



**BlueCross BlueShield
of Vermont**

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Corporate Medical Policy

Transplants

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Description of Procedure or Service

Heart

A heart transplant consists of replacing an end-stage diseased heart with a healthy donor heart

Heart/Lung

A combined heart/lung transplant is intended to prolong survival and improve function in patients with end-stage cardiopulmonary or pulmonary disease. The technique involves a coordinated triple operative procedure consisting of procurement of a donor heart-lung block, excision of the heart and lungs of the recipient, and implantation of the heart and lungs into the recipient. A heart/lung transplant refers to the transplantation of 1 or both lungs and heart from a single cadaver donor.

Lung

A lung transplant refers to single-lung or double-lung replacement. In a single-lung transplant, only 1 lung from a cadaver donor is provided to the recipient. In a double-lung transplant, both the recipient's lungs are removed and replaced by the donor's lungs.

In a lobar transplant, a lobe of the donor's lung is excised, sized appropriately for the recipient's thoracic dimensions, and transplanted. Donors for lobar transplant have been primarily living- related donors, with 1 lobe obtained from each of 2 donors (e.g., mother and father) in cases where a bilateral transplant is required. There are also cases of cadaver lobe transplants.

Liver

Recipients

Liver transplantation is now routinely performed as a treatment of last resort for patients with end-stage liver disease. Patients are prioritized for transplant according to length of time on the waiting list and severity of illness criteria developed by the United Network of Organ Sharing (UNOS).

Donors

Due to the scarcity of donor livers, a variety of strategies have been developed to expand the donor pool. For example, split graft refers to dividing a donor liver into 2 segments that can be used for 2 recipients. Living donor transplantation of the left lateral segment is now commonly performed between parent and child.

Small bowel

A small bowel transplant is typically performed in patients with short bowel syndrome. This is a condition in which the absorbing surface of the small intestine is inadequate due to extensive disease or surgical removal of a large portion of small intestine. Etiologies of short bowel syndrome include volvulus, atresias, necrotizing enterocolitis, Crohn's disease, gastroschisis, thrombosis of the superior mesenteric artery, desmoid tumors, and trauma. Patients with short bowel syndrome are unable to obtain adequate nutrition from enteral feeding and become dependent on total parenteral nutrition (TPN). Patients with complications from TPN may be considered candidates for small bowel transplant. Complications include catheter-related mechanical problems, infections, hepatobiliary disease, and metabolic bone disease. While cadaveric intestinal transplant is the most commonly performed transplant, there has been recent interest in using living donors.

Note: A small bowel transplant may be performed in conjunction with other visceral organs, including the liver, duodenum, jejunum, ileum, pancreas, or colon. When the small bowel and liver are transplanted in conjunction other gastrointestinal organs, the procedure is referred to as a multivisceral transplant.

Pancreas and Pancreas/Kidney Transplant

Transplantation of a normal pancreas is the only treatment method for delivering insulin in response to glucose concentration. Metabolic glucose control is intended to prevent, halt, or reverse the secondary complications of insulin dependent diabetes mellitus (IDDM). Achievement of insulin independence with resultant decreased morbidity and increased quality of life is the primary health outcome of pancreas transplantation. While pancreas transplantation is generally not considered a life-saving treatment, in a small subset of patients who experience life-threatening complications from IDDM, pancreas transplantation could be considered life saving.

Transplant candidates include: (1) IDDM patients with renal failure who may be given a cadaveric simultaneous pancreas/kidney transplant (SPK); (2) IDDM patients who may be given a cadaveric pancreas transplant at a period of time following kidney transplantation from either a cadaveric or a living-related donor (pancreas after kidney, i.e., PAK); and (3) non-uremic IDDM patients with specific severely disabling and potentially life-threatening diabetic problems who may be offered a pancreas transplant alone (PTA). The experience with SPK transplants is more extensive than that of other transplant options.

Autologous bone marrow transplantation (BMT)

A procedure in which a person's own bone marrow/stem cells are removed, stored, and then given back to the person after intensive treatment.

Allogeneic Stem Cell Transplantation, including Peripheral, Umbilical Cord Blood, and Bone Marrow Transplants.

A procedure in which a person receives stem cells/bone marrow from a genetically similar but not identical donor.

Policy Guidelines

A. General Transplant Information

Benefits are subject to all terms, limitations and conditions of the subscriber contract.

The Plan will provide coverage for organ transplants when it is determined to be medically necessary.

Prior Approval is required by the Plan for all transplants except kidney and cornea.

For New England Health Plan (NEHP) members an approved referral authorization from the PCP is required.

Requests for prior approval must be in writing from the provider, and must include the following information:

- The patient's current medical condition, and clinical information relating specifically to transplant necessity; and
- The qualification of the physicians performing the transplant procedure; and
- The qualification of the facility hosting the transplant procedure; and
- Protocols and informed consent documents for bone marrow or stem cell transplants; and
- Protocols and informed consent documents for organ transplants that do not follow standard protocols.

