Hematopoietic Cell Transplantation for Primary Amyloidosis or Waldenstrom's Macroglobulinemia

Policy # 00138
Original Effective Date: 01/28/2002
Current Effective Date: 05/01/2025

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 Non-Hodgkin Lymphomas is addressed separately in medical policy 00062.

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 primary systemic amyloidosis to be **eligible for coverage**.**

Based on review of available data, the Company may consider autologous hematopoietic cell transplantation (HCT) as salvage therapy of chemosensitive Waldenstrom's macroglobulinemia (WM) 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) to treat primary systemic amyloidosis to be **investigational.***

Based on review of available data, the Company considers allogeneic hematopoietic cell transplantation (HCT) to treat Waldenstrom's macroglobulinemia (WM) to be **investigational.***

Background/Overview

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. The typical age at diagnosis is about 50 to 65 years. 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. This chemotherapy regimen has yielded higher response and longer survival rates than colchicine or prior therapies. 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. 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.

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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.

Waldenström Macroglobulinemia

Waldenström macroglobulinemia is a clonal disorder of B lymphocytes that accounts for 1% to 2% of hematologic malignancies, with an estimated 1500 new cases annually in the United States. Symptoms include weakness, headaches, stroke-like symptoms (confusion, loss of coordination), vision problems, excessive bleeding, unexplained weight loss, and frequent infections. The median age of WM patients is 63 to 68 years, with men comprising 55% to 70% of cases. Median survival of WM ranges from 5 to 10 years, with age, hemoglobin concentration, serum albumin level, and B_2-microglobulin level as predictors of outcome.

The Revised European American Lymphoma and World Health Organization classification and a consensus group formed at the Second International Workshop on Waldenström's Macroglobulinemia recognize WM primarily as a lymphoplasmacytic lymphoma with an associated immunoglobulin M (IgM) monoclonal gammopathy. The definition also requires the presence of a characteristic pattern of bone marrow infiltration with small lymphocytes demonstrating plasmacytic differentiation with variable cell surface antigen expression. The Second International Workshop indicated no minimum serum concentration of IgM is necessary for a diagnosis of WM.

Treatment

The goal of therapy for patients with WM is to achieve symptomatic relief and reduce organ damage without compromising quality of life. Treatment of WM is indicated only in symptomatic patients and should not be initiated solely on the basis of serum IgM concentration. Clinical and laboratory findings that indicate the need for therapy of diagnosed WM include a hemoglobin concentration less than 10 g/dL; platelet count less than 100,000/mL; significant adenopathy or organomegaly; symptomatic Ig-related hyperviscosity (>50 g/L); severe neuropathy; amyloidosis; cryoglobulinemia; cold-agglutinin disease; or evidence of disease transformation.

Primary chemotherapeutic options in patients that may undergo autologous HCT often combine rituximab with other agents (eg, dexamethasone, cyclophosphamide, bortezomib, bendamustine), but other agents may also be used including purine analogues (cladribine, fludarabine). Plasma exchange is indicated for acute treatment of symptomatic hyperviscosity.

Conventional Preparative Conditioning for HCT

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 subsequent graft-versus-malignancy effect that develops after engraftment of allogeneic stem cells within patients' bone marrow space. While the slower graft-versus-malignancy effect is considered 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 preengraftment opportunistic infections secondary to loss of endogenous bone marrow function and organ damage and failure caused by the cytotoxic drugs. Furthermore, in any allogeneic HCT, immune suppressant drugs are required to minimize graft rejection and graft-versus-host disease, which also increases susceptibility of the patient 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 prior to engraftment, but not graft-versus-host disease.

Reduced-Intensity Conditioning for Allogeneic HCT

Reduced-intensity conditioning (RIC) refers to the pretransplant use of lower doses or less intense regimens of cytotoxic drugs or radiotherapy than are used in conventional full-dose myeloablative conditioning treatments. The goal of RIC is to reduce disease burden but also to minimize as much as possible associated 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 arbitrary, with numerous versions employed, all seek to balance the competing effects of nonrelapse mortality and relapse due to residual disease. RIC 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 *reduced-intensity conditioning* will refer to all conditioning regimens intended to be nonmyeloablative, as opposed to fully myeloablative (conventional) regimens.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

The U.S. 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.

