Medical Policy

Blue Cross Blue Shield Blue Care Network of Michigan

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***Current Policy Effective Date: 11/1/23**
(See policy history boxes for previous effective dates)

Title: Bone Marrow - Hematopoietic Cell Transplant for Waldenström's Macroglobulinemia

Description/Background

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

WALDENSTRÖM MACROGLOBULINEMIA

Waldenström macroglobulinemia (WM) is a clonal disorder of B lymphocytes that accounts for 1% to 2% of hematologic malignancies, with an estimated 1,500 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 to10 years, with age, hemoglobin concentration, serum albumin level, and β_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 (LPL) 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
There is no standard therapy for the treatment of symptomatic WM. Whenever possible, individuals should be encouraged to participate in clinical trials. The goal of therapy for individuals with WM is to achieve symptomatic relief and reduce organ damage without compromising quality of life. Treatment of WM is indicated only in symptomatic individuals 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 hemoglobin concentration less than 10g/dL; platelet count less than 100,000/µL; 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 individuals who may undergo autologous hematopoietic cell transplantation (HCT) often combine rituximab with other agents (e.g., 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 (e.g., 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 (GVM) effect that develops after engraftment of allogeneic stem cells within the recipients bone marrow space. While the slower GVM 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 individuals 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 allogeneic HCT, immune suppressant drugs are required to minimize graft rejection and graft-versus-host disease, which also increases susceptibility of the recipient 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 recipient before undergoing bone marrow ablation. As a consequence, autologous HCT is typically performed as consolidation therapy when the recipients disease is in complete remission. Individuals 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 non-relapse mortality in the period during which the beneficial GVM effect of allogeneic transplantation develops. Although the definition of RIC remains arbitrary, with numerous versions employed,

all seek to balance the competing effects of NRM 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.

Regulatory Status

The U.S. Food and Drug Administration regulates human cells and tissues intended for implantation, transplantation, or infusion through the Center for Biologics Evaluation and Research, under Code of Federal Regulation (CFR) title 21, parts 1270 and 1271. Hematopoietic stem cells are included in these regulations.

Medical Policy Statement

Autologous hematopoietic cell transplantation is established as salvage therapy of chemosensitive Waldenström's macroglobulinemia. It is a useful therapeutic option when indicated.

Allogeneic hematopoietic cell transplantation is considered experimental/investigational to treat Waldenström's macroglobulinemia. It has not been shown to improve clinical outcomes better than established therapies.

Inclusionary and Exclusionary Guidelines

Clinical documentation supplied to the health plan must demonstrate that attending staff at the transplant center have considered all contraindications as part of their overall evaluation of potential organ transplant recipients and have decided to proceed.

Inclusions:
Autologous hematopoietic cell transplantation for chemosensitive Waldenström's macroglobulinemia individuals who have relapsed after initially responding to treatment, including chemotherapy, alone or in various combinations, with agents such as:

- Alkylating agents (chlorambucil, cyclophosphamide, melphalan)
- Purine analogues (cladribine, fludarabine)
- Monoclonal antibody agents (rituximab)

Exclusions:
Allogeneic hematopoietic cell transplantation for Waldenström's macroglobulinemia.

CPT/HCPCS Level II Codes *(Note: The inclusion of a code in this list is not a guarantee of coverage. Please refer to the medical policy statement to determine the status of a given procedure)*

Established codes:

38204*	38206 *	38207	38208*	38209 *	38210*
38211*	38212*	38213*	38214*	38215*	38232*
38241	S2150*				

Other codes (investigational, not medically necessary, etc.):

38205	38230	38240	38242	S2140	S2142

***** *Allogeneic* hematopoietic cell transplantation for Waldenström's macroglobulinemia is experimental/investigational

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Potential contraindications for transplant:

Note: Final patient eligibility for transplant is subject to the judgment and discretion of the requesting transplant center.

The selection process for approved tissue transplants is designed to obtain the best result for each patient. Therefore, relative contraindications to HCT may include, but are not limited to:

- Poor cardiac function: Ejection fraction should be greater than 45% with no overt symptoms of congestive heart failure.
- Poor pulmonary function: Pulmonary function tests must be greater than or equal to 50% of predicted value.
- Poor renal function: Renal creatinine clearance should be greater than 40 ml/min or creatinine must be less than or equal to 2mg/dl.
- Poor liver function: There should be no history of severe chronic liver disease.
- Presence of HIV or an active form of hepatitis B, hepatitis C or human T-cell lymphotropic virus (HTLV-1).

