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Subject: Autologous Bone Marrow and Stem Cell Transplantation

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DESCRIPTION:

Hematopoietic Stem-Cell Transplantation

Hematopoietic stem-cell transplantation (HSCT) refers to a procedure in which hematopoietic stem cells are infused to restore bone marrow function in those with cancer who receive bone-marrow-toxic doses of cytotoxic drugs, with or without whole-body radiation therapy. Bone marrow stem cells may be obtained from the transplant recipient (i.e., autologous HSCT) or from a donor (i.e., allogeneic HSCT). They can be harvested from bone marrow, peripheral blood, or umbilical cord blood and placenta shortly after delivery of neonates. Although cord blood is an allogeneic source, the stem cells in it are antigenically “naïve” and thus are associated with a lower incidence of rejection or graft-versus-host disease (GVHD).

Immunologic compatibility between infused stem cells and the recipient is not an issue in autologous HSCT. However, immunologic compatibility between donor and recipient is a critical factor for achieving a good outcome of allogeneic HSCT. Compatibility is established by typing of human leukocyte antigens (HLA) using cellular, serologic, or molecular techniques. HLA refers to the tissue type expressed at the HLA A, B, and DR loci on each arm of chromosome 6. Depending on the disease being treated, an acceptable donor will match the individual at all or most of the HLA loci.

The success of autologous HSCT is predicated on the ability of cytotoxic chemotherapy with or without radiation to eradicate cancerous cells from the blood and bone marrow. This permits subsequent engraftment and repopulation of bone marrow space with presumably normal hematopoietic stem cells obtained from the candidate prior to undergoing bone marrow ablation. As a consequence, autologous HSCT is typically performed as consolidation therapy when the individual’s disease is in complete

remission. Those who undergo autologous HSCT are susceptible to chemotherapy-related toxicities and opportunistic infections prior to engraftment, but not GVHD.

POSITION STATEMENT:

REQUIRED: Certificate of Medical Necessity

NOTE: Submitting a completed Certificate of Medical Necessity with your request for Autologous Bone Marrow and Stem Cell Transplantation is required.

Click the link below to open the form. Complete all fields on the form thoroughly. Print and submit a copy of the form with your faxed request.

Bone Marrow/Stem Cell Transplants – Certificate of Medical Necessity (*Word.doc*)

In accordance with **Chapter 59-B of the Florida Administrative Code [(1) – (6)]:**

(1) Autologous hematopoietic stem cell transplantation is covered when performed for one of the following indications:

- Acute myelogenous leukemia (stem cells collected in remission)
- Hodgkin's lymphoma
- Non-Hodgkin's lymphoma
- Ewing's sarcoma, chemotherapy sensitive after first relapse
- Neuroblastoma
- Germ cell tumor, after failure of first therapy but not progressing on salvage therapy
- Multiple myeloma (including double bone marrow transplant)
- Primary amyloidosis
- Primitive neuroectodermal tumor PNET (including medulloblastoma and pinealoblastoma), chemotherapy sensitive after first relapse
- Medulloblastoma and other PNET tumors, metastatic, at diagnosis
- Severe aplastic anemia unresponsive to immunosuppression

In cases where treatment for any of the above conditions includes a clinical trial that conforms to subsection (6) (below), routine care costs associated with the bone marrow transplant will be covered.

(2) Autologous hematopoietic stem cell transplantation is covered for the following indications when the bone marrow transplantation procedure is performed in the context of a well-designed clinical treatment trial (as described in subsection (6):

- Chronic lymphocytic leukemia
- Plasma cell dyscrasias other than multiple myeloma (e.g., Waldenstrom's)
- Breast carcinoma
- Ewing's sarcoma, localized, greater than 8 cm or metastatic at presentation
- Soft tissue sarcoma, pediatric, after failure of first therapy
- Wilm's tumor, at relapse
- Germ cell tumor, high risk, at diagnosis

- Multiple autologous bone marrow transplants for pediatric solid tumors
- Metastatic malignant melanoma
- Autoimmune disorders

(3) The following rare diseases, where there are no existing clinical trials available, are covered for bone marrow transplant at the Blood and Marrow Transplant Clinical Trials Network (BMT CNT) core or non-core facilities when deemed medically necessary:

- Myelofibrosis
- Chronic myelomonocytic leukemia (CMML)
- Paroxysmal nocturnal hemoglobinuria (PNH)
- POEMS syndrome

(4) Transplants from living related donors incompatible for one HLA-A, -B, and -DRB1 loci are covered for bone marrow transplant at BMT CTN core or non-core medical facilities.