Plan approvals are limited to one year following the request. The provider may request an extension of the Plan's approval and forward updated medical information to the medical services department.

In some instances, an organ transplant candidate may request to be listed at multiple facilities. These requests are also subject to Plan Prior Approval as noted above, and certain conditions or restrictions may apply as they relate to duplicative services or charges.

For all TVHP and VHP members if a network facility has the capacity to perform the requested transplant, members must use one of these facilities in order to obtain benefits. There are no standard benefits for transplant services.

In addition to Preferred transplant facilities, transplant candidates undergoing organ transplant have access to the Blue Quality Centers for Transplant (BQCT), a centers of

excellence program. BQCT institutions are selected based on their ability to meet defined clinical quality criteria that are unique for each type of transplant.

Transplant candidates except for cornea and kidney are referred to Specialty Case Management. The case manager will provide information about BQCT and approved facilities, and can assist in arranging for the transplant to occur at a BQCT facility when applicable. Not all transplant candidates are appropriate for Case Management at the time of request for benefit approval, however, transplant candidates will be followed by Medical Services and will be placed in Case Management when appropriate and when written consent is obtained from the member.

For the purposes of re-insurance, claims will be reviewed by medical services to verify if they are transplant related except for corneal and kidney transplants.

When service or procedure is covered

Benefits are available for the following services related to transplants:

- search for a donor;
- surgical removal of an organ;
- storage and transportation costs for the organ, partial organ or bone marrow; and
- costs directly related to the solid organ or bone marrow donation, including costs resulting from complications of the donor's surgery.

The Plan pays benefits for transplants as follows:

- for transplants using a deceased donor, we limit benefits for the search, removal, storage and transportation of the organ to \$35,000 per solid organ transplant.
- for transplants using a live donor, we limit benefits for surgical expenses and storage and transportation of the organ to \$65,000 for each covered organ transplant procedure completed;
- if we cover both the recipient and the donor, each receives benefits under his or her own Contract;
- if we cover the recipient, but not the donor, both receive benefits under the recipient's Contract (benefits available to the recipient will be paid first);
- no benefits are available if we cover the donor, but not the recipient.
- benefits for transplant-related office visits, labs or Prescription Drugs are subject to the terms and conditions in the other sections of your Contract, including Co-payments and the General Exclusions..

When Service or Procedure is not covered

- no benefits are available for the purchase price of any organ or bone marrow that is sold rather than donated, and/or charges for transplant services, which are provided at no cost to organ recipients through government programs, foundations or charitable groups.
- no benefits are available if we cover the donor, but not the recipient

- harvesting of tissue for storage purposes **only** is not eligible for coverage

Time Period for Recipient Benefits

Transplant benefit covers the transplant recipient's expenses directly related to the transplant procedures when they are incurred:

- from 30 days before the procedure to 365 days after the procedure for bone marrow transplants; or
- from five days before the procedure to 365 days after the procedure for all other transplants.
- Benefits for transplant-related Services within this time period are subject to the lifetime transplant benefit maximum listed on the Outline of Coverage.

Time Period for Living Donor Benefits

- To be covered, costs must be incurred within 120 days from the date of the donor's surgery.
- If the covered organ transplant procedure is not completed, we provide benefits only if the covered organ transplant procedure was scheduled to occur within 24 hours of the donor's surgery.
- Such covered donor expenses will be reimbursed subject to the Deductibles, Co-payments and Coinsurance and terms of the transplant recipient's Contract

Lifetime Transplant Maximum

We provide benefits for all transplant Services within the time periods specified above up to a lifetime transplant maximum that is listed on your Outline of Coverage. This maximum transplant benefit is separate from your lifetime benefit maximums for other Services Covered under your Contract.

B. Organ Specific Policy

Cornea and kidney transplants are not covered by the Plan's reinsurance, therefore the reinsurance section outlining requirements and procedures does not apply.

Heart

Human heart transplantation may be considered **medically necessary** for selected patients with end-stage heart failure.

Human heart transplantation is considered **investigational** in HIV+ recipients.

Heart/lung

Heart/lung transplantation may be considered **medically necessary** for carefully selected patients with end-stage cardiac and pulmonary disease including, but not limited to, one of the following diagnoses:

- irreversible primary pulmonary hypertension with heart failure;
- non-specific severe pulmonary fibrosis;
- Eisenmenger complex with irreversible pulmonary hypertension and heart failure;
- cystic fibrosis with severe heart failure;
- chronic obstructive pulmonary disease with heart failure;
- emphysema with severe heart failure;
- pulmonary fibrosis with uncontrollable pulmonary hypertension or heart failure.

Heart/lung transplantation is considered **investigational** in HIV+ recipients. (See Rationale section for further discussion.)

Lung

Lung transplantation may be considered **medically necessary** for carefully selected patients with irreversible, progressively disabling, end-stage pulmonary disease including but not limited to 1 of the conditions listed below.

