POLICY AND PROCEDURE MANUAL

Policy Title: Hematopoietic Cell Transplant for Primary Immunodeficiency Disorders
Policy Number: F.30

Primary Department: Medical Management
Affiliated Department(s): N/A

NCQA Standard: N/A
URAC Standard: N/A

Last Revision Date: 03/04/2016
Revision Dates: 02/13/2015; 03/04/2016
Effective Date: 03/27/2015
Next Review Date: 03/2017
Review Dates: 03/27/2015; 03/25/2016

Special Instructions Alert: N/A

<table>
<thead>
<tr>
<th>State/Program</th>
<th>MI</th>
<th>IL</th>
<th>IA</th>
<th>Commercial</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medicare:</td>
<td>☐SNP ☐MA ☐PDP</td>
<td>☐SNP ☐MA ☐PDP</td>
<td>☐SNP ☐MA ☐PDP</td>
<td>☐Exchange</td>
</tr>
<tr>
<td>Medicaid:</td>
<td>☐TANF ☐SPD ☐SCHIP</td>
<td>☐TANF ☐SPD ☐SCHIP</td>
<td>☐TANF ☐SPD ☐SCHIP</td>
<td>☐TANF ☐SPD ☐SCHIP</td>
</tr>
<tr>
<td>Commercial:</td>
<td>☐Exchange</td>
<td>☐Exchange</td>
<td>☐Exchange</td>
<td>☐Exchange</td>
</tr>
</tbody>
</table>

Definition:

Severe Combined Immunodeficiency: Is a group of disorders with several genetic causes. Children with SCID lack virtually all immune protection from bacteria, viruses, and fungi.

Wiskott–Aldrich Syndrome: Wiskott–Aldrich syndrome is characterized by thrombocytopenia with small platelets, eczema and recurrent infections.

Familial Hemophagocytic Lymphohistiocytosis: Familial HLH is characterized by episodes of fever, hepatosplenomegaly and cytopenias.

Chediak–Higashi Syndrome: Chediak–Higashi syndrome is characterized by oculocutaneous albinism, recurrent infections and the presence of giant granules in hematopoietic and other cells.

Severe Congenital Neutropenia: Severe congenital neutropenia is characterized by an absolute neutrophil count less than 0.2 × 10^9 per liter.

Chronic Granulomatous Disease: Chronic granulomatous disease is characterized by recurrent pyogenic infections in patients with normal neutrophil numbers. Patients present with deep tissue infections and sepsis due to catalase-positive organisms such as Staphylococcus aureus and Aspergillus fumigatus.

HIGM1= Hyper IgM Syndrome (CD40 Ligand Deficiency): Individuals may have high or normal levels of immunoglobulin M (IgM) antibody. People with X-linked hyper IgM syndrome have low levels of three other classes of antibodies: immunoglobulin G (IgG), immunoglobulin A (IgA), and immunoglobulin E (IgE).

Griscelli Syndrome Type 2: These individuals have immune system abnormalities in addition to having hypopigmented skin and hair.
X-linked Lymphoproliferative Disease | X-linked lymphoproliferative disease (XLP) is a disorder of the immune system and blood-forming cells that is found almost exclusively in males. These individuals experience an exaggerated immune response to the Epstein-Barr virus (EBV) which leads to hemophagocytic lymphohistiocytosis (HLH).

Leukocyte Adhesion Defect Type 1 | This is an immunosystem malfunction where bacterial and fungal infections most commonly occur on the skin and mucous membranes such as the moist lining of the nose and mouth.

**Policy:** Primary immune deficiency diseases (PIDD) are due to genetic factors which cause people to be more susceptible to infections. There are more than 200 different forms of PIDDs. These diseases are classified by either adaptive immunity (i.e., T-cell, B-cell or combined immunodeficiencies) or of innate immunity (e.g., phagocyte and complement disorders). The treatment of PIDD’s is complex and generally requires both supportive and definitive strategies. Ig replacement therapy is the mainstay of therapy for B-cell disorders, and is also an important supportive treatment for many patients with combined immunodeficiency disorders. The treatment of innate immunodeficiency disorders varies depending on the type of defect, but may involve antifungal and antibiotic prophylaxis, cytokine replacement, vaccinations and bone marrow transplantation. It is important to utilize early transplantation before the development of serious infections that contribute to a significant increase in the risk of mortality following HSCT.

**Criteria for Allogeneic Hematopoietic Cell Transplantation:**
Meridian considers allogeneic hematopoietic cell transplantation medically necessary for members with the following primary immunodeficiencies:

- Defective T and B lymphocytes
  - Wiskott–Aldrich syndrome
  - HIGM1= hyper IgM syndrome (CD40 ligand deficiency);
- Dysfunctional T lymphocytes
  - Chediak-Higashi syndrome
  - Familial hemophagocytic lymphohistiocytosis (HLH) (defects in perforin, MUNC, etc.)
  - Griscelli syndrome type 2
  - XLP=X-linked lymphoproliferative disease
- Absent T- and B-lymphocyte function
  - SCID
- Absent or defective neutrophil function
  - Kostmann syndrome= Severe congenital neutropenia
  - Chronic granulomatous disease
  - Leukocyte adhesion defect Type 1

