



MASSACHUSETTS

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Medical Policy

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

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Policy Number: 075

BCBSA Reference Number: 8.01.17

NCD/LCD: National Coverage Determination (NCD) for Stem Cell Transplantation Formerly 110.8.1 (110.23)

Related Policies

- Hematopoietic Cell Transplantation for Waldenström Macroglobulinemia, #[322](#)
- Placental/Umbilical Cord Blood as a Source of Stem Cells, #[285](#)

Policy

Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity

MULTIPLE MYELOMA

A single or second (salvage) autologous hematopoietic cell transplantation may be **MEDICALLY NECESSARY** to treat multiple myeloma.

Tandem autologous-autologous hematopoietic cell transplantation may be **MEDICALLY NECESSARY** to treat multiple myeloma in patients who fail to achieve at least a near-complete or very good partial response after the first transplant in the tandem sequence.

Definition of near-complete response and very good partial response

- A near complete response, as defined by the European Group for Blood and Marrow Transplant (EBMT) is the disappearance of M protein at routine electrophoresis, but positive immunofixation.
- A very good partial response has been defined as a 90% decrease in the serum paraprotein level.

Tandem transplantation with an initial round of autologous hematopoietic cell transplantation followed by a non-marrow-ablative conditioning regimen and allogeneic hematopoietic cell transplantation (i.e., reduced-intensity conditioning transplant) may be **MEDICALLY NECESSARY** to treat newly diagnosed multiple myeloma patients.

Allogeneic hematopoietic cell transplantation, myeloablative or nonmyeloablative, as upfront therapy of newly diagnosed multiple myeloma or as salvage therapy, is **INVESTIGATIONAL**.

POEMS syndrome

Autologous hematopoietic cell transplantation may be considered **MEDICALLY NECESSARY** to treat disseminated POEMS syndrome.*

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

Allogeneic and tandem hematopoietic cell transplantation are **INVESTIGATIONAL** to treat POEMS syndrome.

Medicare HMO BlueSM and Medicare PPO BlueSM Members

Medical necessity criteria and coding guidance can be found through the link below.

[National Coverage Determinations \(NCDs\)](#)

National Coverage Determination (NCD) for Stem Cell Transplantation Formerly 110.8.1 (110.23)

Note: To review the specific NCD, please remember to click “accept” on the CMS licensing agreement at the bottom of the CMS webpage.

Prior Authorization Information

Inpatient

- For services described in this policy, precertification/preauthorization **IS REQUIRED** for all products if the procedure is performed **inpatient**.

Outpatient

- For services described in this policy, see below for products where prior authorization **might be required** if the procedure is performed **outpatient**.

	Outpatient
Commercial Managed Care (HMO and POS)	Prior authorization is required .
Commercial PPO and Indemnity	Prior authorization is required .
Medicare HMO Blue SM	Prior authorization is required .
Medicare PPO Blue SM	Prior authorization is required .

CPT Codes / HCPCS Codes / ICD Codes

Inclusion or exclusion of a code does not constitute or imply member coverage or provider reimbursement. Please refer to the member’s contract benefits in effect at the time of service to determine coverage or non-coverage as it applies to an individual member.

Providers should report all services using the most up-to-date industry-standard procedure, revenue, and diagnosis codes, including modifiers where applicable.

The following codes are included below for informational purposes only; this is not an all-inclusive list.

The above **medical necessity criteria MUST** be met for the following codes to be covered for **Commercial Members: Managed Care (HMO and POS), PPO, Indemnity, Medicare HMO Blue and Medicare PPO Blue:**

CPT Codes

CPT codes:	Code Description
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38206	Blood-derived hematopoietic progenitor cell harvesting for transplantation, per collection; autologous
38232	Bone marrow harvesting for transplantation; autologous
38241	Bone marrow or blood-derived peripheral stem-cell transplantation; autologous