A lobar lung transplant from a living or cadaver donor may be considered **medically necessary** for children and adolescents with end-stage pulmonary disease including but not limited to 1 of the conditions listed below.

Codes

- Bilateral bronchiectasis 494
 - 748.61 for congenital bronchiectasis
- Alpha-1 antitrypsin deficiency 277.6
- Primary pulmonary hypertension 416.0
- Cystic fibrosis (both lungs to be transplanted) 277.00 – 277.01
- Bronchopulmonary dysplasia 770.7
- Interstitial pulmonary fibrosis 515
- Idiopathic pulmonary fibrosis 516.3
- Sarcoidosis 135; 517.8
- Scleroderma 710.1
- Lymphangiomyomatosis 235.7
- Emphysema 492.8
- Eosinophilic granuloma 277.8
- Bronchiolitis obliterans 491.8
- Recurrent pulmonary embolism 415.1

- Pulmonary hypertension due to cardiac disease 402.10
- Chronic obstructive pulmonary disease 496
- Eisenmenger's syndrome 745.4

Lobar or lung transplantation is considered **investigational** in HIV+ recipients

Liver

A liver transplant, using a cadaver or living donor, may be considered **medically necessary** for carefully selected patients with end-stage liver failure due to irreversibly damaged livers. Etiologies of end stage liver disease include, but are not limited to, the following:

- Hepatocellular diseases
 - Alcoholic cirrhosis
 - Viral hepatitis (either A, B, C, or non-A, non-B)
 - Autoimmune hepatitis
 - Alpha-1 antitrypsin deficiency
 - Hemochromatosis
 - Protoporphyrria
 - Wilson's disease
- Cholestatic liver diseases
 - Primary biliary cirrhosis
 - Primary sclerosing cholangitis with development of secondary biliary cirrhosis
 - Biliary atresia
- Vascular disease
 - Budd-Chiari syndrome
- Primary hepatocellular carcinoma
- Inborn errors of metabolism
- Trauma and toxic reactions
- Miscellaneous
 - Polycystic disease of the liver
 - Familial amyloid polyneuropathy

Liver transplantation is considered **investigational** in the following patients:

- HIV-positive patients (see further discussion in Rationale section)
- Patients with an extrahepatic malignancy including cholangiocarcinoma
- Patients with hepatocellular carcinoma that has extended beyond the liver
- Patients with an active infection
- Patients with ongoing alcohol and/or drug abuse. (Evidence for abstinence may vary among liver transplant programs, but generally a minimum of 3 months is required.)

Small bowel

A small bowel transplant using a cadaveric intestine may be considered **medically necessary** in adult and pediatric patients with short bowel syndrome (SBS) who have established long-term dependency on total parental nutrition (TPN) and have developed severe complications due to total parental nutrition (TPN).

A small bowel transplant may be considered **investigational** for adults who are able to tolerate TPN.

Small bowel transplant is considered **investigational** in HIV+ recipients (see Rationale section for further discussion.)

Small bowel transplant using living donors is considered **investigational** for adults and children. (See Rationale section for further discussion)

Pancreas and Pancreas/Kidney

A combined pancreas-kidney transplant may be considered **medically necessary** in diabetic patients with uremia.

Pancreas transplant after a prior kidney transplant may be considered **medically necessary** in patients with insulin dependent diabetes.

Pancreas transplant alone may be considered **medically necessary** in patient with severely disabling and potentially life-threatening complications due to hypoglycemia unawareness and labile diabetes that persists in spite of optimal medical management.

Pancreas retransplant after a failed primary pancreas transplant may be considered **medically necessary**.

Pancreas retransplant after 2 or more prior failed pancreas transplants is considered **investigational**.

Pancreas transplant is considered **investigational** in HIV+ recipients.

C. Autologous Bone Marrow and Peripheral Stem Cell

Breast Cancer

Stem cell transplants for women with metastatic breast cancer may be considered **medically necessary** for the following circumstances:

- Previously untreated

- Currently responsive to primary systemic chemotherapy
- Relapse following response to first-line therapy

We do not cover stem cell transplants for women with metastatic breast cancer who are refractory to systemic therapy, because there is insufficient evidence to show that women who do not respond to systemic therapy will benefit from high-dose chemo with stem cell support.

Lymphomas

Hodgkin's Lymphoma

Autologous Stem cell transplants for Hodgkin's Lymphoma may be considered **medically necessary** for the following circumstances:

- Stage III or Stage IV A or B patients who are either in relapse, or refractory to primary chemotherapy

Non-Hodgkin's Lymphoma

Autologous Stem cell transplants for Non-Hodgkin's Lymphoma may be considered **medically necessary** for the following circumstances:

- Stage III or IV A or B, intermediate and high-grade NHL in second or subsequent clinical remission
- Stage IV A or B, high-grade NHL with 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.
- To achieve or consolidate clinical remission for those in a first or subsequent chemosensitive relapse, whether or not their lymphoma has undergone transformation to a higher grade.

