# Hematopoietic Cell Transplantation for Plasma Cell Dyscrasias, Including Multiple Myeloma and POEMS Syndrome

**Policy #** 00060
Original Effective Date: 01/28/2002
Current Effective Date: 04/13/2020

*Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc.(collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.*

*Note: Hematopoietic Cell Transplantation for Primary Amyloidosis or Waldenstrom's Macroglobulinemia is addressed separately in medical policy 00138.*

## When Services Are Eligible for Coverage

*Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:*

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

**Multiple Myeloma**

## When Services Are Eligible for Coverage

*Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:*

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider a single or second (salvage) autologous hematopoietic cell transplantation (HCT) to treat multiple myeloma to be **eligible for coverage.****

Based on review of available data, the Company may consider tandem** autologous-autologous hematopoietic cell transplantation (HCT) to treat multiple myeloma be **eligible for coverage.****

**Tandem transplantation refers to a planned infusion (transplant) of previously harvested hematopoietic stem cells with a repeat hematopoietic cell infusion (transplant) that is performed within 6 months of the initial transplant. This is distinguished from a repeat transplantation requested or performed more than 6 months after the first transplant, and is used as salvage therapy after failure of initial transplantation or relapsed disease.

Based on review of available data, the Company may consider tandem transplantation with an initial round of autologous hematopoietic cell transplantation (HCT) followed by a non-marrow-ablative conditioning regimen and allogeneic hematopoietic cell transplantation (HCT) (i.e., reduced-intensity conditioning transplant) to treat newly diagnosed multiple myeloma patients to be **eligible for coverage.****

# When Services Are Considered Investigational

*Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.*

Based on review of available data, the Company considers allogeneic hematopoietic cell transplantation (HCT), myeloablative or nonmyeloablative, as initial therapy of newly diagnosed multiple myeloma or as salvage therapy to be **investigational.***

**POEMS Syndrome**

# When Services Are Eligible for Coverage

*Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:*

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider autologous hematopoietic cell transplantation (HCT) to treat disseminated POEMS syndrome to be **eligible for coverage.****

Hematopoietic Cell Transplantation for Plasma Cell Dyscrasias, Including Multiple Myeloma and POEMS Syndrome

Policy # 00060
Original Effective Date: 01/28/2002
Current Effective Date: 04/13/2020

# When Services Are Considered Investigational

*Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.*

Based on review of available data, the Company considers allogeneic and tandem hematopoietic cell transplantation (HCT) to treat POEMS syndrome to be **investigational.***

# Policy Guidelines

The International Working Group on Myeloma has updated the European Group for Blood and Marrow Transplant criteria to describe a complete response to multiple myeloma therapy. The criteria include negative immunofixation on the serum and urine; disappearance of soft tissue plasmacytomas; and 5% or fewer plasma cells in bone marrow aspiration.

Patients with disseminated POEMS syndrome may have diffuse sclerotic lesions or disseminated bone marrow involvement.

# Background/Overview

**Multiple Myeloma**

MM is a systemic malignancy of plasma cells that represents approximately 10% of all hematologic cancers. It is treatable but rarely curable. At diagnosis, most patients have generalized disease, and the selection of treatment is influenced by patient age, general health, prior therapy, and the presence of disease complications.

The disease is staged by estimating tumor mass, based on various clinical parameters such as hemoglobin, serum calcium, number of lytic bone lesions, and the presence or absence of renal failure. MM usually evolves from an asymptomatic premalignant stage (termed *monoclonal gammopathy of undetermined significance*). Treatment is usually reserved for patients with symptomatic disease (usually progressive myeloma), whereas asymptomatic patients are observed because there is little evidence that early treatment of asymptomatic MM prolongs survival compared with therapy delivered at the time of symptoms or end-organ damage. In some patients,

an intermediate asymptomatic but more advanced premalignant stage is recognized and referred to as smoldering MM. The overall risk of disease progression from smoldering to symptomatic MM is 10% per year for the first 5 years, approximately 3% per year for the next 5 years, and 1% for the next 10 years.

**POEMS Syndrome**

POEMS syndrome (also known as osteosclerotic myeloma, Crow-Fukase syndrome, or Takatsuki syndrome) is a rare, paraneoplastic disorder secondary to a plasma cell dyscrasia. This complex, multiorgan disease was first described in 1938, but the acronym POEMS was coined in 1980, reflecting hallmark characteristics of the syndrome: polyneuropathy, organomegaly, endocrinopathy, M protein, and skin changes. No single test establishes the presence of POEMS syndrome. Its pathogenesis is undefined, although some evidence has suggested it is mediated by an imbalance of proinflammatory cytokines including interleukin (IL)-1β, IL-6, and tumor necrosis factor α; vascular endothelial growth factor may also be involved. However, specific criteria have been established, and the syndrome may entail other findings in the constellation of signs and symptoms, as shown in Table 1. Both major criteria and at least 1 of the minor criteria are necessary for diagnosis.

**Table 1. Criteria and Associations for POEMS Syndrome**

| ***Major Criteria*** | ***Minor Criteria*** | ***Known Associations*** | ***Possible Associations*** |
|---|---|---|---|
| Polyneuropathy | | | |
| | Sclerotic bone lesions | Clubbing | Pulmonary hypertension |
| Monoclonal plasma-proliferative disorder | | | |
| | Castleman disease | Weight loss | Restrictive lung disease |
| | Organomegaly (splenomegaly, | Thrombocytosis | Thrombotic diatheses |

| ***Major Criteria*** | ***Minor Criteria*** | ***Known Associations*** | ***Possible Associations*** |
|---|---|---|---|
| | hepatomegaly, lymphadenopathy) | | |
| | Edema (edema, pleural effusion, ascites) | Polycythemia | Arthralgias |
| | Endocrinopathy (adrenal, thyroid, pituitary, gonadal, parathyroid, pancreatic) | Hyperhidrosis | Cardiomyopathy (systolic dysfunction) |
| | Skin changes (hyperpigmentation, hypertrichosis, plethora, hemangiomata, white nails) | | Fever |
| | Papilledema | | Low vitamin $B_{12}$ levels |
| | | | Diarrhea |

