



Subject: *Allogeneic Stem Cell Transplant*

Number: *200306-0005*

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Important note

Even though this policy may indicate that a particular service or supply is considered covered, this conclusion is not based upon the terms of your particular benefit plan. Each benefit plan contains its own specific provisions for coverage and exclusions. Not all benefits that are determined to be medically necessary will be covered benefits under the terms of your benefit plan. You need to consult the terms of your own benefit plan to determine if there are any exclusions or other benefit limitations applicable to this service or supply. If there is a discrepancy between this policy and your plan of benefits, the provisions of your benefits plan will govern. However, applicable state mandates will take precedence with respect to fully insured plans and self-funded non-ERISA (e.g., government, school boards, church) plans. Unless otherwise specifically excluded, Federal mandates will apply to all plans. With respect to Medicare and Medicaid members, this policy will apply unless Medicare and Medicaid policies extend coverage beyond this Medical Policy & Criteria Statement. Medicare and Medicaid policies will only apply to benefits paid for under Medicare or Medicaid rules, and not to any other health benefit plan benefits. CMS's Coverage Issues Manual can be found on the following website:

<http://cms.hhs.gov/manuals/pub06pdf/pub06pdf.asp>

Overview

A stem cell – commonly referred to as bone marrow – transplant may be medically necessary for patients with certain diagnoses. Stem cells from bone marrow, peripheral blood or the patient's own umbilical cord blood are used in the transplant. The different types of stem cell transplants are allogeneic, autologous, and syngeneic.

In an **allogeneic** transplant, stem cells are harvested from a donor. In an autologous transplant, stem cells are harvested from the patient's own bone marrow for retransplant after high dose (cytotoxic) chemotherapy. Syngeneic transplant refers to stem cells harvested from an identical twin. The use of this form of transplant is limited due to the rarity of identical twins.

The terms stem cell infusion, re-infusion, support or transplant are used interchangeably in this policy; they essentially have the same meaning in this application. The focus of this policy is the allogeneic stem cell transplant (ASCT). There is a separate policy for autologous stem cell transplants (AuSCT).

Policy and criteria

NOTE: These services require prior authorization by the Plan Medical Director.

Please refer to the **Transplant Policy** for additional information regarding covered and non-covered services.

When services are covered:

We cover ASCT (including bone marrow, peripheral blood, and umbilical cord blood as per the guidelines below) for the following conditions.

Reduced intensity transplant (nonmyeloablative ASCT or mini-allograft transplant) is covered for any of the following diagnoses if the member is eligible according to the designated transplant facility's

protocol for conventional ASCT. In the absence of a formal protocol, the member must meet the criteria stated in this policy. This particular procedure in these cases represents a technical modification of an established procedure.

Leukemias:	Exclusions
<ul style="list-style-type: none"> • ALL (Acute Lymphocytic Leukemia) in the first or subsequent remission when the member is 55 years of age or younger and meets ANY of the following high-risk criteria: <ul style="list-style-type: none"> ○ Presence of chromosomal abnormalities, including ANY of the following: <ul style="list-style-type: none"> ▪ Philadelphia (Ph) chromosome; or ▪ Presence of t (9,22); or ▪ Presence of t (4,11); or ○ At a minimum, patient partially responds to chemotherapy but fails to achieve complete remission within 6 weeks of the start of induction therapy; or ○ B-cell lineage with white blood cell count > 30,000/uL. • ANLL (Acute Non-Lymphocytic Leukemia) in the first or subsequent remission • CGL (Chronic Granulocytic Leukemia) • CML (Chronic Myelogenous Leukemia) 	<p>Autologous or tandem (or sequential) transplants for the treatment of ALL as these treatments are considered investigational and experimental for this indication.</p> <p>Chronic Lymphocytic Leukemia (CLL) – there is not enough scientific evidence to show that this procedure prolongs survival compared to standard chemotherapy</p>

Lymphomas:	Exclusions
<p>Hodgkin’s Lymphoma (HL) or Hodgkin’s Disease (HD)</p> <ul style="list-style-type: none"> • Stage III or IV A or B patients who are either in relapse, or refractory to primary chemotherapy; AND • First or second relapse and maximal chemotherapy and/or radiotherapy has induced only a partial remission; OR the patient is in a second, complete remission; AND • Chemo-responsive disease (see note below); AND • The patient is less than 55 years of age; AND • Performance status (ECOG score) 0 to 1; AND • Organ function intact, as evidenced by <ul style="list-style-type: none"> ○ Cardiac function – LVEF \geq 45% predicted ○ Pulmonary function – FVC/FEV1/DLCO \geq 50%; AND • No comorbid disease that may substantially limit his/her ability to survive marrow ablation <p>Note: Chemo-responsiveness means a tumor demonstrates complete or partial (at least 50% decrease) remission.</p> <p>Non-Hodgkin’s Lymphoma (NHL)</p> <ul style="list-style-type: none"> • Stage III or IV A or B, intermediate and high-grade NHL in 	<p>Tandem transplants for the treatment of HL/HD as this treatment is considered investigational and experimental for this indication.</p> <p>Patients with Small Lymphocytic Lymphoma (SLL)</p> <p>Autologous or tandem transplants for the treatment of NHL as these treatments are considered investigational and experimental for this indication.</p>