HCPCS Codes

HCPCS codes:	Code Description
S2150	Bone marrow or blood-derived peripheral stem-cell (peripheral or umbilical), allogeneic or autologous, harvesting, transplantation, and related complications including pheresis and cell preparation/storage; marrow ablative therapy; drugs, supplies, hospitalization with outpatient follow-up; medical/surgical, diagnostic, emergency, and rehabilitative services; and the number of days of pre- and post-transplant care in the global definition

ICD-10-PCS Procedure Codes

ICD-10-PCS procedure codes:	Code Description
30233G0	Transfusion of Autologous Bone Marrow into Peripheral Vein, Percutaneous Approach
30233G0	Transfusion of Autologous Bone Marrow into Peripheral Vein, Percutaneous Approach
30233G0	Transfusion of Autologous Bone Marrow into Peripheral Vein, Percutaneous Approach
30233X0	Transfusion of Autologous Cord Blood Stem Cells into Peripheral Vein, Percutaneous Approach
30233Y0	Transfusion of Autologous Hematopoietic Stem Cells into Peripheral Vein, Percutaneous Approach
30233Y0	Transfusion of Autologous Hematopoietic Stem Cells into Peripheral Vein, Percutaneous Approach
30243G0	Transfusion of Autologous Bone Marrow into Central Vein, Percutaneous Approach
30243G0	Transfusion of Autologous Bone Marrow into Central Vein, Percutaneous Approach
30243G0	Transfusion of Autologous Bone Marrow into Central Vein, Percutaneous Approach
30243X0	Transfusion of Autologous Cord Blood Stem Cells into Central Vein, Percutaneous Approach
30243Y0	Transfusion of Autologous Hematopoietic Stem Cells into Central Vein, Percutaneous Approach
30243Y0	Transfusion of Autologous Hematopoietic Stem Cells into Central Vein, Percutaneous Approach
30263G0	Transfusion of Autologous Bone Marrow into Central Artery, Percutaneous Approach
30263G0	Transfusion of Autologous Bone Marrow into Central Artery, Percutaneous Approach
30263G0	Transfusion of Autologous Bone Marrow into Central Artery, Percutaneous Approach
30263X0	Transfusion of Autologous Cord Blood Stem Cells into Central Artery, Percutaneous Approach
30263Y0	Transfusion of Autologous Hematopoietic Stem Cells into Central Artery, Percutaneous Approach
3E03305	Introduction of Other Antineoplastic into Peripheral Vein, Percutaneous Approach
3E03305	Introduction of Other Antineoplastic into Peripheral Vein, Percutaneous Approach
3E03305	Introduction of Other Antineoplastic into Peripheral Vein, Percutaneous Approach
3E03305	Introduction of Other Antineoplastic into Peripheral Vein, Percutaneous Approach
3E04305	Introduction of Other Antineoplastic into Central Vein, Percutaneous Approach

3E04305	Introduction of Other Antineoplastic into Central Vein, Percutaneous Approach
3E04305	Introduction of Other Antineoplastic into Central Vein, Percutaneous Approach
3E04305	Introduction of Other Antineoplastic into Central Vein, Percutaneous Approach
3E05305	Introduction of Other Antineoplastic into Peripheral Artery, Percutaneous Approach
3E05305	Introduction of Other Antineoplastic into Peripheral Artery, Percutaneous Approach
3E05305	Introduction of Other Antineoplastic into Peripheral Artery, Percutaneous Approach
3E05305	Introduction of Other Antineoplastic into Peripheral Artery, Percutaneous Approach
3E06305	Introduction of Other Antineoplastic into Central Artery, Percutaneous Approach
3E06305	Introduction of Other Antineoplastic into Central Artery, Percutaneous Approach
3E06305	Introduction of Other Antineoplastic into Central Artery, Percutaneous Approach
3E06305	Introduction of Other Antineoplastic into Central Artery, Percutaneous Approach

The following CPT, HCPCS and ICD Procedure codes are considered investigational for Commercial Members: Managed Care (HMO and POS), PPO, Indemnity, Medicare HMO Blue and Medicare PPO Blue:

CPT Codes

CPT codes:	Code Description
38205	Blood-derived hematopoietic progenitor cell harvesting for transplantation, per collection; allogeneic
38230	Bone marrow harvesting for transplantation; allogeneic
38240	Bone marrow or blood-derived peripheral stem-cell transplantation; allogeneic

HCPCS Codes

HCPCS codes:	Code Description
S2140	Cord blood harvesting for transplantation, allogeneic
S2142	Cord blood-derived stem-cell transplantation, allogeneic

ICD-10-PCS Procedure Codes

ICD-10-PCS procedure codes:	Code Description
30233G1	Transfusion of Nonautologous Bone Marrow into Peripheral Vein, Percutaneous Approach
30233G1	Transfusion of Nonautologous Bone Marrow into Peripheral Vein, Percutaneous Approach
30233G1	Transfusion of Nonautologous Bone Marrow into Peripheral Vein, Percutaneous Approach
30233X1	Transfusion of Nonautologous Cord Blood Stem Cells into Peripheral Vein, Percutaneous Approach
30233Y1	Transfusion of Nonautologous Hematopoietic Stem Cells into Peripheral Vein, Percutaneous Approach
30233Y1	Transfusion of Nonautologous Hematopoietic Stem Cells into Peripheral Vein, Percutaneous Approach
30243G1	Transfusion of Nonautologous Bone Marrow into Central Vein, Percutaneous Approach
30243G1	Transfusion of Nonautologous Bone Marrow into Central Vein, Percutaneous Approach
30243G1	Transfusion of Nonautologous Bone Marrow into Central Vein, Percutaneous Approach

30243X1	Transfusion of Nonautologous Cord Blood Stem Cells into Central Vein, Percutaneous Approach
30243Y1	Transfusion of Nonautologous Hematopoietic Stem Cells into Central Vein, Percutaneous Approach
30243Y1	Transfusion of Nonautologous Hematopoietic Stem Cells into Central Vein, Percutaneous Approach
30263G1	Transfusion of Nonautologous Bone Marrow into Central Artery, Percutaneous Approach
30263G1	Transfusion of Nonautologous Bone Marrow into Central Artery, Percutaneous Approach
30263G1	Transfusion of Nonautologous Bone Marrow into Central Artery, Percutaneous Approach
30263X1	Transfusion of Nonautologous Cord Blood Stem Cells into Central Artery, Percutaneous Approach
30263Y1	Transfusion of Nonautologous Hematopoietic Stem Cells into Central Artery, Percutaneous Approach
30263Y1	Transfusion of Nonautologous Hematopoietic Stem Cells into Central Artery, Percutaneous Approach

Description

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 the generalized disease, and the selection of treatment is influenced by patient age, general health, prior therapy, and the presence of disease complications.^{1,2,3}

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.^{1,2} 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 five years, approximately 3% per year for the next five years, and 1% for the next ten years.^{1,2}

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.^{4,5} 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.⁶ 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)-1 β , IL-6, and tumor necrosis factor α ; vascular endothelial growth factor may also be involved.^{5,7} 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 one of the minor criteria are necessary for diagnosis.⁷

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, hepatomegaly, lymphadenopathy)	Thrombocytosis	Thrombotic diatheses
	Edema (edema, pleural effusion, ascites)	Polycythemia	Arthralgias
	Endocrinopathy (adrenal, thyroid, pituitary, gonadal, parathyroid, pancreatic)	Hyperhidrosis	Cardiomyopathy (systolic dysfunction)
	Skin changes (hyperpigmentation, hypertrichosis, plethora, hemangiomas, 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 100,000.⁸ Other large series had been described in the United States^{5,7,9} and India.¹⁰ In general, patients with POEMS have superior overall survival compared with that of MM (nearly 14 years in a large series).⁷ However, given the rarity of POEMS, no randomized controlled trials of therapies have been reported.¹¹ 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.^{5,7} 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.^{5,12}

HCT is a procedure in which hematopoietic stem cells are infused to restore bone marrow 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. Although cord blood is an allogeneic source, the stem cells in it are antigenically “naive” and thus are associated with a lower incidence of rejection or graft-versus-host disease. Cord blood is discussed in detail in policy #285.