Follicular Non-Hodgkin's Lymphoma

Autologous Stem cell transplants for patients who have Follicular Non-Hodgkin's Lymphoma who have failed primary therapy may be considered **medically necessary**.

Small Lymphocytic Lymphoma

We do not cover patients with SLL (Small Lymphocytic Lymphoma)

Neuroblastoma:

Autologous stem cell transplants for children over 1 year of age who are in remission may be considered **medically necessary**

We do not cover stem cell transplants for 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 progression compared to conventional chemotherapy.

Leukemias:

- **ALL** (Acute Lymphoblastic Leukemia), in first complete remission when there is a high risk for relapse (adults and children) may be considered **medically necessary**.
- **ANLL** (Acute Non-Lymphocytic Leukemia) in the first or subsequent remission may be considered **medically necessary**.

We do not cover autologous stem cell transplants for patients:

- **ALL in adults** in second or subsequent complete remission and **adults** not in complete remission because it hasn't been shown to improve health outcomes compared to conventional therapy.
- **CLL** (Chronic Lymphocytic Leukemia), because there is not enough scientific evidence to show that this procedure prolongs survival compared to standard chemotherapy.
- **CML** (Chronic Myelogenous Leukemia) because there is not enough scientific evidence to show that this procedure prolongs survival compared to standard chemotherapy. See policy on allogeneic stem cell transplants.

Multiple Myeloma

Patients with newly diagnosed or responsive disease, may be considered **medically necessary** for the following circumstances:

- Patients with newly diagnosed previously untreated disease
- Patients in complete or partial remission from treatment
- Patients in a relapse that is responding to treatment

We do not cover stem cell transplants for patients

- Patients with refractory disease, including
 - Patients with primary resistance
 - Patients in resistant relapse
- Patient is pregnant
- Patient is HIV positive (with or without AIDS)
- Evidence of heart disease:
 - 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)
- 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

Testicular, mediastinal, retroperitoneal, and ovarian germ cell tumors that are refractory to standard dose chemotherapy may be considered **medically necessary** for the following circumstances as follows:

- 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

We do not cover Patients who have not failed standard-dose chemotherapy with platinum-based according to the above guidelines, because there is not enough scientific evidence to suggest improved survival or control of disease progression compared to conventional chemotherapy

We do not cover autologous BMT or autologous peripheral stem cell support (APSCT) for the following indications:

- **Epithelial Ovarian Cancer** because the scientific data does not include enough patients with long term follow-up to show conclusions about improved survival. The morbidity and mortality of this treatment is greater than with standard therapy.
- **Solid Tumors (other than those listed above)** in adults because it has not been shown to prolong survival, and in some cases, there is greater mortality. Studies examined melanoma, colorectal and gastric cancer, and small cell lung cancer. Studies of other solid tumors did not report survival data.

We do not cover high-dose chemotherapy with or without autologous stem cell support for autoimmune diseases including but not limited to rheumatoid arthritis, systemic lupus erythematosus (SLE), systemic sclerosis, and multiple sclerosis, because there is insufficient evidence concerning its effectiveness on health outcomes.

We do not cover high-dose chemotherapy with autologous stem cell support for patients with primary amyloidosis, because there is insufficient evidence concerning its effectiveness on health outcomes.

Note that we do not cover services to collect and bank umbilical cord blood for future possible use, when there is no current need.

D. Allogeneic Peripheral, Umbilical Cord Blood, & Bone Marrow Transplants

Allogeneic stem cell transplants (including bone marrow, peripheral blood, and umbilical cord blood- see guidelines below) may be considered **medically necessary** for the following conditions:

Leukemias:

- ALL (Acute Lymphocytic Leukemia) in the first or subsequent remission
- ANLL (Acute Non-Lymphocytic Leukemia) in the first or subsequent remission
- CGL (Chronic Granulocytic Leukemia)
- CML (Chronic Myelogenous Leukemia)

We do not cover Chronic Lymphocytic Leukemia (CLL) because there is not enough scientific evidence to show that this procedure prolongs survival compared to standard chemotherapy

Lymphomas:

Hodgkin's Lymphoma

- Stage III or IV A or B patients who are either in relapse, or refractory to primary chemotherapy

Non-Hodgkin's Lymphoma

- Stage III or IV A or B, intermediate and high-grade NHL in second or subsequent clinical remission
- Stage IV A or B, high-grade NHL with 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.
- To achieve or consolidate clinical remission for those in a first or subsequent chemosensitive relapse, whether or not their lymphoma has undergone transformation to a higher grade.

Follicular Non-Hodgkin's Lymphoma for patients who have failed primary therapy.