The prevalence of POEMS syndrome is unclear. A national survey in Japan showed a prevalence of about 0.3 per 100000. Other large series had been described in the United States and India. In general, patients with POEMS have superior overall survival compared with that of MM (nearly 14 years in a large series). However, given the rarity of POEMS, no RCTs of therapies have been reported. Numerous approaches have included ionizing radiation, plasmapheresis, intravenous immunoglobulin, interferon-α, corticosteroids, alkylating agents, azathioprine, tamoxifen, trans-retinoic acid, and high-dose chemotherapy with autologous hematopoietic cell transplantation (HCT) support. Optimal treatment involves eliminating the plasma cell clone (eg, by surgical excision or local radiotherapy for an isolated plasmacytoma) or systemic chemotherapy in patients

with disseminated disease (eg, medullary disease or multiple plasmacytomas). Given the underlying plasma cell dyscrasia of POEMS syndrome, newer approaches to MM, including bortezomib, lenalidomide, and thalidomide, are also under investigation.

**Hematopoietic Cell Transplantation**

HCT is a procedure in which hematopoietic stem cells are intravenously infused to restore bone marrow and immune function in cancer patients who receive bone marrow-toxic doses of cytotoxic drugs with or without whole-body radiotherapy. Hematopoietic stem cells may be obtained from the transplant recipient (autologous HCT) or a donor (allogeneic HCT [allo-HCT]). They can be harvested from bone marrow, peripheral blood, or umbilical cord blood shortly after delivery of neonates.

Immunologic compatibility between infused hematopoietic stem cells and the recipient is not an issue in autologous HCT. In allogeneic stem cell transplantation, immunologic compatibility between donor and patient is a critical factor for achieving a successful outcome. Compatibility is established by typing of human leukocyte antigens (HLA) using cellular, serologic, or molecular techniques. HLA refers to the gene complex expressed at the HLA-A, -B, and -DR (antigen-D related) loci on each arm of chromosome 6. An acceptable donor will match the patient at all or most of the HLA loci.

**Conditioning for Hematopoietic Cell Transplantation**

**Conventional Conditioning**

The conventional ("classical") practice of allo-HCT involves administration of cytotoxic agents (e.g., cyclophosphamide, busulfan) with or without total body irradiation at doses sufficient to cause bone marrow ablation in the recipient. The beneficial treatment effect of this procedure is due to a combination of the initial eradication of malignant cells and subsequent graft-versus-malignancy effect mediated by non-self-immunologic effector cells. While the slower graft-versus-malignancy effect is considered the potentially curative component, it may be overwhelmed by existing disease in the absence of pretransplant conditioning. Intense conditioning regimens are limited to patients who are sufficiently medically fit to tolerate substantial adverse effects. These include opportunistic infections secondary to loss of endogenous bone marrow function and organ damage or failure caused by cytotoxic drugs. Subsequent to graft infusion in allo-HCT, immunosuppressant drugs are

required to minimize graft rejection and graft-versus-host disease, which increases susceptibility to opportunistic infections.

The success of autologous HCT is predicated on the potential of cytotoxic chemotherapy, with or without radiotherapy, to eradicate cancerous cells from the blood and bone marrow. This permits subsequent engraftment and repopulation of the bone marrow with presumably normal hematopoietic stem cells obtained from the patient before undergoing bone marrow ablation. Therefore, autologous HCT is typically performed as consolidation therapy when the patient's disease is in complete remission. Patients who undergo autologous HCT are also susceptible to chemotherapy-related toxicities and opportunistic infections before engraftment, but not graft-versus-host disease.

**Reduced-Intensity Conditioning Allogeneic Hematopoietic Cell Transplantation**
RIC refers to the pretransplant use of lower doses of cytotoxic drugs or less intense regimens of radiotherapy than are used in traditional full-dose myeloablative conditioning treatments. Although the definition of RIC is variable, with numerous versions employed, all regimens seek to balance the competing effects of relapse due to residual disease and non-relapse mortality. The goal of RIC is to reduce disease burden and to minimize associated treatment-related morbidity and non-relapse mortality in the period during which the beneficial graft-versus-malignancy effect of allogeneic transplantation develops. RIC regimens range from nearly total myeloablative to minimally myeloablative with lymphoablation, with intensity tailored to specific diseases and patient condition. Patients who undergo RIC with allo-HCT initially demonstrate donor cell engraftment and bone marrow mixed chimerism. Most will subsequently convert to full-donor chimerism. In this review, the term reduced-intensity conditioning will refer to all conditioning regimens intended to be nonmyeloablative.

**MM treatment overview**
In the prechemotherapy era, the median survival for a patient diagnosed with MM was approximately 7 months. After the introduction of chemotherapy (eg, the alkylating agent melphalan in the 1960s), prognosis improved, with a median survival of 24 to 30 months and 10-year survival of 3%. In a large group of patients with newly diagnosed MM, there was no difference in overall survival reported during a 24-year period from 1971-1994, with a trend toward improvement during 1995-2000, and a statistically significant benefit in overall survival during 2001-2006. These data

suggested that autologous HCT was responsible for the trends during 1994-2000, while novel agents have contributed to the improvement since 2001.

The introduction of novel agents and better prognostic indicators has been the major advances in the treatment of this disease. Novel agents such as the proteasome inhibitor bortezomib and the immunomodulatory derivatives thalidomide and lenalidomide first showed efficacy in relapsed and refractory myeloma and now have been integrated into first-line regimens. With the introduction of these novel treatments, it is now expected that most patients with MM will respond to initial therapy, and only a small minority will have refractory disease.

