POLICY AND PROCEDURE MANUAL

Policy Title: Hematopoietic Cell Transplantation for Multiple Myeloma	**Policy Number: F.25**
Primary Department: Medical Management	**NCQA Standard: N/A**
Affiliated Department(s): N/A	**URAC Standard: N/A**
Last Revision Date: 10/2018 **Revision Dates: 01/2015; 08/2015; 08/2016; 09/2017; 12/2017; 10/26/2018** **Effective Date: 03/27/2015**	**Next Review Date: 12/2019** **Review Dates: 03/27/2015; 09/25/2015; 09/23/2016; 09/28/2017; 12/13/2017; 12/19/2018**
Applicable Lines of Business: ☐MeridianCare ☒MeridianHealth ☐MeridianComplete ☒MeridianChoice	
Applicable States: ☐All ☒MI ☒IL ☐OH ☐_____ ☐_____	
Applicable Programs: ☒All ☐Other _____	
Policy is to be published: Internally Only ☐ Internally & Externally ☒	

Definitions:

Multiple Myeloma	Multiple Myeloma (MM) is a systemic malignancy of plasma cells that represents approximately 10% of all hematologic cancers in the United States. The plasma cells proliferate in the bone marrow and often results in extensive skeletal destruction with osteolytic lesions, osteopenia, kidney damage, and/or pathologic fractures. It is treatable but rarely curable.

Policy: Autologous hematopoietic cell transplantation (HCT), performed either at the time of initial diagnosis or at relapse, is considered the standard of care for younger patients (less than 70 years of age) with newly diagnosed multiple myeloma (MM) . While neither chemotherapy nor autologous HCT produces a cure, event-free survival and overall survival are prolonged following autologous HCT when compared with treatment with conventional chemotherapy alone. In contrast, allogeneic HCT has the potential for cure, although at a cost of increased treatment-related mortality. The use of allogeneic HCT for MM is not discussed as it is currently considered investigational and experimental.

Procedures:
Criteria for Coverage:
Meridian Health Plan (MHP) considers *single* ***autologous*** hematopoietic stem cell transplantation (SCT) medically necessary for the treatment of Multiple Myeloma when all of the required documentation listed below are met and if one of the following criteria is met:

1. 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 and/or urine] *or* in bone marrow infiltration, sustained for at least one month).
2. Refractory to primary therapy in an individual with relapse or progressive disease

Meridian Health Plan considers *tandem **autologous*** hematopoietic stem cell transplantation (SCT) from an haploidentical to fully matched related donor or well-matched unrelated donor (i.e., meeting National Donor Marrow Program (NDMP) criteria for selection of unrelated donors) medically necessary for the treatment of Multiple Myeloma when all of the required documentation below are met and if one of the following criteria is met:

1. Members with active myeloma; and
2. Planned 1st and 2nd transplantation should be within a 6-month period

Required Documentation:

As consideration for hematopoietic stem cell transplantation these guidelines **MUST** be met:

1. Cardiac function evaluation:
    a. Left ventricular ejection fraction equal or greater than 40 %
    b. If present, coronary artery disease and cardiac arrhythmias must me controlled/stable
2. Pulmonary function evaluation:
    a. 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.
3. Renal function with a serum creatinine < 2 mg/dl of Cl_{cr} > 50 ml/min
4. Liver function studies indicate no frank cirrhosis.
5. No active infection must be present including any of the following:

    a. Human immunodeficiency virus (HIV)
    b. Hepatitis B virus (HBV)
    c. Hepatitis C virus (HCV)
    d. Human T-cell lymphotropic virus (HTLV)-1
    e. Dental exam and x-rays to identify and treat potential sources of infection from the oral cavity

6. Karnofsky rating 70% or greater and/or Eastern Cooperative Oncology Group (ECOG) performance status less than 2
7. Documentation of member's ability to understand the risks of the procedures.
8. Emotional and psychiatric stability, including a strong family or alternative support network (documented by formal social work evaluation)
9. Absence of psychiatric disease that would interfere with the member's ability to comply with the pre- or post-transplant therapeutic regimen

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.

Member Assessment of Compliance with Plan of Care (applicable for ages 10 and above):

- Alcohol screen- abstinence for the past 6 months prior to actual transplant approval, if member history includes use of alcohol. If no history exists then 1 negative alcohol screen must be submitted for members with no history of past alcohol use
- Drug screen-abstinence for the past 6 months prior to actual transplant approval if history exists of drug use. If no history exists then 1 negative drug screen must be submitted for members with no history of positive drug screen.
- Nicotine screening- abstinence for the past 6 months prior to actual transplant approval if history of smoking. If no history exists then 1 negative cotinine level must be submitted

Refusal or failure to undergo monthly testing for those members with a history of alcohol, tobacco, and/or drug use will be interpreted as a positive test result.