Immunologic compatibility between infused hematopoietic stem cells and the recipient is not an issue in autologous HCT. However, immunologic compatibility between donor and patient is a critical factor for achieving a good outcome of allo-HCT. Compatibility is established by typing of human leukocyte antigen (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 six. Depending on the disease being treated, an acceptable donor will match the patient at all or most of the HLA loci (except umbilical cord blood).

Conditioning for HCT

Conventional Conditioning

The conventional (“classical”) practice of allo-HCT involves administration of cytotoxic agents (eg, cyclophosphamide, busulfan) with or without total body irradiation at doses sufficient to destroy endogenous hematopoietic capability in the recipient. The beneficial treatment effect of this procedure is due to a combination of initial eradication of malignant cells and subsequent graft-versus-malignancy effect mediated by non-self-immunologic effector cells that develop after engraftment of allogeneic stem cells within the patient’s bone marrow space. While the slower graft-versus-malignancy effect is

considered to be the potentially curative component, it may be overwhelmed by extant disease without the use of pretransplant conditioning. However, intense conditioning regimens are limited to patients who are sufficiently fit medically to tolerate substantial adverse effects that include pre-engraftment opportunistic infections secondary to loss of endogenous bone marrow function and organ damage and failure caused by the cytotoxic drugs. Furthermore, in any allo-HCT, immunosuppressant drugs are required to minimize graft rejection and graft-versus-host disease, which also increases susceptibility to opportunistic infections.

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

Reduced-Intensity Conditioning Allo-HCT

RIC refers to the pretransplant use of lower doses or less intense regimens of cytotoxic drugs or radiotherapy that are used in traditional full-dose myeloablative conditioning treatments. The goal of RIC is to reduce disease burden and to minimize as much as possible associated treatment-related morbidity and non-relapse mortality in the period during which the beneficial graft-versus-malignancy effect of allogeneic transplantation develops. Although the definition of RIC remains arbitrary, with numerous versions employed, all seek to balance the competing effects of non-relapse mortality and relapse due to residual disease. RIC regimens can be viewed as a continuum in effects, 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, which may be supplemented with donor lymphocyte infusions to eradicate residual malignant cells.

For our purposes, the term *reduced-intensity conditioning* will refer to all conditioning regimens intended to be nonmyeloablative as opposed to fully myeloablative (traditional) regimens.

MM treatment overview

In the prechemotherapy era, the median survival for a patient diagnosed with MM was approximately seven 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 2001-2006.² These data suggested that autologous HCT was responsible for the trends during 1994-2000, while novel agents have contributed to the improvement since 2001.²

The introduction of novel agents and better prognostic indicators has been the major advances in the treatment of this disease.^{13,14} 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.^{13,14,15} 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.¹⁶

Summary

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, randomized controlled trials (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 one or two 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 four 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 three 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.

Policy History

Date	Action
3/2019	BCBSA National medical policy review. Description, summary and references updated. Policy statements unchanged.
1/2019	Outpatient prior authorization is required for all commercial products including Medicare Advantage. Effective 1/1/2019.
2/2018	New references added from BCBSA National medical policy. Title clarified.
1/2018	Clarified coding information.
12/2016	Coverage clarified for Medicare Advantage based on National Coverage Determination (NCD) for Stem Cell Transplantation Formerly 110.8.1 (110.23). 12/14/2016
11/2015	New references added from BCBSA National medical policy.
4/2015	BCBSA National medical policy review. Policy clarified.
1/2015	Clarified coding information.
5/2014	Updated Coding section with ICD10 procedure and diagnosis codes, effective 10/2015.
2/2014	BCBSA National medical policy review. New medically necessary and investigational indications described; policy title changed. Effective 2/1/2014.
12/2012	Updated to add new CPT code 38243.
11/2011-4/2012	Medical policy ICD 10 remediation: Formatting, editing and coding updates. No changes to policy statements.
12/2011	Minor change to policy statements (added phrase “in the tandem sequence” to the medically necessary tandem autologous-autologous statement).
7/2011	Medical Policy Group – Hematology and Oncology. No changes to policy statements.
9/2010	Medical Policy Group – Hematology and Oncology. No changes to policy statements.
9/1/2010	Medical Policy 075 effective 9/1/2010.