# FDA or Other Governmental Regulatory Approval

**U.S. Food and Drug Administration (FDA)**

The FDA regulates human cells and tissues intended for implantation, transplantation, or infusion through the Center for Biologics Evaluation and Research, under Code of Federal Regulation, Title 21, parts 1270 and 1271. Hematopoietic stem cells are included in these regulations.

# Rationale/Source

Multiple myeloma (MM) is a systemic malignancy of plasma cells that represents approximately 10% of all hematologic cancers. POEMS syndrome, characterized by polyneuropathy, organomegaly, endocrinopathy, M protein, and skin changes, is a rare, paraneoplastic disorder secondary to a plasma cell dyscrasia. Plasma cell dyscrasias are treatable but rarely curable. In some cases, autologous or allogeneic hematopoietic cell transplantation (HCT) is considered as therapy.

**Newly Diagnosed MM**

For individuals who have newly diagnosed MM who receive autologous HCT as initial treatment, the evidence includes several prospective, RCTs that compared conventional chemotherapy with high-dose chemotherapy plus autologous HCT. The relevant outcomes include overall survival (OS) and treatment-related morbidity. In general, the evidence has suggested OS rates are improved with autologous HCT compared with conventional chemotherapy in this setting. Limitations of the published evidence include patient heterogeneity, variability in treatment protocols, short follow-up periods, inconsistency in reporting important health outcomes, and inconsistency in reporting or

collecting outcomes. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have newly diagnosed MM who receive tandem autologous HCT, the evidence includes several RCTs. The relevant outcomes include OS and treatment-related morbidity. Compared with single autologous HCT, a number of RCTs have demonstrated tandem autologous HCT improved OS and recurrence-free survival in newly diagnosed MM. The available RCTs compare reduced-intensity conditioning allogeneic HCT (allo-HCT) following a first autologous HCT with single or tandem autologous transplants. The RCTs were based on genetic randomization (ie, patients with a human leukocyte antigen-identical sibling who were offered reduced-intensity conditioning allo-HCT following autologous HCT), whereas other patients underwent either 1 or 2 autologous transplants. Although the body of evidence has shown inconsistencies regarding OS and disease-free survival rates, some studies have shown a survival benefit with tandem autologous HCT followed by reduced-intensity conditioning allo-HCT, although at the cost of higher transplant-related mortality compared with conventional treatments. Factors across studies that may account for differing trial results include different study designs, nonuniform preparative regimens, different patient characteristics (including risk stratification), and criteria for advancing to a second transplant. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have newly diagnosed MM who receive allo-HCT with as initial or salvage treatment, the evidence includes nonrandomized studies. The relevant outcomes include OS and treatment-related morbidity. Studies have reported on patients with both myeloablative conditioning and reduced-intensity conditioning. Limitations of the published evidence include patient sample heterogeneity, variability in treatment protocols, short follow-up periods, inconsistency in reporting important health outcomes, and inconsistency in reporting or collecting outcomes. Nonmyeloablative allo-HCT as first-line therapy is associated with lower transplant-related mortality but a greater risk of relapse; convincing evidence is lacking that allo-HCT improves survival better than autologous HCT. The evidence is insufficient to determine the effects of the technology on health outcomes.

**Relapsed or Refractory MM**
For individuals who have relapsed MM after failing an autologous HCT who receive autologous HCT, the evidence includes an RCT, a retrospective study, a systematic review summarizing data from 4 series of patients who relapsed after a first autologous HCT, and a review summarizing recent studies on a second autologous HCT in relapsed myeloma. The relevant outcomes include OS and treatment-related morbidity. Despite some limitations of the published evidence, including patient sample heterogeneity, variability in treatment protocols, and short follow-up periods, the available trial evidence has suggested OS rates are improved with autologous HCT compared with conventional chemotherapy in this setting. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have refractory, multiple myeloma after failing the first HCT who receive tandem autologous HCT, the evidence includes 3 RCTs and a review. The relevant outcomes include OS and treatment-related morbidity. The evidence has shown tandem autologous HCT improves OS rates in this setting. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

**POEMS Syndrome**
For individuals who have POEMS syndrome who receive HCT, the evidence includes case reports and series. The relevant outcomes include OS and treatment-related morbidity. No RCTs of HCT of any type have been performed in patients with POEMS syndrome of any severity, nor is it likely such studies will be performed because of the rarity of this condition. Available case reports and series are subject to selection bias and are heterogeneous concerning treatment approaches and peritransplant support. However, for patients with disseminated POEMS syndrome, a chain of evidence and contextual factors related to the disease and MM would suggest improvement in health outcomes with autologous HCT. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

# Supplemental Information

**Clinical Input from Physician Specialty Societies and Academic Medical Centers**
While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process, through the provision of appropriate reviewers,

input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted.

**2017 Input**
In response to requests, input was received from 1 specialty medical society, 1 academic medical center, and 2 Blue Distinction Centers for Transplant while this policy was under review in 2017. There was a consensus that allogeneic hematopoietic cell transplantation (HCT) is investigational for newly diagnosed multiple myeloma and as salvage therapy after primary graft failure and for the primary progressive disease.

**2013 Input**
In response to requests, input was received from 3 academic medical centers and 6 Blue Distinction Centers for Transplant while this policy was under review in 2013. There was near-consensus that autologous HCT is medically necessary for POEMS syndrome and near-consensus that allogeneic and tandem HCT are investigational for POEMS syndrome.

**2010 Input**
In response to requests, input was received from 2 academic medical centers while this policy was under review in 2010. One reviewer agreed with the current policy statement related to tandem autologous HCT followed by reduced-intensity conditioning allogeneic HCT and the others disagreed. Those providing input agreed with the other policy statements. (The conclusion that allogeneic HCT is investigational for salvage therapy was a late addition to the policy and was not sent for clinical input.)

