Policy Title: Initial Bone Marrow Transplant

Policy Number: F.07

Primary Department: Medical Management

Affiliated Department(s): N/A

NCQA Standard: N/A

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Special Instructions Alert:

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Definitions:

Stem cell transplantation: Process in which stem cells are harvested from either a patient’s (autologous) or donor’s allogeneic bone marrow or peripheral blood for intravenous infusion.

Autologous stem cell transplants: Must be used to effect hematopoietic reconstitution following severely myelotoxic doses of chemotherapy and/or radiotherapy used to treat various malignancies.

Allogeneic stem cell transplant: May also be used to restore function in recipients having an inherited or acquired deficiency or defect.

Bone marrow and peripheral blood stem cell transplantation: Process which includes mobilization, harvesting, and transplant of bone marrow or peripheral blood stem cells and the administration of high dose chemotherapy or radiotherapy prior to the actual transplant. A bone marrow or peripheral blood stem cell transplantation is covered, including the donor search when it is deemed that the member meets criteria for transplant.

Policy:

To ensure that the selection criteria are consistently followed and documented.

Procedure:

1. **Pre-transplant Evaluation** needs to include documentation of a psychosocial evaluation to assess a member’s ability to undergo this type of procedure and his/her support system to cope and adhere to the treatment plan. A psychiatric disorder or substance abuse problem warrant further evaluation and
follow-up. Therefore the following must be met of all candidates in addition to the disease specific criteria:

a. All patients who are being considered for HSCT must have a thorough assessment of their psychosocial situation, including support systems and coping skills, and careful assessment and documentation of past history or current diagnosis of substance abuse or dependence. If there are any indicators of current or past psychiatric disorders, referral for a formal psychiatric evaluation should also occur.

b. Transplantation Evaluation Rating Scale (TERS) to classify patients’ level of adjustment in 10 aspects of psychosocial functioning: current or past psychiatric diagnoses (Axis I and II), substance use/abuse, compliance, health behaviors, quality of family/social support, prior history of coping, coping with disease and treatment, quality of affect and mental status.

c. If substance abuse is identified, and if the disease is slow growing and transplant is not imperative and/or when other treatment is needed before transplantation, a referral be made to an addiction medicine specialist and chemical dependency treatment is begun before transplantation is offered. For those patients who require HSCT immediately, consultation must be obtained with an addiction medicine specialist and/or psychiatrist with experience in addiction during the patient’s hospital stay. This collaboration can serve to address both the management of acute withdrawal, if needed, and institute psychotherapeutic, educational and medical modalities to begin the recovery process. The patient must agree to a referral for ongoing chemical dependency treatment should be made once the patient is stable enough, medically, to participate in an addiction recovery program.

2. Also, a member needs to be assessed for his/her ability to tolerate the proposed cancer treatment and physiologic reserve. Therefore the following must be met of all candidates in addition to the disease specific criteria:

a. Karnofsky score greater than or equal to 70%* (see appendix) or

b. Eastern Cooperative Oncology Group (ECOG) grade 0-2*(see appendix)

Disease Specific Covered Indications:

A. Allogeneic Hematopoietic Stem Cell Transplantation (HSCT)

- Leukemia—Acute Myelogenous Leukemia (AML), Acute Lymphoblastic Leukemia (ALL), Chronic Myelogenous Leukemia (CML), Chronic Lymphoblastic Leukemia (CLL)
- Leukemia in remission (bone marrow contains < 5% blasts, normal level of RBCs, WBCs, and platelets and no signs and symptoms of malignancy)*
  - The National Comprehensive Cancer Network guidelines must be met (http://www.nccn.org/index.asp)
- Aplastic anemia when it is reasonable and necessary
- Severe combined immunodeficiency disease (SCID)
- Wiskott-Aldrich Syndrome
- Myelodysplastic Syndromes (MDS) pursuant to Coverage with Evidence Development (CED) in the context of a Medicare-approved, prospective clinical study.
  - The National Comprehensive Cancer Network guidelines must be met (http://www.nccn.org/index.asp)
- Myelofibrosis with myeloid metaplasia
- Primary refractory Hodgkin’s and non-Hodgkin’s lymphoma
  - The National Comprehensive Cancer Network guidelines must be met (http://www.nccn.org/index.asp)
- B-Thalassemia major(homozygous) for patients (need to meet all criteria set forth below for allogenic bone marrow or peripheral stem cell transplant):
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- with minimal or no portal fibrosis, hepatomegaly, or active hepatitis and
- who have an HLA matched donor and
- who show deterioration with conventional treatments including transfusions, splenectomy, and chelation (deferasirox or deferoxamine)