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Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to regulations, other plan medical policies, and accredited national guidelines.

Hematopoietic cell transplantation 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 who have primary amyloidosis who receive autologous HCT, the evidence includes a network meta-analysis, randomized controlled trials, nonrandomized comparative studies, and large case series. The relevant outcomes are overall survival, 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 a meaningful improvement in the net health outcome.

For individuals who have primary amyloidosis who receive allogeneic (allo-) HCT, the evidence includes case reports. The relevant outcomes are overall survival, disease-specific survival, change in disease status, and treatment-related morbidity and mortality. Evidence on the use of allo-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.

Hematopoietic cell transplantation refers to a procedure in which hematopoietic stem cells are infused to restore bone marrow function in 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). 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.

For individuals who have Waldenström macroglobulinemia who receive HCT, the evidence includes case series. Relevant outcomes are overall survival, change in disease status, quality of life, and treatment-related mortality and morbidity. Several retrospective series have evaluated HCT for Waldenström macroglobulinemia. Analyses of registry data have found 5-year overall survival rates of 52% after allogeneic HCT and 68.5% after autologous HCT. The total number of patients studied is small and there is a lack of published controlled studies. The evidence is insufficient to determine the effects of the technology on health outcomes.

Clinical input obtained in 2011 and national and international clinical guidelines support the use of autologous HCT as salvage therapy for patients with chemosensitive Waldenström macroglobulinemia. Allogeneic HCT is recommended in the context of clinical trials. Thus, autologous HCT may be considered medically necessary as salvage therapy for patients with chemosensitive Waldenström macroglobulinemia. Allogeneic HCT for patients with Waldenström macroglobulinemia is considered investigational.

Supplemental Information

Primary Amyloidosis

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.

In response to requests, input was received from 5 academic medical centers, including 3 transplant centers, while this policy was under review in 2011. There was support for the policy statements on hematopoietic stem transplantation in the treatment of amyloidosis.

Practice Guidelines and Position Statements

Guidelines or position statements will be considered for inclusion in 'Supplemental Information' if they were issued by, or jointly by, a US professional society, an international society with US

representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

American Society for Transplantation and Cellular Therapy
In 2020, the American Society for Transplantation and Cellular Therapy (ASTCT) issued guidelines on indications for HCT and immune effector therapy. ASTCT gave the rating of N (not generally recommended; neither evidence nor clinical practice supports the routine use) for the use of allogeneic HCT in the treatment of primary amyloidosis in adults. ASTCT gave a rating of S (standard of care) for the use of autologous HCT in the treatment of primary amyloidosis in adults.

National Comprehensive Cancer Network
The National Comprehensive Cancer Network (NCCN) guidelines on systemic light chain amyloidosis (v. 1.2025) recommend assessing organ involvement based on amyloidosis consensus criteria in newly diagnosed disease. Next, patients should be evaluated for stem cell transplant candidacy. The current guidelines prefer the regimen of daratumumab and bortezomib/cyclophosphamide/dexamethasone as initial systemic therapy in most patients.

International Workshops on Waldenström Macroglobulinaemia
In 2017, the International Workshops on Waldenström Macroglobulinaemia published guidelines on the treatment of several paraproteinaemic neuropathies, one of which is primary, or amyloid light chain, amyloidosis. First-line treatment for eligible patients includes an autologous cell transplant preceded by a high-dose regimen combining rituximab with another agent such as a purine analogue, bendamustine, or bortezomib.

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

Medicare National Coverage
The Centers for Medicare & Medicaid Services has determined that the evidence is adequate to conclude that, when recognized clinical risk factors are employed to select patients for transplantation, high-dose melphalan together with autologous stem cell transplantation can provide a net health benefit for Medicare beneficiaries of any age group with primary amyloidosis (110.23, formerly 110.8.1).

This technique "is reasonable and necessary for Medicare beneficiaries of any age with primary amyloid light chain (AL) amyloidosis who meet the following criteria:

- Amyloid deposition in 2 or fewer organs, and,
- Cardiac left ventricular ejection fraction (EF) of greater than 45%."

In addition, autologous HCT "must be used to effect hematopoietic reconstitution following severely myelotoxic doses of chemotherapy … and/or radiotherapy used to treat various malignancies."