Patients with any of the following are excluded because science has not been shown this to improve the health in these cases

- sickle cell trait
- transplant donor who is not HLA-identical
- Patients with Small Lymphocytic Lymphoma (SLL)

Allogeneic stem cell transplants, peripheral blood, and umbilical cord blood- see guidelines below) may be considered **medically necessary** for **Sickle cell anemia** when patients meet all the following conditions:

- documented homozygous sickle cell anemia
- children or very young adults (some studies use < age 16)
- who have an HLA-identical related donor
- one or more of the following features associated with increased risk of stroke or organ damage:
 - prior stroke (CVA)
 - recurrent chest syndrome
 - recurrent vaso-occlusive ("pain") crises
 - red blood cell allo-immunization on chronic transfusion

Allogeneic stem cell transplants (including bone marrow, peripheral blood, and umbilical cord blood- see guidelines below) may be considered **medically necessary** for the following conditions:

Aplastic Anemia

For patients with 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 x10⁹/L, granulocytes < 0.5 x10⁹/L, and reticulocytes < 1% (corrected for hematocrit).

6/6 antigen matched related or unrelated donor *or*

5/6 antigen matched family member donor, for patients failing antithymocyte globulin therapy

Thalassemia (homozygous beta-thalassemia)

For patients with beta thalassemia major, using a 6/6 antigen matched, related or unrelated donor

Myelodysplasia/myelofibrosis for patients with refractory anemia (idiopathic, or secondary to drug or toxin exposure), who have an HLA-identical donor. Patients must have 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

Severe Combined Immunodeficiency (SCID)

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

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

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

Mucopolysaccharidosis (Hunter's, Hurler's, etc.)

for patients with Hunter's, Hurler's, Sanfilippo, or Maroteaux-Lamy, who are neurologically intact, using a 5 or 6 of 6 antigen matched, HLA molecular typing negative family member donor

Mucopolipidoses (Gaucher's, metachromic leukodystrophy, etc.)

for patients with Gaucher's, metachromic leukodystrophy, globoid cell leukodystrophy, or adrenoleukodystrophy, who are neurologically intact, and have failed conventional therapy (such as diet modification or enzyme therapy), using a 5 or 6 of 6 antigen matched, HLA molecular typing negative family member donor

Kostmann's Syndrome (severe infantile agranulocytosis)

Leukocyte Adhesion Deficiencies

X-linked Lymphoproliferation Syndrome

Amegakaryocytic Thrombocytopenia

We do not cover **allogeneic stem cell transplants** for the following indications:

- **Solid Tumors**
- **Ovarian Cancer**
- **Polycythemia vera**

We do not cover **salvage HDC/AlloSCS after HDC/AuSCS**, for patients with recurrent neuroblastoma, metastatic breast cancer, germ cell tumors in relapse or any other solid tumor, because there is no evidence that this procedure improves health outcomes of patients with solid tumors.

We do not cover **salvage HDC/AlloSCS for relapse of incomplete remission after HDC/AuSCS**, for patients with multiple myeloma, Hodgkin's lymphoma, acute myeloblastic leukemia, and acute lymphoblastic leukemia.

We do not cover **reduced intensity transplants (nonmyeloablative allogeneic stem cell transplants, mini transplants, transplant lite) for renal cancer and other solid tumors of solid tissues or organs**. While this new approach shows promise especially for those patients in whom standard transplantation might not be possible, we await long-term data to determine whether these transplants are as effective as standard allogeneic stem cell transplantations. See individual consideration guidelines for details.

Storage for future use, in case of a future need for transplant

Not Covered

Non-hematologic malignancies, because there is not enough evidence to show whether health outcome is improved or not for patients with these tumors

Unrelated donors or related donors with fewer than 5 HLA loci match. There are currently clinical trials underway to address these issues, but results are not available yet.

Reduced Intensity Allogeneic Transplants for Myeloma Patients:

For patients at high risk for complications from standard allogeneic transplantation, or patients who have failed conventional therapy. Standard intensity allogeneic transplantation may also be appropriate for some patients with primary refractory disease. For patients at high risk for relapse after, or who have failed autologous stem cell transplantation.

Patients with young physiological age may also be appropriate candidates. (Allogeneic stem cell transplantation is not currently considered standard of care for myeloma patients over age 55.)

Reduced Intensity Allogeneic Transplants for CML Patients: Patients who are refractory to standard transplantation, or have relapsed after standard transplantation, or as the initial transplant after failing standard treatment.

Reduced Intensity Allogeneic Transplants for NHL and HL Patients: For patients at high risk for treatment failure or who have already failed other therapy.

Reduced Intensity Allogeneic Transplants for Myelodysplasia Patients: For patients at high risk for transplant-related complications; many myelodysplasia patients have a higher incidence of such complications.

Reduced Intensity Allogeneic Transplants for AML/ALL Patients: For patients in remission who are at high risk for relapse. Reduced-intensity transplants are not effective for patients with active leukemia.

