



Subject: *Autologous Stem Cell Transplant*

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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 autologous stem cell transplant (AuSCT). There is a separate policy for allogeneic stem cell transplants (ASCT).

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 AuSCT (including bone marrow, peripheral blood, and umbilical cord blood as per the guidelines below) for the following conditions:

Breast Cancer:	Exclusions
Breast Cancer in accordance with state mandate Chapter 458 (1/13/94), according to the rules and regulations of the	Patients who are refractory to systemic therapy, because there is insufficient

<p>Department of Public Health. According to state law, treatment must conform to that of NCI-sponsored protocols (CALBG 9082, ECOG/SWOG INT 0121, PBT-1) or conform to standards set by the department of public health. We cover stem cell transplants for women with metastatic breast cancer, in any of the following circumstances:</p> <ul style="list-style-type: none"> • Previously untreated • Currently responsive to primary systemic chemotherapy • Relapse following response to first-line therapy 	<p>evidence to show that women who do not respond to systemic therapy will benefit from high-dose chemo with stem cell support.</p>
<p>Lymphomas:</p>	<p>Exclusions</p>
<p>Hodgkin's Lymphoma</p> <p>Stage III or Stage IV A or B patients who are either in relapse or refractory to primary chemotherapy</p> <p style="text-align: center;">OR</p> <p>Stage IIIB, Stage IVA or B patients, or patients with relapsed disease of ANY Stage; AND</p> <p>Maximal primary chemotherapy and/or radiotherapy has induced only a partial remission; AND</p> <p>Patient is in a 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</p> <p>Patient is 65 years of age or younger; AND</p> <p>Performance status (ECOG score) of 0 to 1; AND</p> <p>Organ function is intact, as indicated by;</p> <ul style="list-style-type: none"> • Cardiac function – LVEF \geq 45% predicted • Pulmonary function – FVC/FEV1/DLCO \geq 50% <p>Non-Hodgkin's Lymphoma</p> <p>Stage III¹⁰ or IV A or B, intermediate and high-grade NHL in second or subsequent clinical remission</p> <p>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</p> <p style="text-align: center;">OR</p>	<p>Patients with SLL (Small Lymphocytic Lymphoma)</p> <p>Patients with NHL and ANY of the following contraindications:</p> <ul style="list-style-type: none"> • Evidence of low-grade histology • Comorbid diseases (e.g., uncontrolled HTN, poorly controlled DM) • Evidence of serious organ dysfunction

<p>Patient has any one of the following histology types:</p> <ul style="list-style-type: none"> • Intermediate-grade 1 <ul style="list-style-type: none"> ○ Follicular, large-cell Diffuse, small-cleaved cell Diffuse, mixed and large-cell Diffuse, large-cell <p style="text-align: center;">OR</p> <ul style="list-style-type: none"> • High-grade 1 <ul style="list-style-type: none"> ○ Large-cell immunoblastic Lymphoblastic Small non-cleaved cell, Burkitt's lymphoma; <p style="text-align: center;">AND</p> <ul style="list-style-type: none"> • Chemo-responsive disease* <p>*Note: Chemo-resistant disease in which the disease is relapsed and widely metastatic and ASCT cannot be offered because an HLA-matched donor is available will also be considered.</p> <p style="text-align: center;">AND</p> <ul style="list-style-type: none"> • Organ function is intact, as evidenced by: <ul style="list-style-type: none"> ○ Renal – creatinine clearance > 40 ml/min or serum < 2 mg/ml ○ Hepatic – no history of severe chronic liver disease (direct bilirubin ≤ 1.5 mg/dl) ○ Cardiac – no symptomatic CHF ○ Pulmonary – FVC/FEV1/DLCO ≥ 60% of predicted <p>Responsiveness is when the tumor is in complete or partial (reduced by at least 50%) remission.</p> <p>Follicular Non-Hodgkin's Lymphoma for patients who have failed primary therapy</p> <p>Mantle cell lymphoma in first clinical remission</p>	
<p>Neuroblastomas:</p>	<p>Exclusions</p>
<p>For children over 1 year of age who are in remission</p>	<p>High-grade glial tumors of the brain in adults, because there is not enough scientific evidence that this procedure improves survival or control of disease</p>

