mucopolysaccharidoses.
10. Congenital amegakaryocytic thrombocytopenia.
11. Metachromatic leukodystrophy.

12. Sickle cell disease.
13. Chronic Lymphocytic Leukemia (CLL) when previous therapy has failed or when the CLL is refractory to conventional therapy.
14. Hyperesinophilic Syndrome.
15. Multiple myeloma when HCD with ABMT or PSCT has failed.
16. X-linked hyper-IgM Syndrome.
17. Chediak-Higashi Syndrome.
18. Langerhans Cell Histiocytosis, refractory to conventional treatment.
19. Hodgkin's disease.

D. Unirradiated donor lymphocyte infusion (donor buffy coat infusion, donor leukocyte infusion or donor mononuclear cell infusion) is 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. The medical record must document that the patient:

1. Is in relapse following an adequate trial of HDC with allogeneic stem cell transplantation of CML or AML; and
2. Qualified (or would have qualified) for authorization for HDC with allogeneic stem cell transplantation according to the provisions set forth in this policy.

E. 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. The list of indications is not all inclusive. Other indications are covered when documented by reliable evidence as safe, effective and comparable or superior to standard care (proven).

1. Aplastic anemia.
2. Acute lymphocytic or non-lymphocytic leukemias.
3. Chronic myelogenous leukemia.
4. Severe combined immunodeficiency.
5. Wiskott-Aldrich syndrome.
6. Infantile malignant osteopetrosis.
7. Blackfan-Diamond anemia.
8. Fanconi anemia.

9. Neuroblastoma.
10. X-linked lymphoproliferative syndrome.
11. Hunter syndrome.
12. Hurler syndrome.
13. Congenital amegakaryocytic thrombocytopenia.
14. Sickle cell anemia.
15. Globoid cell leukodystrophy.
16. Adrenoleukodystrophy.
17. Kostmann's Syndrome.
18. Lesch-Nyhan disease.
19. Intermediate and high grade non-Hodgkin's lymphoma.
20. Thalassemia major.
21. Myelodysplastic Syndrome.
22. X-linked hyper-IgM Syndrome.
23. Langerhans Cell Histiocytosis, refractory to conventional treatment.

F. Syngeneic (identical twin donor) stem cell transplantation is covered for the treatment of Hodgkin's disease.

G. TRICARE will reimburse costs for donor searches.

1. Charges for donor searches must be fully itemized and billed by the transplant center.

2. Costs for donor searches will be cost-shared in accordance with established reimbursement guidelines for outpatient diagnostic testing.

3. 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.

H. For the purposes of 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:

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1. Patients with undifferentiated leukemia, Chronic Myelogenous Leukemia (CML), aplastic anemia, Acute Lymphocytic Leukemia (ALL) or Acute Myelogenous Leukemia (AML), when histocompatible related or unrelated donors are not available, a 3 antigen mismatch is allowed for related donors.

2. 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 2-3 antigen mismatch is allowed.

I. **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 prior to the actual transplant. When **BMT, PSCT, or UCBT** is covered, all necessary steps are included in coverage. 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. In the event that the patient expires prior to the stem cell reinfusion being completed, benefits for the harvesting may be allowed.

J. Benefits are allowed for Hepatitis B and pneumococcal vaccines for patients undergoing transplantation.

K. Benefits may be allowed for Deoxyribonucleic Acid-Human leucocyte Antigen (DNA-HLA) tissue typing in determining histocompatibility.

L. 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.

M. Charges for the umbilical cord blood bank may be allowed only for patients who have undergone a covered transplant.

N. 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 Diagnostic 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.

