

MEDICA®

UTILIZATION MANAGEMENT POLICY

TITLE: BONE MARROW OR STEM CELL (PERIPHERAL OR UMBILICAL CORD BLOOD) TRANSPLANTATION

Origination Date: December, 1989

Subsequent Endorsement Date(s): 11/1990, 11/1991, 09/1993, 12/1995, 02/1998, 02/1999, 01/2000, 01/2001, 03/2002, 02/2003, 12/2003, 11/2004, 11/2005, 11/2006, 11/2007, 11/2008, 11/2009, 02/2010

This policy was developed with input from specialists in nephrology, transplants, and oncology, and endorsed by the Medical Policy Committee.

PRODUCT APPLICATION

This policy provides general information concerning Medica's administrative processes. It applies to all fully insured Medica Health Plans, Medica Insurance Company, and Medica Health Plans of Wisconsin products, unless a specific limitation or exception exists. For self-insured plans, consult individual plan sponsor benefit documents. If there is a discrepancy between a Utilization Management Policy and a self-insured benefit plan, the provisions of the benefit plan will govern. With respect to Medicare and Medicaid members, this policy will apply unless Medicare or Medicaid policies require different coverage.

IMPORTANT INFORMATION – PLEASE READ BEFORE USING THIS POLICY

Medica updates its Utilization Management Policies regularly, and reserves the right to amend these policies without notice to Medica members. Medica also reserves the right to amend these policies without notice to contracted health care providers unless the amendment materially alters the policy. If the amendment materially alters the policy, Medica will disclose the change to contracted health care providers not less than 45 days prior to implementation of the policy. Medica's Utilization Management Policies contain general information only and do not guarantee coverage. Receipt of benefits is subject to all terms and conditions of the member's coverage document. Members should consult their Certificates of Coverage or Plan Documents/Summary Plan Descriptions to review the provisions relating to a specific coverage determination. If there is a conflict between a Utilization Management Policy and the applicable coverage document, the coverage document will govern. Members may contact Medica Customer Service at the phone number listed on their member identification card to discuss their benefits more specifically. Providers with questions about this Utilization Management Policy may call Medica's Provider Service Center toll free at 1-800-458-5512.

Medica's Utilization Management Policies are not medical advice. Members should consult with appropriate health care providers to obtain needed medical advice, care and treatment.

PURPOSE

To promote consistency between reviewers in utilization management decision-making by providing the criteria that generally determine the medical necessity of bone marrow or stem cell transplantation. The Coverage Issues box below outlines the process for addressing the needs of individuals who do not meet these criteria.

BACKGROUND

I. Definitions

- A. **Transplant or graft** is a portion of the body or a complete organ removed from its natural site and transferred to a separate site in the same or different individual.
- B. **Stem cells** are blood cells at the earliest stage of development in the bone marrow. They can be taken from the bone marrow, peripheral bloodstream, or from umbilical cord blood.
- C. **Chemosensitive** disease is malignant disease that demonstrates at least a partial response to a course of chemotherapy.
- D. A **complete response** indicates that there is no evidence of active disease.