**Practice Guidelines and Position Statements**
**American Society for Blood and Marrow Transplantation**
The ASBMT (2015) published evidence-based guidelines on the use of HCT in patients with multiple myeloma (MM). The ASBMT recognized that much of the evidence from RCTs summarized in the 2015 guidelines came from trials that predated the novel triple-therapy induction regimens. Furthermore, advances in supportive care and earlier disease detection have increasingly influenced decision making and allow individual tailoring of therapy. ASBMT guidelines did not address POEMS or other plasma cell dyscrasias besides MM.

The ASBMT and 3 other groups (2015) published joint guidelines based on an expert consensus conference. These guidelines contained the following recommendations for HCT as salvage therapy:

"...autologous HCT: (1) In transplantation-eligible patients relapsing after primary therapy that did NOT include an autologous HCT, high-dose therapy with HCT as part of salvage therapy should be considered standard; (2) High-dose therapy and autologous HCT should be considered appropriate therapy for any patients relapsing after primary therapy that includes an autologous HCT with initial remission duration of more than 18 months; (3) High-dose therapy and autologous HCT can be used as bridging strategy to allogeneic HCT; (4) The role of post salvage HCT maintenance needs to be explored in the context of well-designed prospective trials that should include new agents, such as monoclonal antibodies, -modulating agents, and oral proteasome inhibitors; (5) Autologous HCT consolidation should be explored as a strategy to develop novel conditioning regimens or post-HCT strategies in patients with short remission (less than 18 months remissions) after primary therapy (and (6) Prospective randomized trials need to be performed to define the role of salvage autologous HCT in patients with MM [multiple myeloma] relapsing after primary therapy comparing to 'best non-HCT' therapy.

Regarding allogeneic HCT... (1) Allogeneic HCT should be considered appropriate therapy for any eligible patient with early relapse (less than 24 months) after primary therapy that included an autologous HCT and/or with high-risk features (ie, cytogenetics, extramedullary disease, plasma cell leukemia, or high lactate dehydrogenase); (2) Allogeneic HCT should be performed in the context of a clinical trial if possible; (3) The role of post allogeneic HCT maintenance therapy needs to be explored in the context of well-designed prospective trials; and (4) Prospective randomized trials need to be performed to define the role of salvage allogeneic HCT in patients with MM relapsing after primary therapy."

**International Myeloma Working Group**
The 2010 conclusions and recommendations of the International Myeloma Working Group consensus statement on the current status of allogeneic HCT (allo-HCT) for MM are as follows: Myeloablative allo-HCT may cure a minority of patients but is associated with high transplant-related mortality, but could be evaluated in well-designed prospective clinical trials. Nonmyeloablative allo-HCT as first-line therapy is associated with lower transplant-related

mortality but a greater risk of relapse and convincing evidence is lacking that allo-HCT improves survival compared with autologous HCT.

**National Comprehensive Cancer Network**
Autologous HCT
The NCCN guidelines (v.2.2020) consider autologous HCT a category 2A recommendation as a follow-up to induction therapy for newly diagnosed MM and as a category 1 recommendation for relapsed or progressive disease if the patient is considered a transplant candidate. For relapsed or progressive disease, the guideline also says, "allogeneic stem cell transplant in multiple myeloma should only be used in the setting of a clinical trial. Current data do not support miniallografting alone."

**Tandem HCT**
The NCCN recommends collecting enough stem cells for 2 transplants in all eligible patients.

**Allo-HCT**
The NCCN recommends the following for allo-HCT: "Allogeneic stem cell transplant may include nonmyeloablative (mini) following autologous stem cell transplant or fully myeloablative, preferably on a clinical trial. Current data do not support miniallografting alone" (category 2A).

**POEMS Syndrome**
The NCCN guidelines do not address the treatment of POEMS syndrome.

**U.S. Preventive Services Task Force Recommendations**
Not applicable.

**Medicare National Coverage**
Medicare has the following national coverage determination for the use of HCT for MM.
"Effective … January … 2016, allogeneic HSCT [hematopoietic stem cell transplantation] for multiple myeloma is covered by Medicare only for beneficiaries with Durie-Salmon Stage II or III multiple myeloma, or International Staging System (ISS) Stage II or Stage III multiple myeloma, and participating in an approved prospective clinical study that meets the criteria below. There must be appropriate statistical techniques to control for selection bias and confounding by age, duration

of diagnosis, disease classification, International Myeloma Working Group (IMWG) classification, ISS stage, comorbid conditions, type of preparative/conditioning regimen, graft vs. host disease (GVHD) prophylaxis, donor type and cell source.

A prospective clinical study seeking Medicare coverage for allogeneic HSCT for multiple myeloma pursuant to CED must address the following question:
Compared to patients who do not receive allogeneic HSCT, do Medicare beneficiaries with multiple myeloma who receive allogeneic HSCT have improved outcomes as indicated by:

- Graft vs. host disease (acute and chronic);
- Other transplant-related adverse events;
- Overall survival; and
- (optional) Quality of life?"

**Ongoing and Unpublished Clinical Trials**
Some currently unpublished trials that might influence this review are listed in Table 2.

**Table 2. Summary of Key Trials**

| NCT No. | Trial Name | Planned Enrollment | Completion Date |
|---|---|---|---|
| ***Ongoing*** | | | |
| NCT01208662[a] | A Randomized Phase III Study Comparing Conventional Dose Treatment Using a Combination of Lenalidomide, Bortezomib, and Dexamethasone (RVD) to High-dose Treatment With Peripheral Stem Cell Transplant in the Initial Management of Myeloma in Patients up to 65 Years of Age | 660 | Sep 2020 |
| NCT00177047 | Autologous Transplantation for Multiple Myeloma | 363 | Jan 2021 |
| NCT01208766 | A Randomized Phase III Study to Compare Bortezomib, Melphalan, Prednisone (VMP) With | 1500 | Apr 2021 |