O. Transportation of the patient 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.

P. 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 Point of Service rules.

IV. EXCLUSIONS

Benefits will not be paid for:

- A. 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.
- B. Expenses waived by the transplant center (i.e., beneficiary/sponsor not financially liable).
- C. Services and supplies not provided in accordance with applicable program criteria (i.e., part of a grant, or research program; unproven procedure).
- D. Administration of an unproven immunosuppressant drug that is not FDA approved.
- E. 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).
- F. Transportation of a donor.
- G. Allogeneic BMT for treatment of low grade non-Hodgkin's lymphoma is not a benefit.
- H. Autologous UCBT therapy as this procedure is considered unproven.
- I. Allogeneic BMT for neuroblastoma as this procedure is considered unproven.
- J. Allogeneic donor BMT (infusion) performed with or after organ transplants for the purpose of increasing tolerance of the organ transplant is considered unproven.
- K. HDC with ABMT or PSCT is not covered for treatment of breast cancer.
- L. HDC with allogeneic BMT is not a benefit for treatment of Waldenstrom's macroglobulinemia.
- M. HDC with stem cell rescue is not a benefit for the treatment of epithelial ovarian cancer.
- N. HDC with allogeneic stem cell transplantation is not covered for the treatment of cold agglutinin disease.
- O. Donor lymphocyte infusion if not specifically listed as covered in [paragraph III.D.](#) under POLICY above.
- P. Immunoablative therapy with bone marrow or peripheral stem cell transplantation is not covered for the treatment of multiple sclerosis.

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Q. Immunoablative therapy with BMT or PSCT is unproven and not covered for the treatment of rheumatoid arthritis and juvenile idiopathic arthritis.

R. Immunoablative therapy with allogeneic BMT or allogeneic PSCT is not covered for the treatment of systemic lupus erythematosus.

V. EFFECTIVE DATES

A. May 1, 1987, for HDC with ABMT or PSCT for Hodgkin's disease, non-Hodgkin's lymphoma and neuroblastoma.

B. November 1, 1987, for HDC with ABMT or PSCT for acute lymphocytic and nonlymphocytic leukemias.

C. November 1, 1983, for HDC with allogeneic BMTs using related donors.

D. July 1, 1989, for HDC with allogeneic BMTs using unrelated donors.

E. July 11, 1996, for HDC with ABMT or PSCT for multiple myeloma.

F. January 1, 1994, for HDC with ABMT and PSCT for Wilms' tumor.

G. January 1, 1995, for allogeneic UCBTs.

H. January 1, 1994, for HDC with ABMT or PSCT for chronic myelogenous leukemia.

I. January 1, 1996, for HDC with ABMT or PSCT for Waldenstrom's macroglobulinemia.

J. January 1, 1996, for allogeneic BMTs using related three antigen mismatch donors for patients with undifferentiated leukemia, Chronic Myelogenous Leukemia (CML), aplastic anemia, Acute Lymphocytic Leukemia (ALL) or Acute Myelogenous Leukemia (AML).

K. October 1, 1996, for HDC with ABMT or PSCT for AL Amyloidosis.

L. January 1, 1995, for allogeneic BMT for hypereosinophilic syndrome.

M. May 1, 1997, for HDC with ABMT or PSCT for trilateral retinoblastoma/pineoblastoma.

N. January 1, 1997, for HDC with ABMT or PSCT for follicular lymphoma.

O. January 1, 1997, for HDC with ABMT or PSCT for non-Hodgkin's lymphoma in first complete remission.

P. November 28, 1997, for HDC with ABMT or PSCT for Hodgkin's disease in second or third remission.

Q. January 1, 1996, for HDC with allogeneic BMT for multiple myeloma.

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- R. July 1, 1999, for HDC with ABMT or PSCT for germ cell tumors in a second or subsequent relapse.
- S. January 1, 1998, for HDC with ABMT or PSCT for osteosarcoma (osteogenic sarcoma).
- T. June 1, 1995, for allogeneic BMT for Chediak-Higashi syndrome.
- U. January 1, 1998, for allogeneic PSCT.
- V. June 1, 2003, for Langerhans Cell Histiocytosis, refractory to conventional treatment.
- W. January 24, 2002, for allogeneic stem cell transplant for Hodgkin's disease.
- X. May 19, 2005, for tandem autologous PSCT for high-risk neuroblastoma.
- Y. January 1, 2006, for HDC with ABMT or PSCT for desmoplastic small round cell tumor.
- Z. April 2, 2009, for immunoablative therapy with ABMT or autologous PSCT for severe systemic lupus erythematosus, refractory to conventional treatment.

AA. November 1, 2007, for Donor Lymphocyte Infusion (DLI) for AML.

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