(5) Any bone marrow transplant performed outside of a clinical trial will be covered when all the following criteria are met:

- The plan of care follows a clinical trial protocol that meets the requirements of subsection (6)
- Patient cannot be enrolled in the proposed clinical trial
- Bone marrow transplant treatment is medically necessary
- Patient is an appropriate candidate for bone marrow transplant, and
- Treatment center is part of the Blood and Marrow Transplant Clinical Trials Network (BMT CTN) as a core or non-core center

(6) A well-designed and conducted clinical treatment trial is one which includes an IRB-approved written protocol. At a minimum, such protocol shall have specific criteria for evaluating the effect of treatment with defined endpoints that are precise, meaningful, and reliable and which allow valid conclusions to be drawn about therapeutic efficacy and safety. Protocols should include an adequate statistical section describing the method of randomization and stratification, if any, expected outcome parameters relating to response rates, time to progression, survival times and other relevant information. Such clinical treatment trials shall be consistent with protocols reviewed and approved by the National Cancer Institute for scientific merit.

Autologous hematopoietic stem cell transplantation also **meets the definition of medical necessity** when performed for one of the following indications (in addition to any mandated coverage in subsections (1) – (6) above):

- **POEMS Syndrome** (polyneuropathy, organomegaly, endocrinopathy, M protein, and skin changes):
  - To treat disseminated POEMS syndrome (e.g., diffuse sclerotic lesions, disseminated bone marrow involvement)
- **Embryonal tumors of the central nervous system (CNS)** [includes medulloblastoma, medulloepithelioma, supratentorial PNETs (pineoblastoma, cerebral neuroblastoma, ganglioneuroblastoma), ependymoblastoma, and atypical teratoid/rhabdoid tumor (AT/RT):
  - As consolidation therapy for previously untreated tumors of the central nervous system (CNS) that show partial or complete response to induction chemotherapy, or stable disease after induction therapy; **OR**
  - To treat recurrent embryonal tumors of the CNS.

- **Testicular tumors:**
    - Tandem or sequential transplant either as salvage therapy or for platinum-refractory disease
- **Ewing's sarcoma:**
    - As initial treatment of high-risk Ewing's sarcoma [eg, the presence of metastatic disease; location of tumor in an area such as the pelvis; larger tumor size; older age of the individual] **OR**
    - For recurrent or refractory Ewing's sarcoma.
- **Germ cell tumors:**
    - In individuals with favorable prognostic factors [eg, those with a testis or retroperitoneal primary site, a complete response to initial chemotherapy, low levels of serum markers, and low-volume disease] that have failed a previous course of conventional-dose salvage chemotherapy, **OR**
    - In individuals with unfavorable prognostic factors [eg, an extratesticular primary site, an incomplete response to initial therapy, high levels of serum markers, high-volume disease, or relapsing mediastinal nonseminomatous germ cell tumors] as initial treatment of first relapse (ie, without a course of conventional-dose salvage chemotherapy), **OR**
    - In individuals with platinum-refractory disease, **OR**
    - Treatment of testicular tumors either as salvage therapy or with platinum-refractory disease
- **Acute lymphoblastic leukemia (ALL):**
    - To treat adult acute ALL in first complete remission but at high risk of relapse:
        - Age older than 35 years, **OR**
        - Leukocytosis at presentation of >30,000/µL (B-cell lineage) or >100,000/µL (T-cell lineage), **OR**
        - "Poor prognosis" genetic abnormalities such as the Philadelphia chromosome [t(9;22)], **OR**
        - Extramedullary disease, **OR**
        - Time to attain complete remission longer than 4 weeks
    - To treat pediatric acute ALL in first complete remission but at high risk of relapse:
        - Poor response to initial therapy, including prior response to prednisone prophase (defined as an absolute blast count of 1000/µL or greater), **OR**
        - Poor treatment response to induction therapy at 6 weeks, with ≥1% minimal residual disease measured by flow cytometry, **OR**
        - All children with T- cell phenotype, **OR**
        - Children with either the t(9;22) or t(4;11), regardless of early response measures
    - To treat pediatric ALL in second or greater remission
    - To treat pediatric refractory ALL
- **Waldenstrom macroglobulinemia:**
    - As salvage therapy of chemotherapy sensitive disease

It should be noted that there are non-malignant diseases that are genetic disorders or that result in bone marrow failure or lead to immunodeficiency syndromes for which bone marrow transplantation may be

appropriate. While these non-malignant diseases are not described in the preceding lists, there are generally accepted and appropriate indications for bone marrow transplantation in these cases. In addition, there are malignant diseases that are uncommon in their occurrence that also are not included in the above lists for which the appropriateness of bone marrow transplantation may be determined on a case by case basis.