- E. A **partial response** is defined as at least a 50% decrease in all measurable tumors, lasting at least four weeks, but less than a complete response.
- F. **Syngeneic** graft describes a graft in which the donor and recipient are genetically identical.
- G. **Allogeneic** graft is one in which the donor and recipient are of different genetic origins.
- H. **Autologous** bone marrow transplant (ABMT) refers to the removal and storage of some of the patient's own bone marrow for restoring bone marrow function after high dose chemotherapy or radiotherapy.
- I. **Donor Lymphocyte Infusion (DLI)** may be performed following allogeneic transplant. Individuals may be infused with lymphocytes obtained via leukapheresis from the original donor. The DLI attempts to induce a beneficial graft-versus-tumor response without the need for additional bone marrow harvest from the donor.
- J. **Bone marrow transplant** is the reconstitution of the full hematopoietic system by transfer of the pluripotent cells present in the bone marrow (stem cells). A marrow transplant involves a transplant not only of the donor myeloid, erythroid, and megakaryocytic systems, but also of lymphoid and macrophage-monocyte systems. There are four types of disease for which marrow transplantation has been widely utilized:
 - 1. **Genetic disease**
For immunologic deficiency diseases, the objective is to replace the recipient's genetically defective lymphoid system with the normal lymphoid tissue of the donor. For genetic diseases such as thalassemia major, the abnormal marrow must be destroyed and replaced by normal marrow.
 - 2. **Aplastic anemia**
May result from several causes; the disease process results in loss of the marrow, and the objective is to replace the defective organ with a normally functioning one.
 - 3. **Hematologic malignancy**
For leukemia and other hematologic malignancies, the objective is the complete destruction of the malignant cell population and unavoidably, normal marrow cells by intensive chemo-radiotherapy followed by restoration of normal marrow function by the transplanted marrow.
 - 4. **Non-hematologic malignancy** (Chemotherapy or high-dose chemotherapy with autologous peripheral stem cell/bone marrow rescue [HDC/ABMT])
For patients with poor-prognosis cancer necessitating treatment with high dose therapy, autologous bone marrow transplantation rescue may be used in selected conditions to reconstitute the devastated marrow population.
- K. **Stem Cell Transplant**
 - 1. **Allogeneic stem cell transplant** employs chemotherapy, immunosuppressive agents and/or radiation to provide adequate immunosuppression to permit engraftment of stem cells from a human donor other than the patient him/herself. The intensity of the agents used for immunosuppression may be either myeloablative or non-myeloablative depending on the disease being treated and specific patient characteristics. Stem cells may be obtained from the bone marrow, peripheral blood, or umbilical cord blood. The stem cell donor may be related or unrelated to the potential recipient.
 - 2. **Autologous stem cell transplant** utilizes the patient's own stem cells to re-establish hematopoietic cell function following intensive doses of chemotherapy, with or without radiation. Stem cells may be obtained from repeated aspirations of bone marrow or from peripheral blood.
 - 3. **Non-myeloablative stem cell transplant (NST)/Reduced-intensity stem cell transplant (RIST)** is a stem cell transplant in which full ablation does not occur. This transplant provides sufficient immunosuppression to achieve donor engraftment, with less toxicity. It is also called a "mini" transplant.
 - 4. **Tandem Transplant** involves two sequential courses of high dose chemotherapy, each followed by stem cell transplant, within a six-month period.
 - 5. **Umbilical cord blood stem cell transplant** employs the infusion of stem cells obtained from the umbilical cord or placenta of a newborn child. A two antigen (Ag) mismatch is acceptable. Cord blood transplantation in patients weighing more than 40 Kg utilizes cord blood from at least two donors ("double cord").

II. Comments

Refer to Appendices for additional terms, definitions and classification tables.

MEDICAL NECESSITY CRITERIA

I. Patient Suitability

- A. All patients should meet the institution's criteria for acceptable heart, lung, kidney, and liver function.
- B. For adult patients, Karnofsky performance score greater than 70 (*See Appendix 2*).

- C. For patients aged 16 and under, a Lansky performance score greater than 50 (*See Appendix 3*).
- D. All patients should demonstrate response to treatment with conventional chemotherapy agents, if this treatment is appropriate.
- E. Additional studies to determine the patient's suitability for transplant may be requested if indicated, including, but not limited to:
 - 1. Cardiac evaluation for persons with diabetes and persons over age 40
 - 2. Pulmonary function tests
 - 3. Serology testing including, but not limited to, hepatitis A, B and C, human immunodeficiency virus (HIV), cytomegalovirus (CMV), varicella, Epstein Barr virus, herpes virus, Rapid Plasma Reagin (RPR), and Fluorescent Treponemal Antibody Absorption (FTA).
 - 4. Psychosocial evaluation and clearance
 - 5. Mammogram for women over age 40
 - 6. Prostate-specific antigen (PSA) and digital rectal exam for men over age 50
 - 7. Pelvic exam with Pap smear for women
 - 8. Dental exam with completion of required dental work prior to transplant
 - 9. Imaging studies
 - 10. Colonoscopy for persons over age 50 with removal of any polyps
 - 11. Immunizations up to date, including Hepatitis A, Hepatitis B, influenza and pneumonia
 - 12. Carotid Doppler ultrasound for individuals with known coronary artery disease.
 - 13. Ankle-Brachial index (ABI).
 - 14. Ophthalmology exam for persons with diabetes (as baseline)
- F. Patient or guardian is able to give informed consent. Patient/guardian and family/social support system are able to comply with the treatment regimen and the necessary follow-up.
- G. For patients with a recent (24 months) history of alcohol or other drug abuse, successful completion of chemical dependency program and documented ongoing abstinence.

