MASSACHUSETTS

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Medical Policy

Hematopoietic Cell Transplantation for Primary Amyloidosis

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Policy Number: 181

BCBSA Reference Number: 8.01.42 (For Plan internal use only)

Related Policies

N/A

Policy

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

Autologous hematopoietic stem-cell transplantation to treat primary systemic amyloidosis is considered **MEDICALLY NECESSARY**.

Allogeneic hematopoietic stem-cell transplantation to treat primary systemic amyloidosis is **INVESTIGATIONAL.**

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**.

Requesting Prior Authorization Using Authorization Manager

Providers will need to use Authorization Manager to submit initial authorization requests for services. Authorization Manager, available 24/7, is the quickest way to review authorization requirements, request authorizations, submit clinical documentation, check existing case status, and view/print the decision letter. For commercial members, the requests must meet medical policy guidelines.

To ensure the service request is processed accurately and quickly:

- Enter the facility's NPI or provider ID for where services are being performed.
- Enter the appropriate surgeon's NPI or provider ID as the servicing provider, *not* the billing group.

Authorization Manager Resources
Refer to our Authorization Manager page for tips, guides, and video demonstrations.

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, and Indemnity:

CPT Codes

CPT codes:	Code Description
38241	Hematopoietic progenitor cell (HPC); autologous transplantation

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 Procedure Codes

ICD-10-PCS procedure codes:	Code Description
30233Y0	Transfusion of Autologous Hematopoietic Stem Cells into Peripheral Vein, Percutaneous Approach
30243Y0	Transfusion of Autologous Hematopoietic Stem Cells into Central Vein, Percutaneous Approach
3E03305	Introduction of Other Antineoplastic into Peripheral Vein, Percutaneous Approach
3E04305	Introduction of Other Antineoplastic into Central Vein, Percutaneous Approach
3E05305	Introduction of Other Antineoplastic into Peripheral Artery, Percutaneous Approach
3E06305	Introduction of Other Antineoplastic into Central Artery, Percutaneous Approach

Description

Primary Amyloidosis
The primary amyloidoses comprise a group of diseases with an underlying clonal plasma cell dyscrasia. They are characterized by the extracellular deposition of pathologic, insoluble protein fibrils with a beta-pleated sheet configuration that exhibits a pathognomonic red-green birefringence when stained with

Congo red dye and examined under polarized light. These diseases are classified by the type of amyloidogenic protein involved and by the distribution of amyloid deposits. In systemic amyloidosis, the unnatural protein is produced at a site that is remote from the site(s) of deposition, whereas, in localized disease, the amyloid light chain protein is produced at the site of deposition. Primary or amyloid light chain amyloidosis, the most common type of systemic amyloidosis, has an incidence of approximately 9 to 14 cases per million person-years with approximately 4000 new cases in the US each year.[1,] The typical age at diagnosis is about 50 to 65 years.[2,] The amyloidogenic protein in primary amyloidosis is an immunoglobulin light chain or light chain fragment produced by a clonal population of plasma cells in the bone marrow. While the plasma cell burden in primary amyloidosis is typically low, ranging from 5% to 10%, this disease also may occur in association with multiple myeloma in 10% to 15% of patients. Deposition of primary amyloidogenic proteins causes organ dysfunction, most frequently in the kidneys, heart, and liver, although the central nervous system and brain may be affected.

Treatment

Historically, this disease has had a poor prognosis, with median survival from diagnosis of approximately 12 months, although outcomes have improved with combination chemotherapy using alkylating agents and autologous hematopoietic cell transplantation (HCT). Emerging approaches include the use of immunomodulating drugs (eg, thalidomide, lenalidomide, pomalidomide) and the proteasome inhibitor, bortezomib. The anti-CD38 monoclonal antibody daratumumab/hyaluronidase-fihj received approval in July 2021 for treatment of newly-diagnosed light chain amyloidosis in combination with bortezomib, cyclophosphamide, and dexamethasone. Regardless of the approach, treatment of primary amyloidosis aims at rapidly reducing the production of amyloidogenic monoclonal light chains by suppressing the underlying plasma cell dyscrasia, with supportive care to decrease symptoms and maintain organ function. The therapeutic index of any chemotherapy regimen is a key consideration in the context of underlying organ dysfunction.

Chemotherapy for the treatment of light chain amyloidosis was introduced in 1972 in the form of melphalan and prednisone.[3,] This chemotherapy regimen has yielded higher response and longer survival rates than colchicine or prior therapies.[3,4,] Survival after oral melphalan with prednisone (typically 12 to 18 months) is longer than for untreated patients or those given older therapies (10 to 14 months), but more effective regimens have been sought. Combination therapy with vincristine, doxorubicin, and dexamethasone, a well-established regimen for myeloma, has been investigated.[3,4,] However, because of its toxicity, vincristine, doxorubicin, and dexamethasone therapy is usually limited to patients without peripheral neuropathy or cardiomyopathy, both common complications of amyloidosis.

Because conventional regimens rarely cure systemic amyloidosis, and because of the close biologic similarity to multiple myeloma, myeloablative chemotherapy with HCT is being investigated for this disease.