Autologous bone marrow transplantation administered with high dose chemotherapy for all other indications is considered **experimental or investigational**, as there is insufficient scientific evidence to establish definite conclusions regarding the efficacy of autologous stem cell transplantation and specifically for the following indications:

- Solid tumors in adults (e.g., lung, colon, rectal, pancreas, stomach, bile duct, esophageal, gallbladder, renal cell, cervical, ovary, uterine, fallopian tube, prostate, nasopharyngeal, paranasal sinus, neuroendocrine tumors, thyroid, thymus, tumors of unknown primary origin)
- Autoimmune diseases such as multiple sclerosis, juvenile idiopathic and rheumatoid arthritis, systemic lupus erythematosus, systemic sclerosis/scleroderma, Crohns disease; chronic inflammatory demyelinating polyneuropathy (CIDP), immune cytopenias, relapsing polychondritis or type I diabetes mellitus (except as mandated in subsection (2) above)
- Breast cancer, except as mandated in subsection (2) above
- Malignant astrocytoma and glioma (including glioblastoma multiforme and oilgodendroglioma)
- Epithelial ovarian cancer
- Acute adult lymphoblastic leukemia (ALL) in second or greater remission or those with relapsed or refractory disease

Processing, cryopreservation, storage and thawing of peripheral stem cells is eligible for coverage if the harvesting and transplantation is covered.

Harvesting (bone marrow and peripheral stem cells) and cryopreservation (storage) services are eligible for coverage when a bone marrow transplant has been identified by the physician as a course of treatment and is planned or anticipated in the future.

Prophylactic collection and storage of cord blood from a neonate **does not meet the definition of medical necessity** when proposed for some unspecified future use as an autologous stem-cell transplant.

BILLING/CODING INFORMATION:

CPT Coding:

38204	Management of recipient hematopoietic progenitor cell donor search and cell acquisition
38206	Blood-derived hematopoietic progenitor cell harvesting for transplantation, per collection; autologous
38207	Transplant preparation of hematopoietic progenitor cells; cryopreservation and storage
38208	Transplant preparation of hematopoietic progenitor cells; thawing of previously frozen

	harvest, without washing, per donor
38209	Transplant preparation of hematopoietic progenitor cells, thawing of previously frozen harvest, with washing, per donor
38210	Transplant preparation of hematopoietic progenitor cells; specific cell depletion within harvest, T-cell depletion
38211	Transplant preparation of hematopoietic progenitor cells; tumor cell depletion
38212	Transplant preparation of hematopoietic progenitor cells; red blood cell removal
38213	Transplant preparation of hematopoietic progenitor cells; platelet depletion
38214	Transplant preparation of hematopoietic progenitor cells; plasma (volume) depletion
38215	Transplant preparation of hematopoietic progenitor cells; cell concentration in plasma, mononuclear, buffy coat layer
38232	Bone marrow, aspiration only, autologous
38241	Hematopoietic progenitor cell (HPC); autologous transplantation

HCPCS Coding:

S2150	Bone marrow or blood-derived stem cells (peripheral or umbilical), allogeneic or autologous, harvesting, transplantation, and related complications; including: pheresis and cell preparation/storage; marrow ablative therapy; drugs; supplies; hospitalization with outpatient follow-up; medical/surgical, diagnostic, emergency, and rehabilitative services; and the number of day of pre- and post-transplant care in the global definition (**non-covered**)

LOINC Codes:

The following information may be required documentation to support medical necessity: physician history and physical including previous transplants, physician progress notes, treatment plan, radiology report(s), operative and/or pathology report(s), laboratory studies, medication history, type of transplant and reason for transplant, smoking/alcohol/drug abuse history, cardiac and pulmonary clearances, psychosocial assessment and all diagnostic testing.