Transplant Policy Guidelines

Candidates for all types of medically necessary transplants should meet all of the following general criteria:

- No history of malignancy within 5 years of transplantation, excluding nonmelanomatous skin cancers
- Absence of active infection
- Documentation of patient compliance with medical management.

Specific Guidelines

Heart

General guidelines

Candidates must meet all of the following criteria:

Adequate pulmonary status

Cardiac Specific

The American College of Cardiology (ACC) has established recipient guidelines for potential heart transplant recipients as follows. These guidelines would be applicable to those patients listed as Status 2.

- Accepted Indications for Transplantation
 - Maximal VO₂ < 10 ml/kg/min with achievement of anaerobic metabolism
 - Severe ischemia consistently limiting routine activity not amenable to bypass surgery or angioplasty
 - Recurrent symptomatic ventricular arrhythmias refractory to ALL accepted therapeutic modalities
- Probable Indications for Cardiac Transplantation
 - Maximal VO₂ <14 ml/kg/min and major limitation of the patient's activities
 - Recurrent unstable ischemia not amenable to bypass surgery or angioplasty
 - Instability of fluid balance/renal function not due to patient noncompliance with regimen of weight monitoring, flexible use of diuretic drugs, and salt restriction
- Inadequate Indications for Transplantation
 - Ejection fraction <20%
 - History of functional class III or IV symptoms of heart failure
 - Previous ventricular arrhythmias
 - Maximal VO₂ >15 ml/kg/min without other indications

Relative contraindications to heart transplant include any condition that may have a significant impact on the likelihood of a successful clinical outcome.

The United Network for Organ Sharing (UNOS) prioritizes donor thoracic organs according to the severity of illness as follows:

Status 1A

A patient is admitted to the listing transplant center hospital and has at least 1 of the following devices or therapies in place:

- Mechanical circulatory support for acute hemodynamic decompensation that includes at least 1 of the following:
 - Left and/or right ventricular assist device implanted
 - Total artificial heart
 - Intra-aortic balloon pump: or
 - Extracorporeal membrane oxygenator (ECMO)
- Mechanical circulatory support
- Mechanical ventilation
- Continuous infusion of inotropes and continuous monitoring of left ventricular filling pressures
- Criteria above are not met, but the patient has a life expectancy without a transplant of less than 7 days

Status 1B

A patient has at least 1 of the following devices or therapies in place:

- left and/or right ventricular device implanted
or
- Continuous infusion of intravenous inotropes

A patient that does not meet Status 1A or 1B is listed as Status 2.

Heart/lung

General:

Adequate pulmonary status

Cardiac Specific

The United Network for Organ Sharing (UNOS) prioritizes donor thoracic organs according to the severity of illness as follows:

Status 1A

A patient is admitted to the listing transplant center hospital and has at least 1 of the following devices or therapies in place:

- Mechanical circulatory support for acute hemodynamic decompensation that includes at least 1 of the following:
 - Left and/or right ventricular assist device implanted
 - Total artificial heart

- Intra-aortic balloon pump: or
- Extracorporeal membrane oxygenator (ECMO)
- Mechanical circulatory support
- Mechanical ventilation
- Continuous infusion of inotropes and continuous monitoring of left ventricular filling pressures
- Criteria above are not met, but the patient has a life expectancy without a transplant of less than 7 days

Status 1B

A patient has at least 1 of the following devices or therapies in place:

- left and/or right ventricular device implanted
or
- continuous infusion of intravenous inotropes

A patient that does not meet Status 1A or 1B is listed as Status 2.

Lung

General

Candidates must meet all of the following criteria:

- Adequate cardiac status
- Absence of infection, or extrapulmonary infection in patients with cystic fibrosis

Lung Specific

Bilateral lung transplantation is typically required when chronic lung infection disease is present, i.e., associated with cystic fibrosis and bronchiectasis. Some, but not all, cases of pulmonary hypertension will require bilateral lung transplantation.

Bronchiolitis obliterans is associated with chronic lung transplant rejection, and thus may be the etiology of a request for a repeat lung transplantation.

Liver

General

Candidates for all liver transplant should meet the following criteria:

Adequate cardiopulmonary status

Liver Specific

The MELD and PELD scores range from 6 (less ill) to 40 (gravely ill). The MELD and PELD scores will change during the course of a patient's tenure on the waiting list. Patients with liver disease related to alcohol or drug abuse must be actively involved in a treatment program.

Patients with polycystic disease of the liver do not develop liver failure but may require transplantation due to the anatomic complications of a hugely enlarged liver. The MELD/PELD score may not apply to these cases. One of the following complications should be present:

- Enlargement of liver impinging on respiratory function
- Extremely painful enlargement of liver
- Enlargement of liver significantly compressing and interfering with function of other abdominal organs

Patients with familial amyloid polyneuropathy do not experience liver disease, per se, but develop polyneuropathy and cardiac amyloidosis due to the production of a variant transthyretin molecule by the liver. The MELD/PELD score may apply to these cases. Candidacy for liver transplant is an individual consideration based on the morbidity of the polyneuropathy. Many patients may not be candidates for liver transplant alone due to coexisting cardiac disease.