Information Pertaining to All Blue Cross Blue Shield Medical Policies

Click on any of the following terms to access the relevant information:

[Medical Policy Terms of Use](#)

[Managed Care Guidelines](#)

[Indemnity/PPO Guidelines](#)

[Clinical Exception Process](#)

[Medical Technology Assessment Guidelines](#)

References

1. Kyle RA, Rajkumar SV. Multiple myeloma. *Blood*. Mar 15 2008;111(6):2962-2972. PMID 18332230
2. Palumbo A, Rajkumar SV. Treatment of newly diagnosed myeloma. *Leukemia*. Mar 2009;23(3):449-456. PMID 19005483
3. Durie BG, Harousseau JL, Miguel JS, et al. International uniform response criteria for multiple myeloma. *Leukemia*. Sep 2006;20(9):1467-1473. PMID 16855634
4. 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
5. Dispenzieri A. POEMS syndrome: update on diagnosis, risk-stratification, and management. *Am J Hematol*. Aug 2012;87(8):804-814. PMID 22806697
6. 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
7. 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
8. 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
9. 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
10. Singh D, Wadhwa J, Kumar L, et al. POEMS syndrome: experience with fourteen cases. *Leuk Lymphoma*. Oct 2003;44(10):1749-1752. PMID 14692529
11. 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
12. Dispenzieri A. How I treat POEMS syndrome. *Blood*. Jun 14 2012;119(24):5650-5658. PMID 22547581
13. Reece DE. Recent trends in the management of newly diagnosed multiple myeloma. *Curr Opin Hematol*. Jul 2009;16(4):306-312. PMID 19491669
14. Reece D HJ, Gertz MA. Myeloma Management 2009: Nontransplant therapy of myeloma, high-dose therapy for myeloma, and a personalized care plan for treatment of myeloma. 2009 American Society of Clinical Oncology Annual Meeting Educational Handbook. 2009:502-509. PMID
15. 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
16. Fonseca R. Strategies for risk-adapted therapy in myeloma. *Hematology Am Soc Hematol Educ Program*. Nov 2007:304-310. PMID 18024644
17. Rajkumar SV. Multiple myeloma: 2011 update on diagnosis, risk-stratification, and management. *Am J Hematol*. Jan 2011;86(1):57-65. PMID 21181954
18. 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
19. 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
20. 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
21. 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
22. 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

23. 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
24. 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
25. 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
26. 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
27. 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
28. Femand 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
29. 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
30. 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
31. 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
32. Stadtmauer EA. Multiple myeloma, 2004--one or two transplants? [editorial]. *N Engl J Med.* Dec 25 2003;349(26):2551-2553. PMID 14695416
33. 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
34. 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
35. 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
36. 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
37. 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
38. 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
39. Lokhorst H, Mutis I. Allogeneic transplantation and immune interventions in multiple myeloma [abstract]. *Hematol Educ.* 2008;2:106-114. PMID
40. 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. PMID
41. 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

42. 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
43. Harousseau JL. The allogeneic dilemma. *Bone Marrow Transplant.* Dec 2007;40(12):1123-1128. PMID 17680016
44. 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
45. Gahrton G, Bjorkstrand B. Allogeneic transplantation in multiple myeloma. *Haematologica.* Sep 2008;93(9):1295-1300. PMID 18757850
46. 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
47. 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
48. 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
49. 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
50. 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
51. 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
52. 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
53. 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
54. 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
55. 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
56. 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
57. 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
58. 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
59. 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
60. 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

61. 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
62. 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 Malignancy Working Party of the European Society for Blood & Marrow Transplantation. *Haematologica.* Jan 2017;102(1):160-167. PMID 27634201
63. 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
64. 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
65. 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
66. 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. Accessed January 2, 2018.
67. 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=gAAAAAgAAAAAA%3d%3d &. Accessed January 2, 2018.