II. Indications

Bone marrow/stem cell transplants are considered a proven/accepted form of treatment for the following diagnoses.

A. **Allogeneic**

- 1. Leukemias
- 2. Lymphomas (*See Appendix 1*)
- 3. Myelodysplastic Syndrome (MDS) and Pre-Leukemic Syndrome
 - a. Myelodysplastic syndrome (MDS)
 - b. Chronic Myelomonocytic Leukemia (CMML), including Juvenile Myelomonocytic Leukemia (JMML)
- 4. Multiple Myeloma/Plasma Cell Disorders
 - a. Multiple Myeloma
 - b. AL Amyloidosis (primary) in patients with amyloid deposition in two or fewer organs and a cardiac left ejection fraction (EF) greater than 45%.
 - c. Waldenstrom's Macroglobulinemia
- 5. Hematological Disorders
 - a. Aplastic Anemia
 - b. Congenital Amegakaryocytic Thrombocytopenia
 - c. Congenital Agranulocytosis (Kostmann Syndrome)
 - d. Chronic Granulomatous Disease
 - e. Diamond-Blackfan Anemia/Blackfan-Diamond Syndrome (pure red cell aplasia)
 - f. Dyskeratosis Congenita
 - g. Fanconi Anemia (FA)
 - h. Paroxysmal Nocturnal Hemoglobinuria (PNH)
 - i. Sickle Cell Disease
 - j. Thalassemia major
- 6. Immunodeficiency Syndromes
 - a. CD40 Ligand Deficiency
 - b. Chediak-Higashi Syndrome
 - c. Hemophagocytic Lymphohistiocytosis (HLH) (same as familial erythrophagocytic lymphohistiocytosis [FEL])
 - d. Leukocyte Adhesion Deficiency
 - e. Omenn Syndrome

- f. Severe combined immunodeficiency disease (SCID)
- g. Wiskott-Aldrich Syndrome
- h. X-linked Lymphoproliferative Syndrome
- 7. Inherited Metabolic Disorders
 - a. Adrenoleukodystrophy
 - b. Globoid Cell Leukodystrophy (Krabbe Disease)
 - c. Hurler Syndrome (MPS-1H)
 - d. Maroteaux-Lamy Syndrome (MPS-VI)
 - e. Metachromatic Leukodystrophy
 - f. Infantile osteopetrosis (also called marble-bone disease, malignant osteopetrosis, or autosomal recessive osteopetrosis)
 - g. Mannosidosis and other liposomal storage diseases

B. Autologous

- 1. Leukemias
 - a. Acute Lymphocytic Leukemia (ALL) (*Allogeneic transplant preferred; request requires medical director review.*)
 - b. Acute Myelogenous Leukemia (AML) (also known as Acute Non-Lymphocytic Leukemia [ANLL])
 - c. Chronic Lymphocytic Leukemia (CLL) (*Allogeneic transplant preferred; request requires medical director review.*)
 - d. Chronic Myelogenous Leukemia (CML) (*Allogeneic transplant preferred; request requires medical director review.*)
- 2. Lymphomas (*See Appendix 1*)
- 3. Multiple Myeloma/Plasma Cell Disorders
 - a. Multiple myeloma
 - b. AL Amyloidosis (primary) in patients with amyloid deposition in two or fewer organs and a cardiac left ejection fraction (EF) greater than 45%.
 - c. Waldenstrom's Macroglobulinemia
- 4. Germ Cell Tumors
 - a. Testicular Germ Cell Tumor
 - b. Ovarian Germ Cell Tumor
 - c. Extragenital Germ Cell Tumor
- 5. Brain Tumors
 - a. Medulloblastoma
 - b. Primitive Peripheral Neuro-ectodermal Tumor (PNET) (*Request requires medical director review.*)
- 6. Other Malignancies
 - a. Neuroblastoma
 - b. Retinoblastoma
 - c. Ewing's Sarcoma
 - d. Rhabdomyosarcoma, very high-risk patients only (*Request requires medical director review.*)