Documentation Table	LOINC Codes	LOINC Time Frame Modifier Code	LOINC Time Frame Modifier Codes Narrative

Physician history and physical	28626-0	18805-2	Include all data of the selected type that represents observations made six months or fewer before starting date of service for the claim
Attending physician visit note	18733-6	18805-2	Include all data of the selected type that represents observations made six months or fewer before starting date of service for the claim.
Treatment plan	18776-5	18805-2	Include all data of the selected type that represents observations made six months or fewer before starting date of service for the claim.
Radiology report	18726-0	18805-2	Include all data of the selected type that represents observations made six months or fewer before starting date of service for the claim
Physician operative report	28573-4	18805-2	Include all data of the selected type that represents observations made six months or fewer before starting date of service for the claim.
Laboratory studies	26436-6	18805-2	Include all data of the selected type that represents observations made six months or fewer before starting date of service for the claim.
Current, discharge, or administered medications	34483-8	18805-2	Include all data of the selected type that represents observations made six months or fewer before starting date of service for the claim.
Transplant Rx	22043-4	18805-2	Include all data of the selected type that represents observations made six months or fewer before starting date of service for the claim.
Transplant Rx at facility	21883-4	18805-2	Include all data of the selected type that represents observations made six months or fewer before starting date of service for the claim.

Transplant risk factors	44758-1	18805-2	Include all data of the selected type that represents observations made six months or fewer before starting date of service for the claim.
Reason for transplant	44756-5	18805-2	Include all data of the selected type that represents observations made six months or fewer before starting date of service for the claim.
History of tobacco use	11366-2	18805-2	Include all data of the selected type that represents observations made six months or fewer before starting date of service for the claim.
Alcohol abuse	42830-0	18805-2	Include all data of the selected type that represents observations made six months or fewer before starting date of service for the claim.
Drug abuse	42831-8	18805-2	Include all data of the selected type that represents observations made six months or fewer before starting date of service for the claim.
Cardiac screen assessment	39257-1	18805-2	Include all data of the selected type that represents observations made six months or fewer before starting date of service for the claim.
Pulmonary consultation note	34103-2	18805-2	Include all data of the selected type that represents observations made six months or fewer before starting date of service for the claim.
Psychosocial well-being, addressed in care plan	58168-6	18805-2	Include all data of the selected type that represents observations made six months or fewer before starting date of service for the claim.
Diagnostic studies (non-lab)	27899-4	18805-2	Include all data of the selected type that represents observations made six months or fewer before starting date of service for the claim.

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT.**

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Advantage Products: The following National Coverage Determination (NCD) was reviewed on the last guideline reviewed date: Stem Cell Transplantation (110.23) located at cms.gov.

DEFINITIONS:

Acquired: not genetic, but produced by influences originating outside the organism.

Allogeneic: having a different genetic constitution, but belonging to the same species. Allogeneic stem cell support provides two theoretical advantages – (1) the lack of tumor contamination associated with the use of autologous stem cells and (2) the possibility of a beneficial graft vs. tumor effect.

Autologous bone marrow cells: stem cells are harvested from the individual's own bone marrow prior to the cytotoxic therapy, then reinfused into the individual after the therapy.

Cryopreservation: preservation by subjection to extremely low temperatures.

HLA: special identifying markers that are on all cells of the body. HLA markers must match fairly closely between donor and recipient, or rejection may occur. HLA identical means that two people have the same markers as each other (this can occur in twins or brothers and sisters).

Leukemia: "liquid" tumors; a type of white blood cell that grows uncontrollably. Names are given depending on which type of white blood cell is abnormal. More sudden types include Acute Lymphoblastic Leukemia (ALL), Acute Non-lymphocytic Leukemia (ANLL), and Acute Myelocytic Leukemia (AML). More gradual types include Chronic Granulocytic Leukemia (CGL), Chronic Myelogenous Leukemia (CML) Chronic Myelomonocytic Leukemia (CMML), and Chronic Lymphocytic Leukemia (CLL).

Lymphoma: tumor of the white blood cells called lymphocytes. Different types include Hodgkin's, (Follicular) Non-Hodgkins (NHL), and Small Lymphocytic Lymphoma (SLL).

Myeloma: tumor of one of the types of white blood cells.

Stem cell support: a machine can separate only the most important cells (stem cells) from a bone marrow sample or blood sample (peripheral blood stem cells, PBSC), to be transplanted back into the same individual later, after treatment. The machine can also be used to remove cancerous stem cells and keep the normal cells. Stem cells can be collected from the bone marrow or from the peripheral blood.