<ul style="list-style-type: none"> • second or subsequent clinical remission; OR • Stage IV A or B, high-grade NHL with a lymphoma mass over 10 cm and with more than one involved extranodal site, in first clinical remission, because these patients have such a high likelihood of recurrence; AND • Patient has a HLA-matched donor; AND • Performance status (ECOG score) of 0 to 1; AND • Organ function intact, as evidences by <ul style="list-style-type: none"> ○ Cardiac function – no symptomatic CHF; and ○ Pulmonary function – FVC/FEV1/DLCO \geq 50% 	
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Lymphomas (continued)	Exclusions
<p>Follicular Non-Hodgkin’s Lymphoma for patients who have failed primary therapy.</p> <p>Mantle cell lymphoma in first clinical remission.</p>	

Sickle cell anemia:	Exclusions
<p>Patients who meet all the following:</p> <ul style="list-style-type: none"> • documented homozygous sickle cell anemia • children and young adults (\leq 25 years of age) • who have an HLA-matched, related donor • one or more of the following features associated with increased risk of stroke or end-organ damage: <ul style="list-style-type: none"> ○ prior stroke (CVA) ○ recurrent chest syndrome ○ recurrent vaso-occlusive ("pain") crises ○ red blood cell allo-immunization on chronic transfusion 	<p>Patients with any of the following are excluded as scientific evidence is not available to show that this will improve the patient’s health in these cases</p> <ul style="list-style-type: none"> • sickle cell trait • transplant donor who is not HLA-identical

ASCT is also covered for the following conditions:

Aplastic Anemia criteria:

- Patient is 40 years of age or younger; AND
- Has severe or very severe aplastic anemia, including congenital diseases (such as Fanconi’s anemia or Diamond-Blackfan syndrome) or acquired diseases (such as due to drug or toxin exposure). Severe is generally defined as:
 - platelets $<$ 20 x10/L, granulocytes $<$ 0.5 x10/L, and reticulocytes $<$ 1% (corrected for hematocrit).
 - 6 of 6 antigen matched related or unrelated donor *or* 5 of 6 antigen matched family member donor, for patients failing antithymocyte globulin therapy; OR
 - Has a HLA-matched, related donor (see Note below for unrelated bone marrow transplantation)

Note: For patients \geq 20 years of age lacking HLA-matched, related donors, ASCT may be considered if they have failed two courses of immunosuppressive therapy (IST). For patients $<$ 20 years of age lacking HLA-matched, related donors, one course of IST should have been tried.

Mucopolysaccharidosis (Hunter's, Hurler's, Sanfilippo or Maroteaux-Lamy) criteria:

- Patient is neurologically intact; AND
- Using a 5 or 6 of 6 antigen matched, HLA molecular typing negative family member donor

Mucopolipidoses (Gaucher's, metachromic leukodystrophy, globoid cell leukodystrophy, or adrenoleukodystrophy) criteria:

- Patient is neurologically intact; AND
- Failed conventional therapy (such as diet modification or enzyme therapy); AND
- Using a 5 or 6 of 6 antigen matched, HLA molecular typing negative family member donor

Myelodysplasia/myelofibrosis criteria:

- Patient is less than 60 years of age; AND
- Has refractory anemia (idiopathic or secondary to drug or toxin exposure); AND
- Using an HLA-identical donor; AND
- Has one or more of the following:
 - excess blasts
 - excess blasts in transformation
 - chronic myelomonocytic leukemia
 - increasing blast counts or ringed sideroblasts, with at least one of the following:
 - neutropenia (WBC <500/mm³)
 - thrombocytopenia (platelets <20,000/mm³)
 - chromosomal abnormalities

Multiple Myeloma when ALL of the following criteria are met:

- Performance status – SWOG/ECOG score 0 to 1; AND
- Adequate organ function
 - Cardiac function – LVEF \geq 45% predicted; and
 - Pulmonary function – FVC/FEV1/DLCO \geq 50%

High-Risk Neuroblastoma defined as ANY one of the following categories:

- Stage IV disease, patients aged 1 to 18 years
- Stage IV or IVS disease, patients <1 year; AND tumor with > 10 copies of the n-mvc gene
- Stage III disease with at least one of the following:
 - At least 10 copies of the n-mvc gene
 - Unfavorable histopathology by the Shimada classification
 - Elevated serum ferritin (> 142 ng/ml by radioimmunoassay or positive by counterimmunoelectrophoresis)
- Stage II disease, patients > 10 years AND > than 10 copies of the n-mvc gene
- Stage I, II or IVS, patients > 1 year at presentation with subsequent development of disseminated disease without interval chemotherapy or radiotherapy

Criteria for high-risk neuroblastoma are:

- As primary treatment for patients in Stage II to III when associated with more than 10 copies of the n-mvc oncogene; OR
- As primary treatment for patients in Stage IV; OR
- As therapy for primary recurrent or refractory* disease for patients who are unlikely to attain a durable remission with further conventional-dose therapy.