III. Additional Infusions and Replantation

- A. Indications for additional infusions
 - 1. Infusion of stem cells for failure to engraft (autologous transplant)
 - 2. Donor leukocyte infusion (DLI) for persistent or relapsed malignant disease (allogeneic transplant)
- B. Indications for retransplantation (*Requests require medical director review.*)
 - 1. Relapse of original disease
 - 2. Failure to engraft or poor graft function
 - 3. Graft rejection

IV. Contraindications

- A. Generally, transplantation is contraindicated in the presence of any medical condition that would itself markedly shorten life expectancy.
- B. Contraindications
 - 1. Active systemic or localized infection
 - 2. Irreversible multi-system organ failure
 - 3. Acquired immunodeficiency syndrome (AIDS), other than AIDS/HIV associated lymphomas
 - 4. Active alcohol and/or other substance abuse

5. Irreversible severe brain damage
 6. Current patient and/or family history of noncompliance, or psychiatric illness or psychological condition that would make compliance with a disciplined medical regimen impossible
 7. Inability to obtain informed consent from patient or guardian
- C. Relative Contraindications* include, but are not limited to:
1. Persisting CNS involvement by malignancy except for primary CNS tumors listed in the Indications section above
 2. Infection that may be aggravated/activated by immunosuppression
 3. HIV infection without AIDS and with sustained CD4 counts greater than 200/mm³, other than AIDS/HIV associated lymphomas
 4. Disease progression despite multiple prior courses of chemotherapy
 5. Presence of major organ dysfunction or disease that will prohibitively increase risk of transplant over accepted, conventional treatments
 6. Cachexia/severe malnutrition
 7. Body mass index equal to or greater than 40kg/m sq (*See Appendix 4*)
 8. Chronic peptic ulcer disease, GI bleeding, diverticulitis

* NOTE: Additional consultation, evaluation, and/or treatment may be indicated in these situations. Refer to Medical Director.

- V. Written documentation from the medical record specifying the medical necessity according to the above criteria is required. Requested documentation may include, but is not limited to:
- A. Information regarding tumor bulk, the extent of prior treatment, and the patient's responsiveness to that treatment
 - B. Patient suitability studies.
 - C. Transplant protocol

COVERAGE ISSUES

1. Prior authorization is required for bone marrow or stem cell transplantation.
2. Coverage may vary according to the terms of the member's coverage document.
3. For Medicare members, refer to the following criteria, as applicable:
 - Centers for Medicare and Medicaid Services. *National Coverage Determination 110.8.1: Stem Cell Transplantation*. Available at: http://www.cms.gov/mcd/viewncd.asp?ncd_id=110.8.1&ncd_version=4&basket=ncd%3A110%2E8%2E1%3A4%3AStem+Cell+Transplantation. Accessed April 26, 2010.
4. Medica has entered into separate contracts with designated facilities to provide transplant-related health services, as described in the member's coverage document.
5. Complex cases require medical director or external review, and as necessary, discussion with the patient's physician.
6. Underlying co-morbidity that significantly alters the risk/benefit of transplant may preclude transplant eligibility.
7. Coverage of costs related to chemotherapy, drugs, other related supplies and services is limited to individuals who have one of the indications listed and are transplant candidates.
8. Coverage of costs related to collection and storage of umbilical cord blood stem cells is addressed in the member's coverage document.
9. Medical director or external review is required for any of the following procedures if not performed in a clinical trial:
 - a. Repeat bone marrow transplants
 - b. Salvage allogeneic transplants for relapse or incomplete remission following autologous transplantation
10. Use of progenitor/stem cells from bone marrow, peripheral blood or umbilical cord blood for non-conventional indications (such as direct injection into the heart muscle, bone or other body tissue) requires medical director or external review. Please refer to the following related Coverage Policy: *Intracoronary Autologous Cell Transplantation for Cardiac Disease*.

11. If the Medical Necessity and Coverage Criteria are met, Medica will authorize benefits within the limits in the member's coverage document.
12. If it appears that the Medical Necessity and Coverage Criteria are not met, the individual's case will be reviewed by the medical director or an external reviewer. Practitioners are advised of the appeal process in their Medica administrative handbook.