Ongoing and Unpublished Clinical Trials
Some currently unpublished trials that might influence this review are listed in Table 1.

Table 1. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT06022939	A Phase III, Randomized Study of Daratumumab, Cyclophosphamide, Bortezomib and Dexamethasone (Dara-VCD) Induction Followed by Autologous Stem Cell Transplant or Dara-VCD Consolidation and Daratumumab Maintenance in Patients with Newly Diagnosed AL Amyloidosis	338	Oct 2030

Waldenstrom's Macroglobulinemia

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.

In response to requests, input was received from 5 academic medical centers, including 3 transplant centers, while this policy was under review in 2011. Input indicated that autologous hematopoietic cell transplantation may be considered medically necessary as salvage therapy for Waldenström macroglobulinemia that is chemosensitive. Input was mixed on use of allogeneic hematopoietic cell transplantation, with comments suggesting the procedure be performed as part of a clinical trial.

Practice Guidelines and Position Statements

National Comprehensive Cancer Network
National Comprehensive Cancer Network guidelines on WM and lymphoplasmacytic lymphoma (v.1.2021) indicate that, for patients with previously treated WM, stem cell transplantation may be appropriate in selected cases with either: high-dose therapy with autologous stem cell rescue or allogeneic cell transplant (myeloablative or nonmyeloablative). The Network noted that allogeneic cell transplantation "should ideally be undertaken in the context of a clinical trial." For potential autologous cell transplantation candidates, the guidelines also provide suggested treatment regimens considered non-stem-cell toxic.

Mayo Clinic Cancer Center
In 2017, the Mayo Clinic Cancer Center updated its guidelines on the diagnosis and management of WM.5, The guidelines noted that patients who are potentially eligible for autologous hematopoietic cell transplantation (HCT; <70years of age and with chemosensitive disease), should consider harvesting stem cells during first remission after a low tumor burden has been achieved. The guidelines recommended: "Autologous HCT should be considered for first or second relapse in transplant-eligible patients with chemosensitive disease, especially if the first remission duration isshort (<2 years). Patients with refractory WM should not be offered [autologous HCT] (level 3, grade B)."

Eighth International Workshop on Waldenström's Macroglobulinemia
In 2016, consensus recommendations from the Eighth International Workshop on Waldenström's Macroglobulinemia were published. The panel concluded that autologous HCT is a treatment option for high-risk WM patients who are eligible for transplant. It further stated that autologous HCT should be offered at early relapses and is not as beneficial once patients have been exposed to more than 3 lines of therapy or in those with chemotherapy-refractory disease. Regarding allogeneic HCT, it stated that this treatment, "when appropriate, should preferably be considered in the context of clinical trials."

Myeloma Foundation of Australian
In 2017, the Myeloma Foundation of Australia published practice guidelines on the treatment of patients with WM. The guidelines provided the following treatment recommendation for HCT: "Younger patients with good physical fitness should be considered for autologous and allogeneic stem cell transplantation at first or second relapse and should avoid stem cell-toxic therapies such as fludarabine (Level III, grade C)."

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

Medicare National Coverage
There is no national coverage determination. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

Ongoing and Unpublished Clinical Trials

Table 2. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT01251575	A Phase II Study to Assess Immunosuppression with Sirolimus Combined with Cyclosporine (CSP) and Mycophenolate Mofetil (MMF) for	77	Feb 2019 (completed)

	Prevention of Acute GVHD After Non-Myeloablative HLA Class I or II Mismatched Donor Hematopoietic Cell Transplantation- A Multi-Center Trial		
NCT02844361	Autologous Stem-cell Transplantation Versus Conventional Chemotherapy for High Risk Waldenström Macroglobulinemia - a Prospective Multicenter Phase IV Trial from China	70	May 2020 (recruitment status unknown as of Jul 2016)

NCT: national clinical trial.