| NCT No. | Trial Name | Planned Enrollment | Completion Date |
|---|---|---|---|
| | High Dose Melphalan Followed by Bortezomib, Lenalidomide, Dexamethasone (VRD) Consolidation and Lenalidomide Maintenance in Patients With Newly Diagnosed Multiple Myeloma | | |
| ***Unpublished*** | | | |
| NCT02322320 | Continued, Long-Term Follow-Up and Lenalidomide Maintenance Therapy for Patients on BMT CTN 0702 (BMT CTN #Q07LT) | 450 | Jun 2019 |
| NCT01191060[a] | Randomized Study Comparing Conventional Dose Treatment Using a Combination of Lenalidomide, Bortezomib and Dexamethasone to High-Dose Treatment With ASCT in the Initial Management of Myeloma in Patients up to 65 Years of Age | 700 | Nov 2018 |
| NCT01109004 | A Trial of Single Autologous Transplant With or Without Consolidation Therapy Versus Tandem Autologous Transplant With Lenalidomide Maintenance for Patients With Multiple Myeloma (BMT CTN 0702) | 750 | Mar 2018 (completed) |
| NCT00998270 | Autologous Bone Marrow Transplantation (BMT) Compared With Allogeneic BMT in Multiple Myeloma | 185 | Oct 2017 (unknown) |

NCT: national clinical trial.
[a] Denotes industry-sponsored or cosponsored trial.

# References

1. Blue Cross and Blue Shield Association, Medical Policy Reference Manual, "Hematopoietic Cell Transplantation for Plasma Cell Dyscrasias, Including Multiple Myeloma and POEMS Syndrome", 8.01.17, 2:2020.
2. Kyle RA, Rajkumar SV. Multiple myeloma. Blood. Mar 15 2008;111(6):2962-2972. PMID 18332230
3. Palumbo A, Rajkumar SV. Treatment of newly diagnosed myeloma. Leukemia. Mar 2009;23(3):449-456. PMID 19005483
4. Durie BG, Harousseau JL, Miguel JS, et al. International uniform response criteria for multiple myeloma. Leukemia. Sep 2006;20(9):1467-1473. PMID 16855634
5. Dispenzieri A. Long-term outcomes after autologous stem cell transplantation in patients with POEMS syndrome. Clin Adv Hematol Oncol. Nov 2012;10(11):744-746. PMID 23271262
6. Dispenzieri A. POEMS syndrome: update on diagnosis, risk-stratification, and management. Am J Hematol. Aug 2012;87(8):804-814. PMID 22806697
7. Bardwick PA, Zvaifler NJ, Gill GN, et al. Plasma cell dyscrasia with polyneuropathy, organomegaly, endocrinopathy, M protein, and skin changes: the POEMS syndrome. Report on two cases and a review of the literature. Medicine (Baltimore). Jul 1980;59(4):311-322. PMID 6248720
8. Dispenzieri A, Kyle RA, Lacy MQ, et al. POEMS syndrome: definitions and long-term outcome. Blood. Apr 1 2003;101(7):2496-2506. PMID 12456500
9. Nasu S, Misawa S, Sekiguchi Y, et al. Different neurological and physiological profiles in POEMS syndrome and chronic inflammatory demyelinating polyneuropathy. J Neurol Neurosurg Psychiatry. May 2012;83(5):476-479. PMID 22338030
10. Dispenzieri A, Moreno-Aspitia A, Suarez GA, et al. Peripheral blood stem cell transplantation in 16 patients with POEMS syndrome, and a review of the literature. Blood. Nov 15 2004;104(10):3400-3407. PMID 15280195
11. Singh D, Wadhwa J, Kumar L, et al. POEMS syndrome: experience with fourteen cases. Leuk Lymphoma. Oct 2003;44(10):1749-1752. PMID 14692529
12. Kuwabara S, Dispenzieri A, Arimura K, et al. Treatment for POEMS (polyneuropathy, organomegaly, endocrinopathy, M-protein, and skin changes) syndrome. Cochrane Database Syst Rev. Jun 13 2012;6(6):CD006828. PMID 22696361

13. Dispenzieri A. How I treat POEMS syndrome. Blood. Jun 14 2012;119(24):5650-5658. PMID 22547581
14. Reece DE. Recent trends in the management of newly diagnosed multiple myeloma. Curr Opin Hematol. Jul 2009;16(4):306-312. PMID 19491669
15. Reece D HJ, Gertz MA. Myeloma Management 2009: Nontransplant therapy of myeloma, high-dose therapy for myeloma, and a personalised care plan for treatment of myeloma. 2009 American Society of Clinical Oncology Annual Meeting Educational Handbook. 2009:502-509.
16. Qiao SK, Guo XN, Ren JH, et al. Efficacy and safety of lenalidomide in the treatment of multiple myeloma: a systematic review and meta-analysis of randomized controlled trials. Chin Med J (Engl). May 5 2015;128(9):1215-1222. PMID 25947406
17. Fonseca R. Strategies for risk-adapted therapy in myeloma. Hematology Am Soc Hematol Educ Program. Nov 2007:304-310. PMID 18024644
18. Rajkumar SV. Multiple myeloma: 2011 update on diagnosis, risk-stratification, and management. Am J Hematol. Jan 2011;86(1):57-65. PMID 21181954
19. Larocca A, Palumbo A. Evolving paradigms in the treatment of newly diagnosed multiple myeloma. J Natl Compr Canc Netw. Oct 2011;9(10):1186-1196. PMID 21975915
20. van de Donk NW, Lokhorst HM, Dimopoulos M, et al. Treatment of relapsed and refractory multiple myeloma in the era of novel agents. Cancer Treat Rev. Jun 2011;37(4):266-283. PMID 20863623
21. Nishihori T, Alsina M. Advances in the autologous and allogeneic transplantation strategies for multiple myeloma. Cancer Control. Oct 2011;18(4):258-267. PMID 21976244
22. Dunavin NC, Wei L, Elder P, et al. Early versus delayed autologous stem cell transplant in patients receiving novel therapies for multiple myeloma. Leuk Lymphoma. Aug 2013;54(8):1658-1664. PMID 23194056
23. Gay F, Oliva S, Petrucci MT, et al. Chemotherapy plus lenalidomide versus autologous transplantation, followed by lenalidomide plus prednisone versus lenalidomide maintenance, in patients with multiple myeloma: a randomised, multicentre, phase 3 trial. Lancet Oncol. Dec 2015;16(16):1617-1629. PMID 26596670
24. Attal M, Harousseau JL. The role of high-dose therapy with autologous stem cell support in the era of novel agents. Semin Hematol. Apr 2009;46(2):127-132. PMID 19389496
25. Attal M, Harousseau JL, Stoppa AM, et al. A prospective, randomized trial of autologous bone marrow transplantation and chemotherapy in multiple myeloma. Intergroupe Francais du Myelome. N Engl J Med. Jul 11 1996;335(2):91-97. PMID 8649495