Rationale

HEMATOPOIETIC CELL TRANSPLANTATION FOR WALDENSTRÖM MACROGLOBULINEMIA

There is no set standard for the treatment of WM, as the rarity of the disease has limited the ability of randomized trials to guide therapy. WM has proven to be incurable with the treatment combinations that have been explored. Treatment attempts are associated with both short- and long-term complications that can decrease quality of life and potentially affect survival, therefore the treatment of asymptomatic individuals is discouraged. The goals of treatment are to control symptoms and prevent end-organ damage, while maximizing quality of life. In symptomatic individuals, most experts differ in their treatment preferences. Toxicity profiles and the clinician's comfort with the regimen used weighs heavily in individual treatment choices.

Clinical Context and Test Purpose

The purpose of hematopoietic cell transplantation is to provide a treatment option that is an alternative to or an improvement on existing therapies in individuals with Waldenström macroglobulinemia.

The following PICOs were used to select literature to inform this review.

Populations

The relevant population of interest are individuals with Waldenström macroglobulinemia.

Interventions

The therapy being considered is hematopoietic cell transplantation.

Comparators

Comparators of interest include chemotherapy, targeted therapy drugs, and biologic therapy drugs.

Outcomes

The general outcomes of interest include overall survival, quality of life, treatment-related mortality, and treatment-related morbidity.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess longer term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

Few published data are available and there is a lack of studies comparing hematopoietic cell transplantation (HCT) to other treatments e.g., chemotherapy in individuals who have Waldenström macroglobulinemia (WM). Several retrospective series have been published.

Review of Evidence

Autologous HCT

Kyriakou et al (2010) evaluated 158 adults with WM reported to the European Group for Blood and Marrow Transplantation (EBMT) between 1991 and 2005. Median time from diagnosis to autologous HCT was 1.7 years (range, 0.3 to 20.3 years), 32% of the patients experienced treatment failure with at least 3 lines of therapy, and 93% had sensitive disease at the time of HCT. Median follow-up for surviving patients was 4.2 years (range: 0.5 to 14.8 years). Non-relapse mortality (NRM) was 3.8% at 1 year. Relapse rate was 52.1% at 5 years. Progression-free survival and overall survival (OS) were 39.7% and 68.5%, respectively, at 5 years and were significantly influenced by number of lines of therapy and chemo-refractoriness at HCT. Authors conclude that autologous HCT is a feasible procedure in young patients with advanced WM but that it should not be offered to individuals with chemo resistant disease and to those who have received more than 3 lines of therapy.

Ansell et al (2022) reviewed the treatment and prognosis of Waldenstrom macroglobulinemia through a meta-analysis of 15 retrospective studies that included 278 patients who underwent autologous HCT across several decades. None of the regimens used were found to demonstrate superior efficacy over another. High dose chemotherapy followed by autologous HCT was rarely used for the treatment of WM. Authors pointed out that the role of autologous HCT in WM is limited, and it is reserved for selected individuals with good performance status in whom other treatment options have been exhausted. Data regarding the efficacy of autologous HCT indicated that most individuals who received autologous HCT had relapsed or refractory disease. Most studies reported overall survival (OS), PFS, and relapse rates (RR) at 3 to 5 years and non-relapse mortality (NRM) at 1 year. Pooled estimates for autologous HCT were OS 76 percent (95% CI 65-86 percent), PFS 55 percent (95% CI 42-68 percent), RR 42 percent (95% CI 30-55 percent), and NRM 4 percent (95% CI 1-7 percent).

Allogeneic HCT

Data from the Center for International Blood and Marrow Transplant Research registry have been published periodically, most recently in 2017. Cornell et al (2017) reported retrospectively on 144 adults with WM entered in the registry between 2001 and 2013 who underwent allogeneic HCT. Patients had relapsed after receiving at least 1 line of prior therapy. Hematopoietic cells were obtained from human leukocyte antigen-matched or -mismatched donors; cord blood stem cells were excluded. Sixty-seven patients received myeloablative conditioning (MAC) and 67 received reduced intensity conditioning (RIC). Over half of patients (n=82 [57%]) had chemosensitive disease. Median follow-up after transplant was 70 months. Overall survival (OS) rates were 74% at 1 year and 52% at 5 years. Patients with chemosensitive disease had significantly better 1 year and 5-year overall survival rates compared with individuals who had chemo-resistant disease. Conditioning intensity (MAC vs RIC) did not impact treatment-related mortality, relapse, or progression free survival rates. Sixty-five deaths were reported, with the most common causes being graft-versus-host disease (28%) and primary disease (23%).