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Policy # 00138
Original Effective Date: 01/28/2002
Current Effective Date: 05/01/2025

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12/06/2001	Medical Policy Committee review
01/28/2002	Managed Care Advisory Council approval
06/24/2002	Format revision. No substance change to policy.
06/01/2004	Medical Director review
06/15/2004	Medical Policy Committee review. Format revision. Rationale and Source added. Clinical criteria revision. Primary amyloidosis eligible for coverage.
06/28/2004	Managed Care Advisory Council
06/07/2005	Medical Director review
06/21/2005	Medical Policy Committee Review Policy revision; investigational status for: 1) HDC with allogeneic SCS for primary systemic Amyloidosis or Waldenstrom's Macroglobulinemia and 2) HDC with autologous SCS in cases where Patient Selection Criteria are not met.
07/15/2005	Managed Care Advisory Council approval
06/07/2006	Medical Director review
06/21/2006	Medical Policy Committee approval. Format revisions, FDA /Governmental, Rationale/Source
09/05/2007	Medical Director review
09/19/2007	Medical Policy Committee approval. No change in policy statement.
09/09/2008	Medical Director review
09/17/2008	Medical Policy Committee approval. Criteria removed from policy.
04/02/2009	Medical Director review
04/15/2009	Medical Policy Committee approval. Investigational statement for when criteria are not met removed from the policy. No change to coverage eligibility.
09/03/2009	Medical Policy Committee approval
09/16/2009	Medical Policy Implementation Committee approval. Title changed from "High-Dose Chemotherapy with Hematopoietic Stem Cell Support to Treat Primary Amyloidosis or Waldenstrom's Macroglobulinemia" to Hematopoietic Stem Cell Support to Treat Primary Amyloidosis or Waldenstrom's Macroglobulinemia "Hematopoietic Stem Cell Transplantation for Primary Amyloidosis or Waldenstrom's Macroglobulinemia." No change to coverage eligibility.
09/09/2010	Medical Policy Committee review
09/15/2010	Medical Policy Implementation Committee approval. Changed the language in the coverage section from high-dose chemotherapy with stem cell support to hematopoietic stem-cell transplantation. Coverage eligibility unchanged.
09/01/2011	Medical Policy Committee review
09/14/2011	Medical Policy Implementation Committee approval. "Based on review of available data, the Company may consider autologous hematopoietic stem-cell transplantation as salvage therapy of chemosensitive Waldenstrom macroglobulinemia to be eligible for coverage" was added to the coverage

	statement. "Autologous hematopoietic stem cell transplantation" was changed to "Allogeneic hematopoietic stem cell transplantation" in the investigational statement for the treatment of Waldenstrom macroglobinemia.
10/11/2012	Medical Policy Committee review
10/31/2012	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
10/03/2013	Medical Policy Committee review
10/16/2013	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
11/06/2014	Medical Policy Committee review
11/21/2014	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
08/03/2015	Coding update: ICD10 Diagnosis code section added; ICD9 Procedure code section removed.
10/29/2015	Medical Policy Committee review
11/16/2015	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
11/03/2016	Medical Policy Committee review
11/16/2016	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
01/01/2017	Coding update: Removing ICD-9 Diagnosis Codes
11/02/2017	Medical Policy Committee review
11/15/2017	Medical Policy Implementation Committee approval. Coverage eligibility unchanged. The word Stem removed from title and policy.
11/08/2018	Medical Policy Committee review
11/21/2018	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
11/07/2019	Medical Policy Committee review
11/13/2019	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
04/02/2020	Medical Policy Committee review
04/08/2020	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
04/01/2021	Medical Policy Committee review
04/14/2021	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
04/07/2022	Medical Policy Committee review
04/13/2022	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
04/06/2023	Medical Policy Committee review
04/12/2023	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

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04/04/2024	Medical Policy Committee review
04/10/2024	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
04/03/2025	Medical Policy Committee review
04/09/2025	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

Next Scheduled Review Date: 04/2026

Coding

The five character codes included in the Louisiana Blue Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)‡, copyright 2024 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.

The responsibility for the content of Louisiana Blue Medical Policy Coverage Guidelines is with Louisiana Blue 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 Louisiana Blue 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 Louisiana Blue 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, 38240, 38241, 38242, 38243
HCPCS	S2140, S2142, S2150
ICD-10 Diagnosis	All related Diagnoses

*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 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.

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.

Hematopoietic Cell Transplantation for Primary Amyloidosis or Waldenstrom's Macroglobulinemia

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NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.