26. Barlogie B, Kyle RA, Anderson KC, et al. Standard chemotherapy compared with high-dose chemoradiotherapy for multiple myeloma: final results of phase III US Intergroup Trial S9321. J Clin Oncol. Feb 20 2006;24(6):929-936. PMID 16432076
27. Blade J, Rosinol L, Sureda A, et al. High-dose therapy intensification compared with continued standard chemotherapy in multiple myeloma patients responding to the initial chemotherapy: long-term results from a prospective randomized trial from the Spanish cooperative group PETHEMA. Blood. Dec 1 2005;106(12):3755- 3759. PMID 16105975
28. Child JA, Morgan GJ, Davies FE, et al. High-dose chemotherapy with hematopoietic stem-cell rescue for multiple myeloma. N Engl J Med. May 8 2003;348(19):1875-1883. PMID 12736280
29. Fermand JP, Ravaud P, Chevret S, et al. High-dose therapy and autologous peripheral blood stem cell transplantation in multiple myeloma: up-front or rescue treatment? Results of a multicenter sequential randomized clinical trial. Blood. Nov 1 1998;92(9):3131-3136. PMID 9787148
30. Palumbo A, Bringhen S, Petrucci MT, et al. Intermediate-dose melphalan improves survival of myeloma patients aged 50 to 70: results of a randomized controlled trial. Blood. Nov 15 2004;104(10):3052-3057. PMID 15265788
31. Koreth J, Cutler CS, Djulbegovic B, et al. High-dose therapy with single autologous transplantation versus chemotherapy for newly diagnosed multiple myeloma: A systematic review and meta-analysis of randomized controlled trials. Biol Blood Marrow Transplant. Feb 2007;13(2):183-196. PMID 17241924
32. Marini C, Maia T, Bergantim R, et al. Real-life data on safety and efficacy of autologous stem cell transplantation in elderly patients with multiple myeloma. Ann. Hematol., 2018 Oct 29;98(2). PMID 30368589
33. Attal M, Harousseau JL, Facon T, et al. Single versus double autologous stem-cell transplantation for multiple myeloma. N Engl J Med. Dec 25 2003;349(26):2495-2502. PMID 14695409
34. Stadtmauer EA. Multiple myeloma, 2004--one or two transplants? [editorial]. N Engl J Med. Dec 25 2003;349(26):2551-2553. PMID 14695416
35. Cavo M, Tosi P, Zamagni E, et al. Prospective, randomized study of single compared with double autologous stem-cell transplantation for multiple myeloma: Bologna 96 clinical study. J Clin Oncol. Jun 10 2007;25(17):2434- 2441. PMID 17485707
36. Maffini E, Storer BE, Sandmaier BM, et al. Long-term follow-up of tandem autologous-allogeneic hematopoietic cell transplantation for multiple myeloma. Haematologica. Sep 27 2018. PMID 30262560

37. Garban F, Attal M, Michallet M, et al. Prospective comparison of autologous stem cell transplantation followed by dose-reduced allograft (IFM99-03 trial) with tandem autologous stem cell transplantation (IFM99-04 trial) in high- risk de novo multiple myeloma. Blood. May 1 2006;107(9):3474-3480. PMID 16397129
38. Moreau P, Garban F, Attal M, et al. Long-term follow-up results of IFM99-03 and IFM99-04 trials comparing nonmyeloablative allotransplantation with autologous transplantation in high-risk de novo multiple myeloma. Blood. Nov 1 2008;112(9):3914-3915. PMID 18948589
39. Bruno B, Rotta M, Patriarca F, et al. A comparison of allografting with autografting for newly diagnosed myeloma. N Engl J Med. Mar 15 2007;356(11):1110-1120. PMID 17360989
40. Rosinol L, Perez-Simon JA, Sureda A, et al. A prospective PETHEMA study of tandem autologous transplantation versus autograft followed by reduced-intensity conditioning allogeneic transplantation in newly diagnosed multiple myeloma. Blood. Nov 1 2008;112(9):3591-3593. PMID 18612103
41. Lokhorst H, Mutis I. Allogeneic transplantation and immune interventions in multiple myeloma [abstract]. Hematol Educ. 2008;2:106-114.
42. Bjorkstrand B, Iacobelli S, Hegenbart U, et al. Autologous stem cell transplantation (ASCT) versus ASCT followed by reduced-intensity conditioning allogeneic SCT with identical sibling donor in previously untreated multiple myeloma: preliminary analysis of a prospective controlled trial by the EBMT [abstract]. Bone Marrow Transplant. 2008;41:S38.
43. Gahrton G, Iacobelli S, Bjorkstrand B, et al. Autologous/reduced-intensity allogeneic stem cell transplantation vs autologous transplantation in multiple myeloma: long-term results of the EBMT-NMAM2000 study. Blood. Jun 20 2013;121(25):5055-5063. PMID 23482933
44. Krishnan A, Pasquini MC, Logan B, et al. Autologous haemopoietic stem-cell transplantation followed by allogeneic or autologous haemopoietic stem-cell transplantation in patients with multiple myeloma (BMT CTN 0102): a phase 3 biological assignment trial. Lancet Oncol. Dec 2011;12(13):1195-1203. PMID 21962393
45. Harousseau JL. The allogeneic dilemma. Bone Marrow Transplant. Dec 2007;40(12):1123-1128. PMID 17680016
46. Crawley C, Iacobelli S, Bjorkstrand B, et al. Reduced-intensity conditioning for myeloma: lower nonrelapse mortality but higher relapse rates compared with myeloablative conditioning. Blood. Apr 15 2007;109(8):3588- 3594. PMID 17158231
47. Gahrton G, Bjorkstrand B. Allogeneic transplantation in multiple myeloma. Haematologica. Sep 2008;93(9):1295- 1300. PMID 18757850