* Primary refractory is defined as a tumor that does not achieve a complete remission after initial standard dose chemotherapy.

Severe Combined Immunodeficiency (SCID) criteria:

- Using a 4, 5, or 6 of 6 antigen matched, HLA molecular typing negative related or unrelated donor

Thalassemia (homozygous beta-thalassemia) criteria:

- For patients with beta thalassemia major, using a 6/6 antigen matched, related or unrelated donor; OR
- In children and young adults when BOTH of the following criteria are met:
 - Patients show deterioration with conventional treatments including transfusions, splenectomy, and deferoxamine; and
 - Have a HLA-matched, related donor

Wiskott-Aldrich Syndrome and Infantile Malignant Osteoporosis (Albers-Schonberg disease, also known as marble bone disease) criteria:

- Using a 6/6 antigen matched, HLA molecular typing negative related or unrelated donor

ASCT is also covered for the following conditions:

- Kostmann's Syndrome (severe infantile agranulocytosis)
- Leukocyte Adhesion Deficiencies
- X-linked Lymphoproliferation Syndrome
- Amegakaryocytic Thrombocytopenia

When services are not covered:

We **do not cover** ASCT – conventional or reduced intensity – for the following indications:

- Autoimmune diseases (including but not limited to Multiple Sclerosis, Systemic Lupus Erythematosus, Systemic Sclerosis, Rheumatoid Arthritis (RA), Juvenile RA, Idiopathic Thrombocytopenic Purpura, Dermatomyositis and Polymyositis)
- Breast Cancer
- CLL
- Melanoma
- Other Solid Tumors
- Ovarian Cancer
- Polycythemia vera
- Renal Cancer
- Testicular Cancer

We do not cover **salvage High Dose Chemotherapy (HDC) and ASCT after HDC and autologous stem cell transplant (AuSCT)** for patients with:

- recurrent neuroblastoma or
- metastatic breast cancer or
- germ cell tumors in relapse or
- any other solid tumor

There is no evidence that this procedure improves health outcomes of patients with solid tumors.

We do not cover **salvage HDC/ASCT for relapse of incomplete remission after HDC/AuSCT** for patients with:

- multiple myeloma,
- non-Hodgkin's or Hodgkin's lymphoma,
- acute myeloblastic leukemia,
- acute lymphoblastic leukemia, and
- neuroblastoma

We do not cover **reduced intensity transplants for renal cancer and other solid tumors of solid tissues or organs**. Currently, there is no long-term data available to determine whether these transplants are as effective as standard ASCT.

We do not cover **tandem or sequential transplant for the treatment of patients with multiple myeloma or high-risk neuroblastoma**. There is insufficient scientific evidence that this approach is effective.

We do not cover **reduced intensity transplants** if the member is **ineligible for conventional ASCT** either according to the designated transplant facility's protocol or the criteria stated in this policy. There is insufficient scientific evidence that mini-allograft is effective equal to or more effective than conventional ASCT or that it has a reduced incidence of morbidity and mortality.

We do not cover **harvesting of tissue for the purpose of storage only**.

<i>Guidelines for use of umbilical cord blood:</i>	Exclusions
<p>We cover the use of umbilical cord stem cells for transplants that are otherwise covered for either HDC with stem cell support, or for bone marrow transplant, when all the following are met:</p> <ul style="list-style-type: none"> • Recipient is a child or adult • There is no other available stem-cell donor with the same or better matching characteristics • Cord blood is HLA mismatched at less than or equal to 1 antigen • Donors may be related or unrelated 	<p>Facility providing umbilical cord blood that is not in compliance with any existing FDA regulations governing umbilical cord transplants. FDA regulations were still being developed as of June 2003.</p> <p>There is a 2 or greater antigen mismatch, because there is insufficient data regarding health outcomes for these procedures</p> <p>There is a suitable stem cell donor of equal or superior HLA match</p> <p>Storage for future use, in case of a future need for transplant</p>

<i>Guidelines for use of allogeneic peripheral blood:</i>	Exclusions
We cover mobilized peripheral blood stem cells from allogeneic	Non-hematologic malignancies, as

<p>donors, when all the following are met:</p> <ul style="list-style-type: none"> • Hematologic malignancies • Donor is related, and HLA matched at 5 or more loci 	<p>there is not enough scientific evidence to show that health outcome is improved or not for patients with these tumors</p> <p>Unrelated donors or related donors with fewer than 5 HLA loci match, as results from clinical trials unavailable (as of June 2003) to speak to this issue.</p>
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<p>Products to which this policy applies:</p> <ul style="list-style-type: none"> ⊕ Commercial Plan (Direct, Select & PPO Plans) ⊕ The Independent Plan ⊕ Fallon Flex ⊕ Major Medical ∅ Medicare Plan – refer to CMS for policy and criteria.
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