- Sickle cell anemia in children or young adults when both of the following are met (allogeneic or peripheral stem cell transplant):
  - Members have an HLA-matched donor and

Members with either a history of stroke or at increased risk of stroke or end-organ damage (factors associated with increased risk of stroke or end-organ damage include recurrent chest syndrome, recurrent vaso-occlusive crises and red blood cell alloimmunization on chronic transfusion therapy)

**Not Covered Indications (Allogeneic HSCT):**
*For Medicaid & Medicare non-covered indications see the special instructions section.*
The maximum age at which a patient is considered eligible for an allogeneic transplant varies and the type of preparative regime will often dictate the upper limit of a patient’s age. Decisions regarding the appropriate age of a candidate is a matter of clinical judgment made by the transplant medical practitioner.

**B. Autologous Stem Cell Transplantation (AuSCT)**
- Acute Leukemia in remission in patients who have a high probability of relapse and who have no human leucocyte antigens (HLA)-matched donor (acute myelogenous leukemia or acute lymphoblastic leukemia but **not covered for acute leukemia not in remission nor chronic myelogenous leukemia**)
  - The National Comprehensive Cancer Network guidelines must be met
(http://www.nccn.org/index.asp)
- Resistant non-Hodgkin’s lymphomas or those presenting with poor prognostic features following an initial response
  - The National Comprehensive Cancer Network guidelines must be met
(http://www.nccn.org/index.asp)
- Recurrent or refractory neuroblastoma
- Advanced Hodgkin’s disease who have failed conventional therapy and have no HLA-matched donor
  - The National Comprehensive Cancer Network guidelines must be met
(http://www.nccn.org/index.asp)
- Multiple Myeloma—**See special instructions below for coverage.**
- AuSCT in combination with high dose melphalan for patients with **primary amyloid light chain amyloidosis** (Not covered for non-primary amyloid light chain amyloidosis), with amyloid deposition in two or fewer organs and a cardiac left ventricular ejection fraction greater than 45%
- Testicular cancer
  - The National Comprehensive Cancer Network guidelines must be met
(http://www.nccn.org/index.asp)

**Non-covered indications (AuSCT):**
- Acute leukemia not in remission
- Chronic granulocytic leukemia
- Solid tumors other than Neuroblastoma
- Tandem transplantation (multiple rounds of AuSCT) for patients with multiple myeloma with the exception of patients who do not achieve complete remission (CR) or a very good partial

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response (VGPR) after the first autologous transplant. For those patients, tandem transplant may be approved within 6 months of the first transplant. (25; 26; 27; 28; 24; 24; 29),

- Non primary amyloid light chain amyloidosis; and
- *For Medicaid & Medicare non-covered indications see the special instructions section.*

C. **Relative Contraindications:**

Many factors affect the outcome of tissue transplantation; the selection process is designed to obtain the best result for each individual. Overall health, age, and disease stage are extremely important considerations in evaluating candidates. Relative but not absolute contraindications to hematopoietic stem-cell transplantation (HSCT) include, but are not limited to:

- **cardiac:** coronary artery disease, congestive heart failure, myocardial infarction or ejection fraction as measured by ECHO or MUGA of less than or equal to 50%, valvular disease with the exception of mitral valve prolapse, atrial fib/flutter, sick sinus syndrome or ventricular arrhythmias
- **liver function:** chronic hepatitis, cirrhosis (bilirubin at the upper limit of normal to greater than 1.5 times ULN and transaminases greater than 2.5 time the upper limit of normal)
- **poor renal function:** creatinine clearance < 50ml/min, on dialysis, or prior renal transplant
- **poor pulmonary function:** diffusion capacity (DLCO) < 65% of predicted or dyspnea at rest requiring O2
- **infection:** presence of human immunodeficiency virus OR an active form of any ONE of the following:
  1. hepatitis B virus (HBV)
  2. hepatitis C virus (HCV)
  3. human T-cell lymphotropic virus (HTLV)-1
  4. dental exam and x-rays to identify and treat potential sources of infection from the oral cavity
- **Karnofsky rating < 70%** and/or Eastern Cooperative Oncology Group (ECOG) performance status > 2
- **Cerebrovascular disease:** TIA or CVA
- **Diabetes:** requiring treatment with insulin or oral hypoglycemics but not diet alone
- **Inflammatory bowel disease:** Crohn’s or Ulcerative Colitis
- **Obesity:** BMI > 35 kg/m²
- **Peptic ulcer:** requiring treatment
- **Rheumatologic:** SLE, RA, polymyositis, mixed CTD, polymyalgia rheumatic
- **Solid tumor prior:** treated at any time in the patient’s past history, excluding non-melanoma skin cancer
- **Positive serum pregnancy test**

The rationale to proceed with transplantation, if a transplant candidate has sub-optimal organ function or a per-existing comorbid conditions (s) must be documented within the candidate’s medical record by the BMT physician.