Patients with hepatocellular carcinoma are appropriate candidates for liver transplant only if the disease remains confined to the liver. Therefore, the patient should be periodically monitored while on the waiting list, and if metastatic disease develops, the patient should be removed from the transplant waiting list. In addition, at the time of transplant a backup candidate should be scheduled. If locally extensive or metastatic cancer is discovered at the time of exploration prior to hepatectomy, the transplant should be aborted, and the backup candidate scheduled for transplant.

Donor Criteria - Living Related Adult-to-Adult Transplant

Donor morbidity and mortality are prime concerns in adult donors undergoing right donor hepatectomy as part of an adult-to-adult living donor liver transplantation. Right hepatectomy is a technically demanding surgery, the success of which may be related to the availability of an experienced surgical team. In 2000, the American Society of Transplant Surgeons proposed the following guidelines for living donors:

- Should be healthy individuals who are carefully evaluated and approved by a multidisciplinary team including hepatologists and surgeons to assure that they can tolerate the procedure
- Should undergo evaluation to assure that they fully understand the procedure and associated risks

- Should be of legal age and have sufficient intellectual ability to understand the procedures and give informed consent
- Should be emotionally related to the recipients
- Must be excluded if the donor is felt or known to be coerced
- Needs to have the ability and willingness to comply with long-term follow-up

Candidates should meet the following criteria:

Adequate cardiopulmonary status

Absence of active infection

HIV-negative status

No history of malignancy within 5 years of transplantation, excluding nonmelanomatous skin cancers

Documentation of patient compliance with medical management.

Small Bowel

General

Candidates for **Small Bowel** transplant should meet the following criteria:

Adequate cardiopulmonary status

HIV-negative status

Small Bowel Specific

Evidence of intolerance of TPN includes, but is not limited to, multiple and prolonged hospitalizations to treat TPN-related complications, or the development of progressive but reversible liver failure. In the setting of progressive liver failure, small bowel transplant may be considered a technique to avoid end-stage liver failure related to chronic TPN, thus avoiding the necessity of a multivisceral transplant.

Pancreas and Pancreas/Kidney

Candidates for all types of pancreas transplant should meet all of the following criteria:

Adequate cardiopulmonary status

Pancreas Specific

Candidates for pancreas transplant alone should additionally meet 1 of the following severity of illness criteria:

- Documentation of severe hypoglycemia unawareness as evidenced by chart notes or emergency room visits; OR
- Documentation of potentially life-threatening labile diabetes as evidenced by chart notes or hospitalization for diabetic ketoacidosis.

Allogeneic peripheral blood

Guidelines for use of umbilical cord blood

We cover **umbilical cord stem cell support** as an acceptable cell source for transplants that are otherwise covered for either high-dose chemo with stem cell support, or for bone marrow transplant, when all the following are met:

- 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

Not covered:

- Facility providing umbilical cord blood that is not in compliance with any existing FDA regulations governing umbilical cord transplants. FDA regulations are currently under development.
- There is a 2 or greater antigen mismatch, because there is insufficient data regarding health outcomes for these procedures
- There is a suitable stem cell donor of equal or superior HLA match

We cover mobilized peripheral blood stem cells from allogeneic donors, when all the following are met:

- Hematologic malignancies
- Donor is related, and HLA matched at 5 or more loci

Not covered :

- Non-hematologic malignancies, because there is not enough evidence to show whether health outcome is improved or not for patients with these tumors
- Unrelated donors or related donors with fewer than 5 HLA loci match. There are currently clinical trials underway to address these issues, but results are not available yet.

Other information

Clinical trials for Cancer Mandate

As required by law, we provide coverage for services and supplies received as part of a qualified clinical trial (for treatment of cancer) when the member is enrolled in that trial. This coverage is provided for services and supplies that are consistent with the study protocol and with the standard of care for someone with the patients' diagnosis, and that would be covered if the patient did not participate in the trials. This coverage may also be provided for investigational drugs and devices that have been approved for use as part of the trial. Coverage for services and supplies that are received as part of a qualified

clinical trial is provided to the same extent as it would have been provided if the patient did not participate in the trial. However, no coverage is provided for:

- Investigational drugs and devices that have not been approved for use in the trial.
- Investigational drugs and devices that are paid for by the manufacturer, distributor or provider of the drug or device, whether or not the drug or device has been approved for use in the trial.
- Non-covered services under the subscriber contract.
- Costs associated with managing the research for the trial.
- Items, services or costs that are reimbursed or otherwise furnished by the sponsor of the trial.
- Costs of services that are inconsistent with widely accepted and established national and regional standards of care.
- Costs of clinical trials that are not "qualified trials."