Syngeneic: genetically identical especially with respect to antigens or immunological reactions. Refers to stem cells harvested from an identical twin.

Tandem transplant: two courses of high dose chemotherapy are given, opposed to the typical one course. Tandem transplants are typically administered at intervals of 2 – 6 months, depending on recovery from prior toxicity.

RELATED GUIDELINES:

Allogeneic Bone Marrow and Stem Cell Transplantation, 02-38240-01

OTHER:

Florida Statute 627.4236 Coverage for bone marrow transplant procedures (excerpt)

(1) As used in this section, the term "bone marrow transplant" means human blood precursor cells administered to a patient to restore normal hematological and immunological functions following ablative or nonablative therapy with curative or life-prolonging intent. Human blood precursor cells may be obtained from the patient in an autologous transplant or from a medically acceptable related or unrelated donor, and may be derived from bone marrow, circulating blood, or a combination of bone marrow and circulating blood. If chemotherapy is an integral part of the treatment involving bone marrow transplantation, the term "bone marrow transplant" includes both the transplantation and the chemotherapy.

(2) An insurer or a health maintenance organization may not exclude coverage for bone marrow transplant procedures recommended by the referring physician and the treating physician under a policy exclusion for experimental, clinical investigative, educational, or similar procedures contained in any individual or group health insurance policy or health maintenance organization contract issued, amended, delivered, or renewed in this state that covers treatment for cancer, if the particular use of the bone marrow transplant procedure is determined to be accepted within the appropriate oncological specialty and not experimental pursuant to subsection. (3) Covered bone marrow transplant procedures must include costs associated with the donor-patient to the same extent and limitations as costs associated with the insured, except the reasonable costs of searching for the donor may be limited to immediate family members and the National Bone Marrow Donor Program.

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COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Medical Policy & Coverage Committee on 03/22/18.

GUIDELINE UPDATE INFORMATION:

08/15/02	Medical Coverage Guideline Reformatted – Revised to reflect criteria set forth in Chapter 59-B of the Florida Administrative Code.

02/15/03	2003 HCPCS coding update.
08/15/03	Reviewed – no changes in coverage statement.
01/01/04	Annual HCPCS coding update.
04/01/04	2nd Quarter 2004 HCPCS coding update.
09/15/04	Scheduled review; no change in coverage statement.
01/01/05	HCPCS coding update: revised descriptor for S2150.
05/15/05	Revision consisting of addition of ICD-9 diagnosis code for primary amyloid light chain amyloidosis (277.3).
09/15/05	Scheduled review; expand list of covered indications to include metastatic malignant melanoma and multiple transplants for pediatric solid tumors.
09/15/06	Scheduled review; coverage statement revised to be consistent with Florida Administrative code 59B-12.
07/15/07	Scheduled review; reformatted guideline; updated references.
01/01/08	Annual HCPCS coding update: removed G0265, G0266, and G0267.
09/15/08	Scheduled review; revise position statement. Add excerpt from Florida Statute. Update references.
09/15/09	Scheduled review; update position statement and references.
10/15/10	Scheduled review; added ICD-10 codes added; revised to reflect criteria set forth in Chapter 59-B of the Florida Administrative Code, and; references updated; guideline reformatted.
09/15/11	Scheduled review; added Medicare program exception and updated references, formatting changes.
01/01/12	Annual HCPCS coding update. Added 38232. Revised 38208 and 38209 descriptors. Deleted 38230.
05/15/12	Revision; reformatted guideline.
06/15/12	Scheduled review. Revised description section and position statement. Added statement regarding cord blood collection and storage. Updated references and reformatted

	guideline.
01/01/13	Annual CPT coding update. Revised code descriptor for 38241.
09/15/13	Revision; updated Florida Administrative Rule 59B-12.001 language.
10/15/13	Scheduled review. Revised position statement and updated references.
11/15/14	Scheduled review. Revised position statement and updated references.
11/15/15	Scheduled review. Revised position statement and updated references.
05/15/16	Revision: updated coverage criteria for adult and pediatric acute lymphoblastic leukemia. Updated references.
01/01/18	Annual CPT/HCPCS coding update: deleted 38220.
04/15/18	Scheduled review. Revised criteria for germ cell tumor and list of conditions considered E/I. Revised Medicare Advantage program exception. Updated references.
01/15/2019	Revision: updated language regarding prophylactic collection and storage of cord blood from a neonate.