**Criteria for Autologous Hematopoietic Cell Transplantation:**
Meridian considers autologous hematopoietic cell transplantation experimental for the treatment of primary immunodeficiency disorders because its effectiveness has not been recognized. Also, as consideration for hematopoietic stem cell transplantation these guidelines must be met:

1. The member meets selection criteria requirements regarding organ function. The following values should be used: cardiac function (left ventricular ejection fraction equal or greater than 45 %); pulmonary function [forced vital capacity (FVC)/forced expiratory volume in 1 second (FEV1)/diffusion capacity of the lung for carbon monoxide (DLCO) equal to or greater than 50 % predicted]; Renal function with a serum creatinine < 2 mg/dl of CrCl > 50 ml/min; Liver function no frank cirrhosis.
2. Emotional and psychiatric stability, including a strong family or alternative support network (documented by formal social work evaluation)
3. Ability to understand the risks of the procedures
4. Karnofsky performance score or Lansky score of 70% or greater or Southwestern Oncology Group (SWOG)/Eastern 6. Cooperative Oncology Group (ECOG) score of 0 to 2
5. No active infection including but not limited to HIV, hepatitis B, hepatitis C, or potential oral sources
6. No persistent or active substance or alcohol abuse
7. Absence of psychiatric disease that would interfere with the member’s ability to comply with the pre- or post-transplant therapeutic regimen

No significant history of medical noncompliance as defined by Meridian Health Plan Policy I.07:

1. For members with a history of tobacco use, if the member fails or refuses to submit to monthly cotinine testing for the preceding 6 months prior to the transplant and while listed, or refuses to actively and continuously participate in an accepted smoking cessation program.
2. For members with a history of alcohol abuse, member fails or refuses to submit to testing for alcohol use. Absence of documentation showing member has not engaged in alcohol use for at least six months prior to transplant and monthly while listed.
3. For members with a history of illicit drug use, member fails or refuses to submit to testing for illegal drug use. Absence of documentation showing member has not engaged in illegal drug use for at least six months prior to transplant and monthly testing while listed.
4. Tobacco, Alcohol and Drug Addiction: Refusal or failure to participate in available addiction interventions for actively using members must be documented in non-compliance determinations.

* 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 should 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.

5. Documentation of non-impactable social issues that substantially increase the risks of an adverse outcome of the medical therapy or transplant at issue
6. Severely Mentally Ill Adults and Severely Emotionally Disturbed Minors: Non-adherence to psychotropic medications or medical regimen in SMI or SED members for whom core symptoms include lack of insight into illness, must be assessed for adequacy of and engagement with psychosocial resource supports in Care Coordination prior to non-compliance determinations.
7. Developmental or Acquired Cognitive Impairment and Dementia: Psychosocial and guardianship support as well as reversibility of impairment must be assessed and documented prior to non-compliance determinations.

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

**Special Instructions:** N/A

**Line of Business Applicability:**
For Medicaid/Medicaid Expansion Plan members, this policy will apply. Coverage is based on medical necessity criteria being met and the codes being submitted and considered for review being included on either
the Michigan Medicaid Fee Schedule (located at: http://www.michigan.gov/mdch/0,1607,7-132-2945_42542_42543_42546_42551-159815--,00.html), the Illinois Medicaid Fee Schedule (located at: http://www.illinois.gov/hfs/MedicalProviders/MedicaidReimbursement/Pages/default.aspx), or the Iowa Medicaid Fee Schedule (located at: http://dhs.iowa.gov/ime/providers/csrp/fee-schedule). If there is a discrepancy between this policy and either the Michigan Medicaid Provider Manual (located at: http://www.michigan.gov/mdch/0,1607,7-132-2945_5100-87572--,00.html), the Illinois Medicaid Provider Manual (located at: http://www.illinois.gov/hfs/MedicalProviders/Handbooks/Pages/default.aspx), or the Iowa Medicaid Provider Manual (located at: http://dhs.iowa.gov/policy-manuals/medicaid-provider) the applicable Medicaid Provider Manual will govern.

For Medicare members, coverage is determined by the Centers for Medicare and Medicaid Services (CMS). If a coverage determination has not been adopted by CMS, this policy applies. Medicare Fee Schedules can be found on the CMS website (https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/FeeScheduleGenInfo/index.html).

For Exchange members, please refer to the Meridian Choice Certificate of Coverage located here: https://share13.mhplan.com/sites/communications/Bronson%20Healthcare/MCH%20Certificate%20of%20Coverage%202016.pdf. If there is a discrepancy between this policy and the Certificate of Coverage for Meridian Choice, the Certificate will govern.

Approved by: __________________________________

Corporate Chief Operating Officer

Date: 04/21/2016

Reviewed and approved by Policy and Procedure Committee: Date: 03/04/2016

Reviewed and approved by Medical Policy Operations Committee: Date: 03/11/2016

Reviewed and approved by Physician Advisory Committee: Date: 03/25/2015

Reviewed and approved by Healthcare Compliance Subcommittee: Date: 04/21/2016

References:
2. Primary immunodeficiency Christine McCusker and Richard Warrington. Allergy, Asthma & Clinical Immunology Nov. 2011, 7(Suppl 1)
3. Primary immunodeficiency diseases: An update from the International Union of Immunological Societies Primary Immunodeficiency Diseases Classification Committee. Geha, Raif S. et al. Journal of Allergy and Clinical Immunology , Volume 120 , Issue 4 , 776 – 794