Policy Implementation/Update information, References

12/04 New policy. 12/05 updated current cert language.

12/06 updated to match current certificate language. Reviewed by CAC 9/07

Scientific background and Reference Resources

Heart

Blue Cross Blue Shield Association (BCBSA) Medical Policy Reference Manual. Heart Transplant Policy: 7.03.09, Issue: 1:2004

Heart/Lung

Blue Cross Blue Shield Association (BCBSA) Medical Policy Reference Manual. Heart/Lung Transplant Policy: 7.03.08, Issue: 1:2004

Lung

Blue Cross Blue Shield Association (BCBSA) Medical Policy Reference Manual. Lung Transplant Policy: 7.03.07; Issue: 1:2004

Liver

Blue Cross Blue Shield Association (BCBSA) Medical Policy Reference Manual. Liver Transplant Policy: 7.03.06; Issue: 1:2004

Small Bowel

Blue Cross Blue Shield Association (BCBSA) Medical Policy Reference Manual. Small Bowel Transplant Policy: 7.03.04; Issue: 1:2004

Pancreas and Pancreas/Kidney

Blue Cross Blue Shield Association (BCBSA) Medical Policy Reference Manual.
Allogeneic Pancreas Transplant Policy: 7.03.02; Issue: 1:2004

Autologous/Allogeneic Stem Cell/bone marrow transplantation

Blue Cross Blue Shield Association (BCBSA) Medical Policy Reference Manual:
High-Dose Chemotherapy with Hematopoietic Stem-Cell Support for Chronic Lymphocytic Leukemia and Small Lymphocytic Lymphoma Policy: 8.01.05; Issue 3:2004; Single or Tandem Courses of High-Dose Chemotherapy plus Hematopoietic Stem-Cell Support for Multiple Myeloma Policy 8.01.17; Issue: 8.01.17; High-Dose Autologous/Allogeneic Stem Cell/bone marrow transplantation Chemotherapy and Hematopoietic Stem-Cell Support for Non-Hodgkin's Lymphomas Policy 8.01.20, Issue 1:2003; High-Dose Chemotherapy and Allogeneic Stem-Cell Support for Myelodysplastic Diseases Policy 8.01.21, Issue 2:2004; High-Dose Chemotherapy and Allogeneic Stem-Cell Support for Genetic Diseases and Acquired Anemias, Policy 8.01.22, Issue 1:2004; High-Dose Chemotherapy and Hematopoietic Stem-Cell Support for Epithelial Ovarian Cancer, Policy 8.01.23, Issue 4:2002; High-Dose Chemotherapy and Hematopoietic Stem-Cell Support for Miscellaneous Solid Tumors in Adults, Policy 8.01.24, Issue 3:2004; High-Dose Chemotherapy and Autologous Stem-Cell Support for Autoimmune Diseases, Including Multiple Sclerosis, Policy 8.01.25, Issue 3:2004; High-Dose Chemotherapy with Hematopoietic Stem-Cell Support for Acute Myelogenous Leukemia, Policy 8.01.26, Issue 4:2002; High-Dose Chemotherapy with Hematopoietic Stem-Cell Support for Breast Cancer, Policy 8.01.27, Issue 4:2002; High-Dose Chemotherapy with Hematopoietic Stem-Cell Support for Primitive Neuroectodermal Tumors (PNET) of the CNS and Ependymoma, Policy 8.01.28, Issue 3:2004; High-Dose Chemotherapy and Hematopoietic Stem-Cell Support for Hodgkin's Disease, Policy 8.01.29, Issue 1:2003; High-Dose Chemotherapy and Hematopoietic Stem-Cell Support for the Treatment of Chronic Myelogenous Leukemia, Policy 8.01.30, Issue 3:2004; High-Dose Chemotherapy and Autologous Stem-Cell Support for Malignant Astrocytomas and Gliomas, Policy 8.01.31, Issue 3:2004; High-Dose Chemotherapy with Hematopoietic Stem-Cell Support as a Treatment of Acute Lymphocytic Leukemia, Policy 8.01.32, Issue 4:2002; High-Dose Chemotherapy with Hematopoietic Stem-Cell Support for Solid Tumors of Childhood, Policy 8.01.34, Issue 3:2004; High-Dose Chemotherapy and Hematopoietic Stem-Cell Support as a Treatment of Germ-Cell Tumors, Policy 8.01.35, Issue 3:2004; Nonmyeloablative Allogeneic Transplants of Hematopoietic Stem Cells for Treatment of Malignancy, Policy 8.01.38, Issue 3:2003; High-Dose Chemotherapy plus Hematopoietic Stem-Cell Support to Treat Primary Amyloidosis or Waldenstrom's Macroglobulinemia, Policy 8.01.42, Issue 1:2004;

Approved by BCBSVT and TVHP Medical Directors

Stephen E. Perkins, M.D. (BCBSVT) and Frank Provato, M.D. (TVHP) Date Approved