Kyriakou et al (2010) retrospectively analyzed data on 86 who had allogeneic HCT for WM. Patients underwent MAC (n=37) or RIC (n=49) regimens. Median age was 49 years (range: 23 to 64 years); 47 patients had received 3 or more previous lines of therapy, and 8 patients had experienced failure on a prior autologous HCT. Fifty-nine (68.6%) patients had chemosensitive disease at the time of allogeneic HCT. Median follow-up of the surviving patients was 50 months. The overall response rate was 75.6%. Relapse rates at 3 years were 11% for MAC and 25% for RIC. The OS at 5 years was 62% for MAC and 64% for RIC. Thirty deaths were reported; causes of death included graft-versus-host disease (23%) and primary disease (23%). The occurrence of chronic graft-versus-host disease was associated with a lower relapse rate.

Ansell et all (2022) reviewed the treatment and prognosis of Waldenstrom macroglobulinemia through a meta-analysis of 15 retrospective studies that included 311 patients who underwent allogeneic HCT across several decades. All patients undergoing allogeneic HCT had relapsed or refractory disease. Most studies reported overall survival (OS), PFS, and relapse rates (RR) at 3 to 5 years and non-relapse mortality (NRM) at 1 year. Pooled estimates for allogeneic HCT were OS 57 percent (95% CI 50-65 percent), PFS 49 percent (95% CI 42-56 percent), NRM 29 percent (95% CI 23-34 percent), RR 23 percent (95% CI 18-28 percent). Acute graft-versus-host disease (GVHD) was reported in 71 percent and usually grade I to II.

Chronic GVHD was reported in 51 percent. Results following allogeneic HCT were heterogeneous, likely reflecting diversity in conditioning regimens, donor type, stem cell source, and GVHD prophylaxis used at different institutions and across time. Authors concluded that Allogeneic HCT carries a much higher risk of non-relapse mortality than autologous HCT and should not be considered outside the context of a clinical trial

Section Summary: Hematopoietic Cell Transplantation for Waldenström Macroglobulinemia

Several retrospective series have evaluated HCT for WM. Analyses of registry data have reported 5-year OS rates of 52% after allogeneic HCT and 68.5% after autologous HCT. The total number of patients studied was small and there is a lack of published controlled studies.

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
NCT01251575	A Phase II Study to Assess Immunosuppression With Sirolimus Combined With Cyclosporine and Mycophenolate Mofetil for Prevention of Acute GVHD After Non-Myeloablative HLA Class I or II Mismatched Donor Hematopoietic Cell Transplantation- A Multi-Center Trial	77	Feb 2019 (completed; last updated Dec 2019)
NCT02844361	Autologous Stem-cell Transplantation Versus Conventional Chemotherapy for High Risk Waldenström Macroglobulinemia - a Prospective Multicentre Phase IV Trial From China	70	May 2020 (Estimated; Last updated Feb 2016)

NCT: national clinical trial

SUMMARY OF EVIDENCE

For individuals who have Waldenström macroglobulinemia who receive hematopoietic cell transplantation (HCT), the evidence includes case series and meta-analysis of 15 studies. 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 recipients 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.

Supplemental Information

CLINICAL INPUT RECEIVED THROUGH 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, Blue Cross Blue Shield Association received input from no physician specialty societies and 5 academic medical centers, including 3 transplant centers, while this policy was under review in 2011. The input indicated that autologous HCT may be considered medically necessary as salvage therapy for Waldenström macroglobulinemia that is chemosensitive. Input was mixed on use of allogeneic HCT, 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 Waldenström macroglobulinemia (WM) and lymphoplasmacytic lymphoma 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 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. The guidelines noted that patients who are potentially eligible for autologous hematopoietic cell transplantation (HCT; <70 years 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 is short (<2 years). Patients with refractory WM should not be offered [autologous HCT] (level 3, grade B).”

Eighth International Workshop on Waldenström’s Macroglobulinemia

In the 2016 consensus recommendations from the Eighth International Workshop on Waldenström Macroglobulinemia, the committee stated that when appropriate, allogeneic HCT, “should preferably be considered in the context of clinical trials.”