Hematopoietic Cell Transplantation

Hematopoietic cell transplantation refers to the infusion of hematopoietic stem cells to restore bone marrow function in cancer patients who receive bone-marrow-toxic doses of drugs with or without whole-body radiotherapy. Hematopoietic stem cells may be obtained from the transplant recipient (autologous HCT) or from a donor (allogeneic HCT). These cells can be harvested from bone marrow, peripheral blood, or umbilical cord blood. 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 (GVHD).

Autologous Hematopoietic Cell Transplantation

Immunologic compatibility between infused hematopoietic stem cells and the recipient is not an issue in autologous HCT. The success of autologous HCT is predicated on the ability of cytotoxic chemotherapy with or without radiation 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 response. Patients who undergo autologous HCT are susceptible to chemotherapy-related toxicities and opportunistic infections before engraftment, but not GVHD.

Allogeneic Hematopoietic Cell Transplantation

Immunologic compatibility between donor and patient is a critical factor for achieving a good outcome of allogeneic HCT. Compatibility is established by typing human leukocyte antigen (HLA) using cellular, serologic, or molecular techniques. Human leukocyte antigen refers to the tissue type expressed at the HLA-A, -B, and -DR loci on each arm of chromosome 6. Depending on the disease being treated, an acceptable donor will match the patient at all or most of the HLA loci.

The conventional ("classical") practice of allogeneic 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 in this procedure is due to a combination of initial eradication of malignant cells and the subsequent graft-versus-malignancy effect that develops 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 events that include pre-engraftment opportunistic infections secondary to loss of endogenous bone marrow function and organ damage and failure caused by cytotoxic drugs. Furthermore, in any allogeneic HCT, immune suppressant drugs are required to minimize graft rejection and GVHD, which also increases susceptibility to opportunistic infections.

Reduced-intensity conditioning (RIC) refers to the pretransplant use of lower doses or less intense regimens of cytotoxic drugs or radiation than are used in conventional full-dose myeloablative conditioning treatments. The goal of RIC is to reduce disease burden and to minimize as much as possible treatment-related morbidity and nonrelapse mortality in the period during which the beneficial graft-versus-malignancy effect of allogeneic transplantation develops. Although the definition of RIC remains variable with numerous versions employed, all seek to balance the competing effects of nonrelapse mortality and relapse due to residual disease. These regimens can be viewed as a continuum in effects, from nearly totally myeloablative to minimally myeloablative with lymphoablation, with intensity tailored to specific diseases and patient condition. Patients who undergo RIC with allogeneic 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 this evidence review, the term RIC will refer to all conditioning regimens intended to be nonmyeloablative, as opposed to fully myeloablative (conventional) regimens.

Summary

Hematopoietic cell transplantation (HCT) refers to the infusion of hematopoietic stem cells to restore bone marrow function in individuals with cancer who receive bone-marrow-toxic doses of drugs with or without whole-body radiotherapy. Hematopoietic stem cells may be obtained from the transplant recipient (autologous HCT) or from a donor (allogeneic HCT).

For individuals with primary amyloidosis who receive autologous hematopoietic cell transplantation (HCT), the evidence includes a network meta-analysis, randomized controlled trials (RCTs), nonrandomized comparative studies, and large case series. Relevant outcomes are overall survival (OS), disease-specific survival, change in disease status, and treatment-related morbidity and mortality. Use of autologous HCT for primary amyloidosis rapidly eradicates the amyloid light chain produced by the clonal plasma cell populations, which is the proximal cause of pathology and subsequent death. This procedure has extended survival rates to a reported 77% at 5 years and 56% at 10 years in patients who respond to treatment. Complete response to treatment has been reported in 34% to 69.6% of patients, while transplant-related mortality rates have declined significantly in more recent studies. Therefore, autologous HCT is an important treatment option for patients who are deemed eligible. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with primary amyloidosis who receive allogeneic HCT, the evidence includes case reports. Relevant outcomes are OS, disease-specific survival, change in disease status, and treatment-related

morbidity and mortality. Evidence on the use of allogeneic HCT is sparse and has shown high treatment-related mortality. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Policy History

Date	Action
3/2024	Annual policy review. Description, summary, and references updated. Policy statements unchanged.
9/2023	Policy clarified to include prior authorization requests using Authorization Manager.
3/2023	Annual policy review. Description, summary, and references updated. Policy statements unchanged.
1/2023	Medicare information removed. See MP #132 Medicare Advantage Management for local coverage determination and national coverage determination reference.
2/2022	Annual policy review. Description, summary, and references updated. Policy statements unchanged.
3/2021	Annual policy review. Description, summary, and references updated. Policy statements unchanged.
10/2020	Clarified coding information
4/2020	Bone marrow harvesting codes were removed. Outpatient prior authorization is not required.
3/2020	Annual policy review. Description, summary, and references updated. Policy statements unchanged.
3/2019	Annual 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.
3/2018	Annual policy review. New references added.
2/2018	Clarified coding information.
1/2017	Annual policy review. New references added.
9/2015	Clarified coding information.
3/2015	Annual policy review. New references added.
6/2014	Updated Coding section with ICD10 procedure and diagnosis codes, effective 10/2015.
5/2014	Annual policy review. New references added.
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.
7/2011	Medical Policy Group – Hematology and Oncology. No changes to policy statements.
5/1/2010	Medical Policy 181 effective 5/1/2010describing covered and non-covered indications.

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

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