Six month abstinence period may be shortened in cases where patient's condition is sufficiently advanced that mortality is reasonably expected before the full abstinence period can be completed. Patients granted a waiver of the six month abstinence period require documentation of participation in a formal outpatient treatment program, when practical, as well as serial blood or urine testing no less frequently than monthly. A positive test result at any time prior to the procurement phase will result in denial.

Network:
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.

Relative Contraindications:
Eligibility for autologous HCT in Multiple Myeloma varies across countries and institutions. In most European countries, transplantation for myeloma is offered primarily to patients younger than 65 years of age. In the United States, a strict age limit is not used. Instead, decisions are made on a case-by-case basis based upon "physiologic age" and vary across institutions.
These are guidelines and the decision on transplant eligibility should be made based on a risk-benefit assessment and the needs and wishes of the patient. There is insufficient evidence at this time that the newer chemotherapeutic programs (eg, bortezomib, thalidomide, lenalidomide) will result in a reduced need for HCT.

Absolute Contraindications:

1. MHP considers ***allogeneic*** hematopoietic stem cell transplant, myeloablative or nonmyeloablative, as therapy of newly diagnosed multiple myeloma or as salvage therapy, as <u>investigational</u> **and therefore not a covered benefit**. There has been limited success with allogeneic stem cell transplantation (allo-SCT) for treatment of myeloma due to related toxicity. A majority of hase 3 trials do not show a survival advantage for allogenic SCT compared with autologous SCT[2.] Also, there are limited randomized trials and this should be considered in the context of clinical trials.

Diagnoses excluded for transplant include members with indolent myeloma, smoldering myeloma[*], and monoclonal gammopathy of uncertain significance (MGUS).

**Smoldering (Asymptomatic) Myeloma*Monoclonal gammopathy of uncertain significance (MGUS).

<u>APPENDICIES:</u>

A. International Staging System (ISS) for Multiple Myeloma

Stage	ISS criteria[6]	Revised- ISS (R-ISS)[6]
1	Serum beta-2 microglobulin < 3.5 mg/l, Serum albumin ≥ 3.5 g/dl	ISS stage 1 and standard-risk chromosomal abnormalities by FISH and Serum LDH ≤ the upper limit of normal
2	Neither stage 1 or 3	Not R-ISS stage 1 or 2
3	Serum beta-2 microglobulin >5.5 mg/l	ISS stage 3 and either high-risk chromosomal abnormalities by FISH -or_ Serum LDH >the upper limit of normal

B.

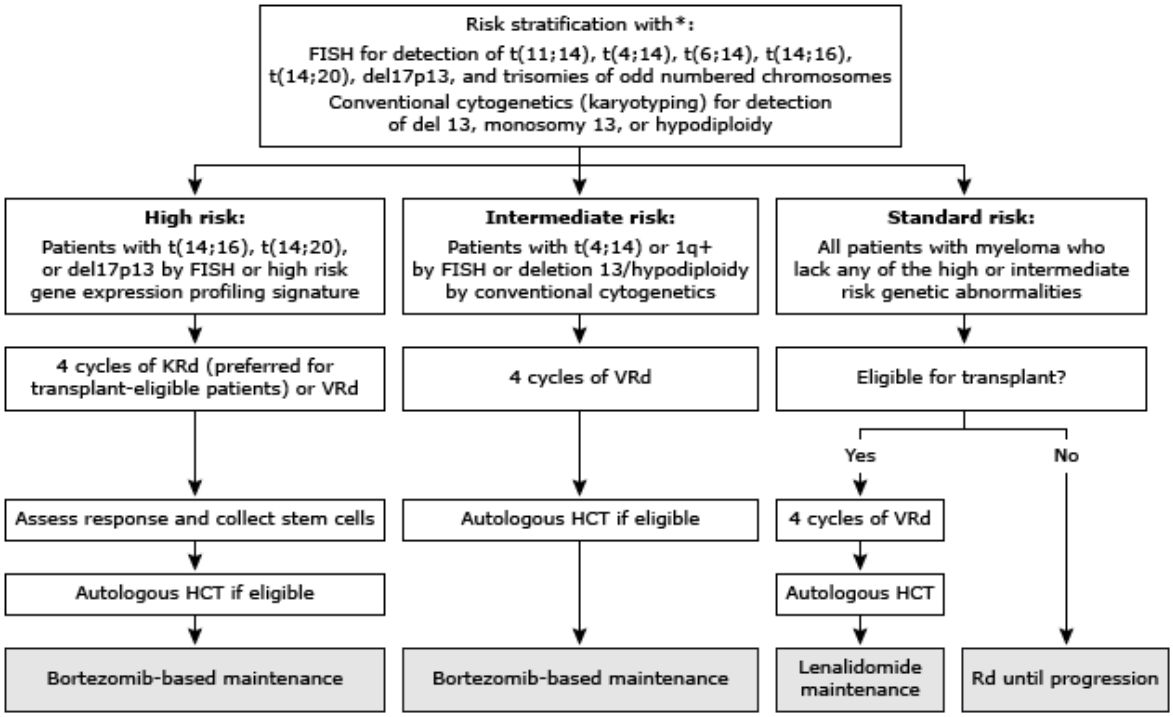
C. Durie-Salmon Staging for Multiple Myeloma