Tenth International Workshop on Waldenström’s Macroglobulinemia

In 2018 (updated in 2019 and 2020), consensus recommendations from the Tenth International Workshop on Waldenström Macroglobulinemia were published. The panel concluded that autologous hematopoietic cell transplantation (HCT) is not appropriate for first line therapy in patients who are responding to induction therapy. Autologous HCT is appropriate following second or subsequent relapses in high-risk WM patients (i.e., aggressive clinical behavior or refractory to previous therapies) with chemosensitive disease, and HCT should not be considered in patients who are BTK inhibitor naïve, provided BTK inhibitors are available.

Myeloma Foundation of Australian

The Myeloma Foundation of Australia (2017) 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)."

British Society for Haematology Guideline
BSH guidelines (2022) recommend against offering autologous stem cell to patients with less than a partial response (Grade C1) but advise that autologous stem cell can be considered as a second- or later line of therapy in selected chemotherapy-responsive patients (e.g., those with amyloidosis who are in first remission), although its use remains contentious because of the new drugs becoming available (Grade C2). Allogeneic SCT should be considered only for highly selected patients who have progressed after immunochemo-therapy and BTK inhibitor therapy (Grade C2).

U.S. PREVENTIVE SERVICES TASK FORCE RECOMMENDATIONS
Not applicable.

Government Regulations
National Coverage Determination:

Medicare National Coverage Determinations Manual, Chapter 1, Part 2, Section 110.23, "Stem Cell Transplantation." Effective date: 1/27/16; Implementation Date: 10/3/16

The Medicare NCD on stem cell transplantation does not specifically mention Waldenström's macroglobulinemia. However, Waldenström's macroglobulinemia (WM) is a rare, (slow-growing) non-Hodgkin lymphoma which is also called lymphoplasmacytic lymphoma.

Under Medicare, autologous stem cell transplant is considered reasonable and necessary for patients with resistant non-Hodgkin's lymphomas or those presenting with poor prognostic features following an initial response.

(The above Medicare information is current as of the review date for this policy. However, the coverage issues and policies maintained by the Centers for Medicare & Medicare Services [CMS, formerly HCFA] are updated and/or revised periodically. Therefore, the most current CMS information may not be contained in this document. For the most current information, the reader should contact an official Medicare source.)

Related Policies

- BMT – Hematopoietic Cell Transplantation for Acute Lymphoblastic Leukemia
- BMT – Hematopoietic Cell Transplantation for Acute Myeloid Leukemia
- BMT – Hematopoietic Cell Transplantation for Autoimmune Diseases
- BMT – Hematopoietic Cell Transplantation for Chronic Lymphocytic Leukemia and Small Cell Lymphocytic Lymphoma – Autologous or Allogeneic
- BMT – Hematopoietic Cell Transplantation for Chronic Myeloid Leukemia
- BMT – Hematopoietic Cell Transplantation for CNS Tumors, Embryonal Tumors and Ependymoma
- BMT – Hematopoietic Cell Transplantation for Epithelial Ovarian Cancer
- BMT – Hematopoietic Cell Transplantation for Genetic Diseases and Acquired Anemias (Allogeneic)

- BMT – Hematopoietic Cell Transplantation for Germ-Cell Tumors
- BMT – Hematopoietic Cell Transplantation for Hodgkin Lymphoma
- BMT – Hematopoietic Cell Transplantation for Miscellaneous Solid Tumors in Adults
- BMT – Hematopoietic Cell Transplantation for Myelodysplastic Syndromes and Myeloproliferative Neoplasms
- BMT – Hematopoietic Cell Transplantation for Non-Hodgkin Lymphomas
- BMT – Hematopoietic Cell Transplantation for Plasma Cell Dyscrasias, Including Multiple Myeloma and POEMS Syndrome
- BMT – Hematopoietic Cell Transplantation for Primary Amyloidosis
- BMT – Hematopoietic Cell Transplantation for Solid Tumors of Childhood
- BMT – Malignant Astrocytomas and Gliomas (Autologous)
- Donor Lymphocyte Infusion for Malignancies Treated with an Allogeneic Hematopoietic Cell Transplant
- Orthopedic Applications of Stem-Cell Therapy (Including Allografts and Bone Substitutes used with Autologous Bone Marrow)