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APPENDIX 1 – Classification of Lymphoid Malignancies

WHO Classification of Lymphoid Malignancies		
<u>B Cell</u>	<u>T Cell</u>	<u>Hodgkin's Disease</u>
Precursor B cell neoplasm	Precursor T cell neoplasm	Nodular lymphocyte-predominant Hodgkin's disease
Precursor B lymphoblastic leukemia/lymphoma (precursor B cell acute lymphoblastic leukemia)	Precursor T lymphoblastic lymphoma/leukemia (precursor T cell acute lymphoblastic leukemia)	
Mature (peripheral) B cell neoplasms	Mature (peripheral) T cell neoplasms	Classical Hodgkin's disease
B cell chronic lymphocytic leukemia/small lymphocytic lymphoma	T cell prolymphocytic leukemia	Nodular sclerosis Hodgkin's disease
B cell prolymphocytic leukemia	T cell granular lymphocytic leukemia	Lymphocyte-rich classic Hodgkin's disease
Lymphoplasmacytic lymphoma	Aggressive NK cell leukemia	Mixed-cellularity Hodgkin's disease
Splenic marginal zone B cell lymphoma (± villous lymphocytes)	Adult T cell lymphoma/leukemia (HTLV-I+)	Lymphocyte-depletion Hodgkin's disease
Hairy cell leukemia	Extranodal NK/T cell lymphoma, nasal type	
Plasma cell myeloma/plasmacytoma	Enteropathy-type T cell lymphoma	
Extranodal marginal zone B cell lymphoma of MALT type	Hepatosplenic T cell lymphoma	
Mantle cell lymphoma	Subcutaneous panniculitis-like T cell lymphoma	
Follicular lymphoma	Mycosis fungoides/Sézary syndrome	
Nodal marginal zone B cell lymphoma (± monocytoid B cells)	Anaplastic large cell lymphoma, primary cutaneous type	
Diffuse large B cell lymphoma	Peripheral T cell lymphoma, not otherwise specified (NOS)	
Burkitt's lymphoma/Burkitt cell leukemia	Angioimmunoblastic T cell lymphoma	
	Anaplastic large cell lymphoma, primary systemic type	

Source: Longo, DL. Malignancies of Lymphoid Cells. In: Fauci A, Braunwald E, Kasper DL, et al. eds. *Harrison's Online*. 17th ed. Columbus, OH: McGraw-Hill; 2008;chap 105.

APPENDIX 2 – Activities of Daily Living
 Karnofsky Performance Scale

Able To Carry On Normal Activity	No Special Care Needed
100%	Normal; no complaints; no evidence of disease
90%	Able to carry on normal activity
80%	Normal activity with effort
Unable to Work; Able to Live at Home, Care For Most Personal Needs	A Varying Amount of Assistance is Needed
70%	Cares for self; unable to carry on normal activity or to do active work
60%	Requires occasional assistance, but is able to care for most needs
50%	Requires considerable assistance and frequent medical care
Moderate to Severe Restrictions	
40%	Disabled; requires special care and assistance
30%	Severely disabled; hospitalization indicated, although death not imminent
20%	Very sick; hospitalization necessary
10%	Moribund; fatal process progressing rapidly

APPENDIX 3 – Pediatric Activity
 Lansky Performance Scale

Able To Carry On Normal Activity	No Special Care Needed
100%	Fully active
90%	Minor restriction in physically strenuous play
80%	Restricted in strenuous play, tires more easily, otherwise active
Mild to Moderate Restriction	
70%	Both greater restriction of, and less time spent in active play
60%	Ambulatory up to 50 percent of time, limited active play with assistance/supervision
50%	Considerable assistance required for any active play; fully able to engage in quiet play
Moderate to Severe Restrictions	
40%	Able to initiate quiet activities
30%	Needs considerable assistance for quiet activity
20%	Limited to very passive activity initiated by others (e.g. TV)
10%	Completely disabled, not even passive play