Facilities performing stem cell transplants must be accredited by the Foundation for the Accreditation of Cellular Therapy and the Joint Accreditation Committee and compliant with the FACT_JACIE International Standards for Cellular Therapy Product Collection, Processing, and Administration manual.

D. **Appendix – KPS and ECOG:**

One tool that assesses a patient’s performance status is the Karnofsky Performance Scale. The scale ranges from 0 to 100%, with 100% representing patients without evidence of disease and 0% being
dead. A status score of 70% denotes those patients that are able to care for themselves but may not be able to effectively work, shop, drive, or care for family members; patients with an irreversible score or less the 70% generally have a poor prognosis.

- 100% – normal, no complaints, no signs of disease
- 90% – capable of normal activity, few symptoms or signs of disease
- 80% – normal activity with some difficulty, some symptoms or signs
- 70% – caring for self, not capable of normal activity or work
- 60% – requiring some help, can take care of most personal requirements
- 50% – requires help often, requires frequent medical care
- 40% – disabled, requires special care and help
- 30% – severely disabled, hospital admission indicated but no risk of death
- 20% – very ill, urgently requiring admission, requires supportive measures or treatment
- 10% – moribund, rapidly progressive fatal disease processes
- 0% – death.

The Eastern Cooperative Oncology Group (ECOG) developed a performance status tool. This tool assesses the patient’s disease progression, the impact of the disease on daily living, and provides information used to determine proper treatment and prognosis. Patients are classified based on the following information:

- 0 – Asymptomatic (Fully active, able to carry on all predisease activities without restriction)
- 1 – Symptomatic but completely ambulatory (Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature. For example, light housework, office work)
- 2 – Symptomatic, <50% in bed during the day (Ambulatory and capable of all self-care but unable to carry out any work activities. Up and about more than 50% of waking hours)
- 3 – Symptomatic, >50% in bed, but not bedbound (Capable of only limited self-care, confined to bed or chair 50% or more of waking hours)
- 4 – Bedbound (Completely disabled. Cannot carry on any self-care. Totally confined to bed or chair)
- 5 – Death

Special Instructions:

Medicare/All States:
In addition to the above policy, the following are also considered disease specific covered indications:

A. Allogeneic Hematopoietic Stem Cell Transplantation (HSCT):

Non-covered indications (Allogeneic HSCT):
- Allogeneic HSCT is not covered as treatment for multiple myeloma.

B. Autologous Stem Cell Transplantation (AuSCT)

- Multiple Myeloma—Single AuSCT (No tandem transplants or multiple rounds of AuSCT are covered) is only covered for Durie-Salmon Stage II or III patients that fit the following requirements (Stage II: intermediate tumor mass, 0.6 - 1.2 x 10^{12} plasma cells/m^2; Stage III: high tumor mass, > 1.2 x 10^{12} plasma cells/m^2):
  - Newly diagnosed or responsive multiple myeloma. This includes those patients with previously untreated disease, those with at least a partial response to prior chemotherapy (defined as a 50% decrease either in measurable paraprotein—serum or urine or in bone marrow infiltration, sustained for at least one month, and those in responsive relapse and...
Adequate cardiac (ejection fraction > 45%), renal (creatinine clearance > 50/ml/min), pulmonary (FEV1 > 80%), and hepatic function (bilirubin < 2.0 and transaminases less than two times normal)

Non-covered indications (AuSCT):
- Acute leukemia not in remission;
- Chronic granulocytic leukemia;
- Solid tumors other than Neuroblastoma;
- Tandem transplantation (multiple rounds of AuSCT) for patients with multiple myeloma;
- Non primary amyloid light chain amyloidosis; and,
- Primary amyloid light chain amyloidosis for members age 64 or older.

Medicaid/All States:
In addition to the above policy, the following are also considered disease specific covered indications:

A. Allogeneic Hematopoietic Stem Cell Transplantation (HSCT):
   - Waldenstrom Macroglobulinemia

Non-covered indications (Allogeneic SCT):
- Infantile malignant osteopetrosis
- Mucopolysaccharidoses
- Kostmann’s syndrome
- Leukocyte adhesion deficiencies
- X-linked lymphoproliferative syndrome
- Recurrent or refractory medulloblastoma and other primitive neuroectodermal tumors
- Recurrent or refractory Ewing’s sarcoma