Stage	Durie-Salmon Criteria
1	All of the following: • Hemoglobin > 10 g/dl • Serum Calcium < or = 12 mg/dl • Bone x-ray, normal bone structure or only solitary bone lesion • Low M-component: IgG < 5 g/dl, or IgA < 3 g/dl or Bence Jones protein < 4 g/24 hr
2	Neither Stage 1 or 3
3	One or more of the following: • Hemoglobin < 8.5 g/dL

	• Serum Calcium > 12 mg/dl • Advanced lytic bone lesions • High M-component: IgG > 7 g/dl, IgA > 5 g/dl or Bence Jones protein > 12 g/24 hr
Subclass= A: Normal renal function (Cr< 2.0 mg/dl) B: Abnormal renal function (Cr>2.0 mg/dl)	

In the United States, the Centers for Medicare and Medicaid Services approves reimbursement for high-dose therapy with autologous HCT in newly-diagnosed patients with myeloma who are less than 78 years old and have Durie-Salmon stage II or III disease, and for selected patients who have been previously treated. Additional details are available on the Centers for Medicare and Medicaid Services website at www.cms.gov

D.



This algorithm illustrates a general approach to the treatment of a patient with newly diagnosed multiple myeloma. The clinician is expected to use his or her independent medical judgment in the context of individual circumstances to make adjustments, as necessary.
FISH: fluorescence in situ hybridization; VRd: bortezomib, lenalidomide, low-dose dexamethasone; KRd: carfilzomib, lenalidomide, low-dose dexamethasone; Rd: lenalidomide plus low-dose dexamethasone; HCT: hematopoietic cell transplantation.
* All myeloma patients are risk-stratified at initial diagnosis based on FISH studies on the bone marrow. If FISH is unavailable, conventional cytogenetics can be used as an alternative but is much less sensitive.

Line of Business Applicability:
This policy applies to Michigan Medicaid, Illinois Medicaid, and Individual plans.

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), or the Illinois Medicaid Fee Schedule (located at:

http://www.illinois.gov/hfs/MedicalProviders/MedicaidReimbursement/Pages/default.aspx). 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), or the Illinois Medicaid Provider Manual (located at: http://www.illinois.gov/hfs/MedicalProviders/Handbooks/Pages/default.aspx) the applicable Medicaid Provider Manual will govern.

For **Individual** members, consult the individual insurance policy. If there is a discrepancy between this policy and the individual insurance policy document, the guidelines in the individual insurance policy will govern.

State specific special instructions:

None: ☒
MI:
IL:
OH:

References:

1. Curr Opin Oncol. 2009 March; 21(2): 162–170. doi:10.1097/CCO.0b013e328324bc04. Stem cell transplantation for multiple myeloma.Shaji Kumar
2. Up to date Autologous hematopoietic cell transplantation in multiple myeloma. Updated: 04/27/2015.
3. UpToDate. Clinical features, laboratory manifestations, and diagnosis of multiple myeloma. Assessed 10/15/18.
4. Michigan Department of Health and Human Services. Medicaid Provider Manual. Billing & Reimbursement for Institutional Providers. (Issue Date: July 1, 2016).
5. Illinois Healthcare and Family Services. Handbook for Providers of Hospital Services, Chapter H-200, Section H-254. Policy and Procedures for Hospital Services. (Issue Date: September 2014).
6. National Comprehensive Cancer Network. Guidelines Version 2.2018; Multiple Myeloma. 10/02/2017.

State Letters/Bulletins					
CMS National/Local Coverage Determination (NCD/LCD)	NCD 110.8.1 Stem Cell Transplantation (v5, 8/4/2010)				
Medicare Managed Care Manual:					
Medicaid CFR:		89 Ill Admin Code Sec. 148.82			
State Administrative Codes:					
Contract Requirements:					
Related Policies:	Member Compliance I.07				