APPENDIX 4 – Body Mass Index (BMI) Conversion Table

		Body Mass Index Table																																			
		Normal					Overweight					Obese					Extreme Obesity																				
BMI	Height (Inches)	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	53	54
		Body Weight (pounds)																																			
58	91	96	100	105	110	115	119	124	129	134	138	143	148	153	158	162	167	172	177	181	186	191	196	201	205	210	215	220	224	229	234	239	244	248	253	258	
59	94	99	104	109	114	119	124	128	133	138	143	148	153	158	163	168	173	178	183	188	193	198	203	208	212	217	222	227	232	237	242	247	252	257	262	267	
60	97	102	107	112	118	123	128	133	138	143	148	153	158	163	168	174	179	184	189	194	199	204	209	215	220	225	230	235	240	245	250	255	261	266	271	276	
61	100	106	111	116	122	127	132	137	143	148	153	158	164	169	174	180	185	190	195	201	206	211	217	222	227	232	238	243	248	254	259	264	269	275	280	285	
62	104	109	115	120	126	131	136	142	147	153	158	164	169	175	180	186	191	196	202	207	213	218	224	229	235	240	246	251	256	262	267	273	278	284	289	295	
63	107	113	118	124	130	135	141	146	152	158	163	169	175	180	186	191	197	203	208	214	220	225	231	237	242	248	254	259	265	270	276	282	287	293	299	304	
64	110	116	122	128	134	140	145	151	157	163	169	174	180	186	192	197	204	209	215	221	227	232	238	244	250	256	262	267	273	279	285	291	296	302	308	314	
65	114	120	126	132	138	144	150	156	162	168	174	180	186	192	198	204	210	216	222	228	234	240	246	252	258	264	270	276	282	288	294	300	306	312	318	324	
66	118	124	130	136	142	148	155	161	167	173	179	186	192	198	204	210	216	223	229	235	241	247	253	260	266	272	278	284	291	297	303	309	315	322	328	334	
67	121	127	134	140	146	153	159	166	172	178	185	191	198	204	211	217	223	230	236	242	249	255	261	268	274	280	287	293	299	306	312	319	325	331	338	344	
68	125	131	138	144	151	158	164	171	177	184	190	197	203	210	216	223	230	236	243	249	256	262	269	276	282	289	295	302	308	315	322	328	335	341	348	354	
69	128	135	142	149	155	162	169	176	182	189	196	203	209	216	223	230	236	243	250	257	263	270	277	284	291	297	304	311	318	324	331	338	345	351	358	365	
70	132	139	146	153	160	167	174	181	188	195	202	209	216	222	229	236	243	250	257	264	271	278	285	292	299	306	313	320	327	334	341	348	355	362	369	376	
71	136	143	150	157	165	172	179	186	193	200	208	215	222	229	236	243	250	257	265	272	279	286	293	301	308	315	322	329	338	343	351	358	365	372	379	386	
72	140	147	154	162	169	177	184	191	199	206	213	221	228	235	242	250	258	265	272	279	287	294	302	309	316	324	331	338	346	353	361	368	375	383	390	397	
73	144	151	159	166	174	182	189	197	204	212	219	227	235	242	250	257	265	272	280	288	295	302	310	318	325	333	340	348	355	363	371	378	386	393	401	408	
74	148	155	163	171	179	186	194	202	210	218	225	233	241	249	256	264	272	280	287	295	303	311	319	326	334	342	350	358	365	373	381	389	396	404	412	420	
75	152	160	168	176	184	192	200	208	216	224	232	240	248	256	264	272	279	287	295	303	311	319	327	335	343	351	359	367	375	383	391	399	407	415	423	431	
76	156	164	172	180	189	197	205	213	221	230	238	246	254	263	271	279	287	295	304	312	320	328	336	344	353	361	369	377	385	394	402	410	418	426	435	443	

The BMI describes relative weight for height. It is calculated as weight (in kilograms) / height (in meters) squared. The National Heart, Lung, and Blood Institute (NHLBI) guidelines classify overweight as a BMI of 25 through 29.9 kg/meter squared, obesity as a BMI equal to or greater than 30 kg/meter squared, and extreme obesity as a BMI equal to or greater than 40 kg/meter squared.

Adapted from: National Heart Lung and Blood Institute. Clinical Guidelines on the Identification, Evaluation and Treatment of Overweight and Obesity in Adults. Available at: http://www.nhlbi.nih.gov/guidelines/obesity/ob_home.htm.