B. Autologous Stem Cell Transplantation (AuSCT)
- Follicle center lymphoma
- Lymphoplasmacytoid lymphoma
- Marginal zone lymphoma
- Burkitt lymphoma
- Diffuse, large cell lymphoma
- Mantle cell lymphoma
- Precursor B-Cell leukemia
- Recurrent or refractory neuroblastoma or neuroblastoma of unfavorable cell type
- Ewing Sarcoma
- Retinoblastoma
- Wilm’s Tumor
- Medulloblastoma
- Pineoblastoma
- Primitive Neuro-ectodermal Tumor (PNET)
- Testicular Germ Cell Tumor
- Extragonadal Germ Cell Tumor
- Seminoma
- Choriocarcinoma
- Embryonal Carcinoma
- Mixed Germ Cell Tumors
- Teratoma
- Yolk-sac Tumor
• Germ Cell tumor of the Ovary
  a. The National Comprehensive Cancer Network guidelines must be met (http://www.nccn.org/index.asp)
• Multiple Myeloma---is only covered for Durie-Salmon Stage II or III patients that fit the following requirements (Stage II: intermediate tumor mass, 0.6 -1.2 x 10^{12} plasma cells/m^2; Stage III: high tumor mass, > 1.2 x 10^{12} plasma cells/m^2):
  a. Newly diagnosed or responsive multiple myeloma. This includes those patients with previously untreated disease, those with at least a partial response to prior chemotherapy (defined as a 50% decrease either in measurable paraprotein—serum or urine or in bone marrow infiltration, sustained for at least one month, and those in responsive relapse and
  b. Adequate cardiac (ejection fraction > 45%), renal (creatinine clearance > 50/ml/min), pulmonary( FEV1 > 80%), and hepatic function (bilirubin < 2.0 and transaminases less than two times normal)

Non-covered indications (AuSCT):
• Acute leukemia not in remission
• Chronic granulocytic leukemia
• Tandem transplantation (multiple rounds of AuSCT) for patients with multiple myeloma
• Non primary amyloid light chain amyloidosis
• Breast cancer

Medicaid/Iowa:
In addition to the above policy, the following are also considered disease specific covered indications:

A. Allogenic stem cell transplants are a covered benefit for the following:
• Aplastic anemia
• Severe combined immunodeficiency disease
• Follicular lymphoma
• Fanconi Anemia
• Paroxysmal hemoglobinuria
• Pure red cell aplasia
• Amegakaryocytosis/Congenital thrombocytopenia
• Beta thalassemia major
• Sickle Cell disease
• Hurler’s syndrome (mucopolysaccharidosis type 1)
• Adrenoleukodystrophy
• Metachromatic leukodystrophy
• Refractory anemia
• Angiogenic myeloid metaplasia (myelofibrosis)
• Familial erythrophagocytic lymphohistiocytosis and other histiocytic disorders
• Acute myelofibrosis
• Diamond-Blackfan anemia
• Epidermolysis bullosa
• Wiskott-Aldrich syndrome; or
• The following types of Leukemia
  a. Acute Myelocytic Leukemia
  b. Chronic Myelogenous Leukemia,
  c. Juvenile myelomonocytic leukemia
  d. Chronic myelomonocytic leukemia
  e. Acute myelogenous leukemia
f. Acute Leukemia

B. Autologous stem cell transplant is a covered benefit for the following:
- Acute Leukemia
- Chronic lymphocytic leukemia
- Plasma cell leukemia
- Non-Hodgkin’s Lymphomas;
- Hodgkin’s lymphoma
- Relapsed Hodgkin’s lymphoma
- Lymphomas presenting poor prognostic features;
- Follicular lymphoma
- neuroblastoma;
- Medulloblastoma
- Advanced Hodgkin’s disease
- Primitive neuroendocrine tumor (PNET)
- Atypical/rhabdoid tumor (ATRT)
- Wilms’ tumor
- Ering’s sarcoma
- Metastatic germ cell tumor or
- Multiple myeloma

Medicaid/New Hampshire:
In addition to the above policy, the following are also considered disease specific covered indications:

A. Allogenic stem cell transplants are a covered benefit for the following:
- Paroxysmal nocturnal hemoglobinuria
- Fanconi’s anemia

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Approved by: __________________________________ Date: 03/28/2014
Corporate Chief Operating Officer

Reviewed and approved by Policy and Procedure Committee: Date: 01/24/2014

Reviewed and approved by Medical Policy Operations Committee: Date: 01/31/2014

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References:

Single versus double autologous stem-cell transplantation for multiple myeloma


26. Cavo M; Tosi P; Zamagni E; Cellini C; Tacchetti P; Patriarca F; Di Raimondo F; Volpe E; Ronconi S; Cangini D; Narni F; Carubelli A; Masini L; Catalano L;

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