	progression compared to conventional chemotherapy.
Leukemias:	Exclusions
<p>ALL (Acute Lymphoblastic Leukemia), in first complete remission when there is a high risk for relapse (adults and children)</p> <p>ANLL (Acute Non-Lymphocytic Leukemia) in the first or subsequent remission</p>	<p>ALL in adults in second or subsequent complete remission and adults not in complete remission as it has not been shown to improve health outcomes compared to conventional therapy.</p> <p>CLL (Chronic Lymphocytic Leukemia) as there is not enough scientific evidence to show that this procedure prolongs survival compared to standard chemotherapy.</p> <p>CML (Chronic Myelogenous Leukemia) as there is not enough scientific evidence to show that this procedure prolongs survival compared to standard chemotherapy.</p>
Multiple Myeloma:	Exclusions
<ul style="list-style-type: none"> • Myeloma Intergroup Trial INT 141 official enrollment in this trial sponsored by the National Cancer Institute (NCI). We are supporting this trial in hopes that the scientific data obtained will help determine the optimal role for BMT in multiple myeloma; OR • Multiple Myeloma patients with newly diagnosed or responsive disease, including: <ul style="list-style-type: none"> ○ Patients with newly diagnosed previously untreated disease ○ Patients in complete or partial remission from treatment ○ Patients in a relapse that is responding to treatment 	<ul style="list-style-type: none"> • Patients with refractory disease, including: <ul style="list-style-type: none"> ○ Patients with primary resistance ○ Patients in resistant relapse <p>as there is not enough data to show that health outcomes will be improved for these patients with multiple myeloma.</p> • Patient is pregnant • Patient is HIV positive (with or without AIDS) • Evidence of heart disease: <ul style="list-style-type: none"> ○ Myocardial infarction within 6 months of treatment ○ Cardiac arrhythmia ○ Cardiomegaly • Other significant heart disease unrelated to myeloma • Previous radiation therapy to bone marrow sites (pelvis, spine), unless the radiation therapist gives approval • Other invasive cancer or other significant medical condition present (including any residual plasmacytoma)

	<ul style="list-style-type: none"> We do not cover tandem high-dose chemoradiotherapy with autologous stem cell support for responsive multiple myeloma We do not cover single or tandem high-dose chemotherapy with autologous stem cell support for resistant multiple myeloma
Germ Cell Cancer:	Exclusions
<p>For testicular, mediastinal, retroperitoneal, and ovarian germ cell tumors that are refractory to standard dose chemotherapy as follows:</p> <ul style="list-style-type: none"> Patients with advanced disease who fail to achieve complete response to second-line standard dose platinum therapy or Patients with minimal or moderate extent of disease who fail to achieve a complete response to third-line standard-dose platinum therapy 	<p>Patients who have not failed standard-dose chemotherapy with platinum-based therapies as there is not enough scientific evidence to suggest improved survival or control of disease progression compared to conventional chemotherapy.</p> <p>As the initial course of therapy as it is considered experimental and investigational for any of these indications.</p> <p>For treatment of epithelial and mixed epithelial/germ cell ovarian cancers as experimental and investigational for this indication.</p>

AuSCT is also covered for the following conditions:

Multiple Myeloma when ALL of the following criteria are met:

- No significant comorbid conditions; AND
- Performance status – Karnofsky score of $\geq 60\%$, or ECOG score of 0 to 2; AND
- No extensive prior chemotherapy or radiation therapy (i.e., more than a year of alkylator-based chemotherapy and/or more than two prior alkylator-based chemotherapies; radiation therapy to no more than 10% of marrow producing bones); AND
- Adequate liver function – bilirubin, SGOT $< 1.5x$ normal; AND
- Adequate major organ function;
 - Cardiac function – LVEF $\geq 45\%$ predicted; and
 - Pulmonary function – FVC/FEV1/DLCO $\geq 50\%$; and
- No evidence of cardiac amyloid; AND
- No evidence of indolent myeloma, smoldering myeloma, and/or monoclonal gammopathy of uncertain significance [MGUS]

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.

When services are not covered:

We do not cover AuSCT for the following indications:

- **Epithelial Ovarian Cancer** – the morbidity and mortality of this treatment is greater than with standard therapy. The scientific data does not include enough patients with long term follow-up to show conclusions about improved survival.
- **Solid Tumors (other than those previously listed)** in adults as it has not been shown to prolong survival, and in some cases, there is greater mortality.

We do not cover **high-dose chemotherapy (HDC) with or without AuSCT for autoimmune diseases** including but not limited to Rheumatoid Arthritis (RA), Juvenile RA, Systemic Lupus Erythematosus (SLE), Systemic Sclerosis, Multiple Sclerosis, Idiopathic Thrombocytopenic Purpura, Dermatomyositis and Polymyositis as there is insufficient evidence concerning its effectiveness on health outcomes.

We do not cover **HDC with AuSCT for patients with primary amyloidosis** as there is insufficient evidence concerning its effectiveness on health outcomes.

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

Note: We do not cover services to collect and bank umbilical cord blood for future possible use, when there is no curative treatment available for the patient's condition.

Products to which this policy applies:	
⊕	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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