48. Giralt S, Koehne G. Allogeneic hematopoietic stem cell transplantation for multiple myeloma: what place, if any? Curr Hematol Malig Rep. Dec 2013;8(4):284-290. PMID 24146203
49. Giralt S, Costa L, Schriber J, et al. Optimizing autologous stem cell mobilization strategies to improve patient outcomes: consensus guidelines and recommendations. Biol Blood Marrow Transplant. Mar 2014;20(3):295-308. PMID 24141007
50. Olin RL, Vogl DT, Porter DL, et al. Second auto-SCT is safe and effective salvage therapy for relapsed multiple myeloma. Bone Marrow Transplant. Mar 2009;43(5):417-422. PMID 18850013
51. Cook G, Williams C, Brown JM, et al. High-dose chemotherapy plus autologous stem-cell transplantation as consolidation therapy in patients with relapsed multiple myeloma after previous autologous stem-cell transplantation (NCRI Myeloma X Relapse [Intensive trial]): a randomised, open-label, phase 3 trial. Lancet Oncol. Jul 2014;15(8):874-885. PMID 24948586
52. Cook G, Ashcroft AJ, Cairns DA, et al. The effect of salvage autologous stem-cell transplantation on overall survival in patients with relapsed multiple myeloma (final results from BSBMT/UKMF Myeloma X Relapse [Intensive]): a randomised, open-label, phase 3 trial. Lancet Haematol. Jul 2016;3(7):e340-351. PMID 27374467
53. Michaelis LC, Saad A, Zhong X, et al. Salvage second hematopoietic cell transplantation in myeloma. Biol Blood Marrow Transplant. May 2013;19(5):760-766. PMID 23298856
54. Ziogas DC, Terpos E, Dimopoulos MA. When to recommend a second autograft in patients with relapsed myeloma? Leuk Lymphoma. Apr 2017;58(4):781-787. PMID 27894207
55. Hahn T, Wingard JR, Anderson KC, et al. The role of cytotoxic therapy with hematopoietic stem cell transplantation in the therapy of multiple myeloma: an evidence-based review. Biol Blood Marrow Transplant. Jan 2003;9(1):4-37. PMID 12533739
56. McCarthy PL, Holstein SA. Role of stem cell transplant and maintenance therapy in plasma cell disorders. Hematology Am Soc Hematol Educ Program. Dec 2 2016;2016(1):504-511. PMID 27913522
57. Qazilbash MH, Saliba R, De Lima M, et al. Second autologous or allogeneic transplantation after the failure of first autograft in patients with multiple myeloma. Cancer. Mar 1 2006;106(5):1084-1089. PMID 16456814
58. Auner HW, Szydlo R, van Biezen A, et al. Reduced intensity-conditioned allogeneic stem cell transplantation for multiple myeloma relapsing or progressing after autologous transplantation: a study by the European Group for Blood and Marrow Transplantation. Bone Marrow Transplant. Nov 2013;48(11):1395-1400. PMID 23708704

59. Schneidawind C, Duerr-Stoerzer S, Faul C, et al. Follow-up of patients with refractory or relapsed multiple myeloma after allogeneic hematopoietic cell transplantation. Clin Transplant. Jul 2017;31(7). PMID 28470884
60. Garderet L, Cook G, Auner HW, et al. Treatment options for relapse after autograft in multiple myeloma - report from an EBMT educational meeting. Leuk Lymphoma. Apr 2017;58(4):797-808. PMID 27650125
61. Autore F, Innocenti I, Luigetti M, et al. Autologous peripheral blood stem cell transplantation and the role of lenalidomide in patients affected by poems syndrome. Hematol Oncol. Sep 15 2017. PMID 28913957
62. D'Souza A, Lacy M, Gertz M, et al. Long-term outcomes after autologous stem cell transplantation for patients with POEMS syndrome (osteosclerotic myeloma): a single-center experience. Blood. Jul 5 2012;120(1):56-62. PMID 22611150
63. Jang IY, Yoon DH, Kim S, et al. Advanced POEMS syndrome treated with high-dose melphalan followed by autologous blood stem cell transplantation: a single-center experience. Blood Res. Mar 2014;49(1):42-48. PMID 24724066
64. Cook G, Iacobelli S, van Biezen A, et al. High-dose therapy and autologous stem cell transplantation in patients with POEMS syndrome: a retrospective study of the Plasma Cell Disorder sub-committee of the Chronic Syndrome Malignancy Working Party of the European Society for Blood & Marrow Transplantation. Haematologica. Jan 2017;102(1):160-167. PMID 27634201
65. Shah N, Callander N, Ganguly S, et al. Hematopoietic stem cell transplantation for multiple myeloma: guidelines from the American Society for Blood and Marrow Transplantation. Biol Blood Marrow Transplant. Jul 2015;21(7):1155-1166. PMID 25769794
66. Giralt S, Garderet L, Durie B, et al. American Society of Blood and Marrow Transplantation, European Society of Blood and Marrow Transplantation, Blood and Marrow Transplant Clinical Trials Network, and International Myeloma Working Group consensus conference on salvage hematopoietic cell transplantation in patients with relapsed multiple myeloma. Biol Blood Marrow Transplant. Dec 2015;21(12):2039-2051. PMID 26428082
67. Lokhorst H, Einsele H, Vesole D, et al. International Myeloma Working Group consensus statement regarding the current status of allogeneic stem-cell transplantation for multiple myeloma. J Clin Oncol. Oct 10 2010;28(29):4521-4530. PMID 20697091

68. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Multiple Myeloma. Version 3.2018. https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf.
69. Centers for Medicare & Medicaid Services. National Coverage Determination (NCD) for Stem Cell Transplantation (Formerly 110.8.1) (110.23). 2016; https://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?NCDId=366&ncdver=1&DocID=110.23&list_type=ncd&bc=gAAAAAgAAAAAAA%3d%3d&.