References

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3. Centers for Medicare and Medicaid Services (CMS), *Medicare Coverage Database*, National Coverage Determination (NCD) for Stem Cell Transplantation (Formerly 110.8.1) (110.23), effective date 1/27/16; https://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?NCDId=366&ncdver=1&SearchType=Advanced&CoverageSelection=Both&NCSelection=NCA%7cCAL%7cNCD%7cMEDCAC%7cTA%7cMCD&ArticleType=SAD%7cEd&PolicyType=Both&s=27&KeyWord=stem+cell+transplantation&KeyWordLookUp=Title&KeyWordSearchType=Exact&kq=true&bc=IAAAACAAAAAAAA%3d%3d&. Accessed July 6, 2023
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5. Kapoor P, Ansell SM, Fonseca R, et al. Diagnosis and management of Waldenstrom macroglobulinemia: Mayo Stratification of Macroglobulinemia and Risk-Adapted Therapy (mSMART) Guidelines 2016. JAMA Oncol. Sep 1 2017;3(9):1257-1265. PMID 28056114
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9. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Waldenstrom's Macroglobulinemia/Lymphoplasmacytic Lymphoma. Version 1.2023; https://www.nccn.org/professionals/physician_gls/pdf/waldenstroms.pdf. Accessed July 6, 2023.
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11. Talaulikar D, Tam CS, Joshua D, et al. Treatment of patients with Waldenstrom macroglobulinaemia: clinical practice guidelines from the Myeloma Foundation of Australia Medical and Scientific Advisory Group. Intern Med J. Jan 2017;47(1):35-49. PMID 28076910

The articles reviewed in this research include those obtained in an Internet based literature search for relevant medical references through 7/6/23, the date the research was completed.

Joint BCBSM/BCN Medical Policy History

Policy Effective Date	BCBSM Signature Date	BCN Signature Date	Comments
5/1/11	3/17/11	3/3/11	Joint policy established. Information previously available on the following policies: • Allogeneic BMT-Established • Allogeneic BMT – Investigational • Autologous BMT – Established • Autologous BMT – Investigational
11/1/12	8/21/12	8/21/12	Policy title changed from, "Bone Marrow/Stem-Cell Transplantation for Primary Amyloidosis or Waldenström's Macroglobulinemia" to "Bone Marrow/Stem-Cell Transplantation for Waldenström's Macroglobulinemia" (separate policy). No change in policy status.
11/1/13	8/22/13	8/27/13	Routine maintenance. References and rationale refreshed.
7/1/15	4/24/15	5/8/15	Routine maintenance. Added procedure codes S2140, S2142 and S2150
7/15/16	4/19/16	4/19/16	Routine approval
5/1/17	2/21/17	2/21/17	Routine maintenance Added procedure code 38207 References and rationale updated Changed "hematopoietic stem cell transplant" to "hematopoietic cell transplant" throughout policy
5/1/18	2/20/18	2/20/18	Routine maintenance
5/1/19	2/19/19		Routine maintenance
11/1/19	8/20/19		Routine maintenance
11/1/20	8/18/20		Routine maintenance
11/1/21	8/17/21		Routine maintenance
11/1/22	8/16/22		Routine maintenance
11/1/23	8/15/23		Routine maintenance (slp) Vendor Managed: N/A

Next Review Date: 3rd Qtr, 2024

BLUE CARE NETWORK BENEFIT COVERAGE
POLICY: BONE MARROW TRANSPLANT FOR WALDENSTRÖM'S MACROGLOBULINEMIA

I. Coverage Determination:

Commercial HMO (includes Self-Funded groups unless otherwise specified)	Covered; criteria apply.
BCNA (Medicare Advantage)	Refer to the Medicare information under the Government Regulations section of this policy.
BCN65 (Medicare Complementary)	Coinsurance covered if primary Medicare covers the service.

II. Administrative Guidelines:

- The member's contract must be active at the time the service is rendered.
- Coverage is based on each member's certificate and is not guaranteed. Please consult the individual member's certificate for details. Additional information regarding coverage or benefits may also be obtained through customer or provider inquiry services at BCN.
- The service must be authorized by the member's PCP except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Services must be performed by a BCN-contracted provider, if available, except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Payment is based on BCN payment rules, individual certificate and certificate riders.
- Appropriate copayments will apply. Refer to certificate and applicable riders for detailed information.
- CPT - HCPCS codes are used for descriptive purposes only and are not a guarantee of coverage.