# Policy History

Original Effective Date: 01/28/2002
Current Effective Date: 04/13/2020

| | |
|---|---|
| 12/06/2001 | Medical Policy Committee review |
| 01/28/2002 | Managed Care Advisory Council approval |
| 12/06/2006 | Medical Director review |
| 12/20/2006 | Medical Policy Committee approval. Coverage eligibility unchanged. |
| 09/05/2007 | Medical Director review |
| 09/19/2007 | Medical Policy Committee approval. Policy statement language regarding tandem transplants in newly diagnosed or responsive multiple myeloma clarified. |
| 09/09/2008 | Medical Director review |
| 09/17/2008 | Medical Policy Committee approval. No change to coverage eligibility. |
| 09/03/2009 | Medical Policy Committee approval |
| 09/16/2009 | Medical Policy Implementation Committee approval. No change to coverage eligibility. |
| 09/09/2010 | Medical Policy Committee review |
| 09/15/2010 | Medical Policy Implementation Committee approval. Policy title changed from "High-Dose Chemotherapy with Stem-Cell Support for Multiple Myeloma" to "Hematopoietic Stem-Cell Transplantation for Multiple Myeloma". Policy language and statements extensively updated to reflect current practice. |
| 09/01/2011 | Medical Policy Committee review |
| 09/14/2011 | Medical Policy Implementation Committee approval. No changes to coverage. |
| 09/06/2012 | Medical Policy Committee review |

Hematopoietic Cell Transplantation for Plasma Cell Dyscrasias, Including Multiple Myeloma and POEMS Syndrome

Policy # 00060
Original Effective Date: 01/28/2002
Current Effective Date: 04/13/2020

| | |
|---|---|
| 09/19/2012 | Medical Policy Implementation Committee approval. Coverage eligibility unchanged. |
| 03/04/2013 | Coding updated |
| 10/03/2013 | Medical Policy Committee review |
| 10/16/2013 | Medical Policy Implementation Committee approval. Title changed. Coverage for POEMS syndrome added. |
| 11/06/2014 | Medical Policy Committee review |
| 11/21/2014 | Medical Policy Implementation Committee approval. No change to coverage. |
| 03/05/2015 | Medical Policy Committee review |
| 03/19/2015 | Medical Policy Implementation Committee approval. Tandem autologous-autologous hematopoietic stem-cell transplantation to treat multiple myeloma clarified. |
| 03/03/2016 | Medical Policy Committee review |
| 03/16/2016 | Medical Policy Implementation Committee approval. No change to coverage. |
| 01/01/2017 | Coding update: Removing ICD-9 Diagnosis Codes |
| 03/02/2017 | Medical Policy Committee review |
| 03/15/2017 | Medical Policy Implementation Committee approval. No change to coverage. |
| 03/01/2018 | Medical Policy Committee review |
| 03/21/2018 | Medical Policy Implementation Committee approval. No change to coverage. |
| 03/07/2019 | Medical Policy Committee review |
| 03/20/2019 | Medical Policy Implementation Committee approval. No change to coverage. |
| 03/05/2020 | Medical Policy Committee review |
| 03/11/2020 | Medical Policy Implementation Committee approval. No change to coverage. |

Next Scheduled Review Date: 03/2021

# Coding

*The five character codes included in the Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)‡, copyright 2019 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.*

Hematopoietic Cell Transplantation for Plasma Cell Dyscrasias, Including Multiple Myeloma and POEMS Syndrome

Policy # 00060
Original Effective Date: 01/28/2002
Current Effective Date: 04/13/2020

*The responsibility for the content of Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines is with Blue Cross and Blue Shield of Louisiana and no endorsement by the AMA is intended or should be implied. The AMA disclaims responsibility for any consequences or liability attributable or related to any use, nonuse or interpretation of information contained in Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines. Fee schedules, relative value units, conversion factors and/or related components are not assigned by the AMA, are not part of CPT, and the AMA is not recommending their use. The AMA does not directly or indirectly practice medicine or dispense medical services. The AMA assumes no liability for data contained or not contained herein. Any use of CPT outside of Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines should refer to the most current Current Procedural Terminology which contains the complete and most current listing of CPT codes and descriptive terms. Applicable FARS/DFARS apply.*

CPT is a registered trademark of the American Medical Association.

Codes used to identify services associated with this policy may include (but may not be limited to) the following:

| Code Type | Code |
|---|---|
| CPT | 38204, 38205, 38206, 38207, 38208, 38209, 38210, 38211, 38212, 38213, 38214, 38215, 38230, 38232, 38240, 38241, 38242, 38243 |
| HCPCS | S2140, S2142, S2150 |
| ICD-10 Diagnosis | C90.00-C90.02, E88.09 |

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or

B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with the Blue Cross and Blue Shield Association technology assessment program (TEC) or other nonaffiliated technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

**NOTICE**: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

Hematopoietic Cell Transplantation for Plasma Cell Dyscrasias, Including Multiple Myeloma and POEMS Syndrome

Policy # 00060
Original Effective Date: 01/28/2002
Current Effective Date: 04/13/2020

**NOTICE:** Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.