Hematopoietic Stem-Cell Transplantation for Primary Amyloidosis

**Number** 8.01.530  
**Effective Date** April 24, 2015  
**Revision Date(s)** 08/09/16; 04/14/15; 05/12/14  
**Replaces** 8.01.42

**Policy**

Autologous hematopoietic stem-cell transplantation may be considered **medically necessary** to treat primary systemic amyloidosis in carefully selected patients with no more than 2 adverse prognostic characteristics:

1. Creatinine clearance <30 mL/min
2. Nephrotic syndrome > 3.5 gm of proteinuria/24 hours
3. Heart failure – Functional classification by NYHA Class 3 or worse OR cardiac left ventricular ejection fraction of < 40%
4. Neuropathy – Moderately severe mixed sensory and motor peripheral neuropathy and/or moderately severe autonomic neuropathy
5. Hepatomegaly with enzyme elevations – Moderately severe liver involvement seen in 70% together with alkaline phosphatase concentration >200 international units/L seen in 25%

Autologous hematopoietic stem-cell transplantation is considered **investigational** in all others situations unless enrolled in a clinical trial. (See **Related Policies**, Clinical Trials)

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

**Related Policies**

7.01.50 Placental and Umbilical Cord Blood as a Source of Stem Cells
8.01.21 Allogeneic Hematopoietic Stem-Cell Transplantation for Myelodysplastic Syndromes and Myeloproliferative Neoplasms
8.01.22 Allogeneic Hematopoietic Stem-Cell Transplantation for Genetic Diseases and Acquired Anemias
8.01.24 Hematopoietic Stem-Cell Transplantation for Miscellaneous Solid Tumors in Adults
8.01.25 Hematopoietic Stem-Cell Transplantation for Autoimmune Diseases
8.01.29 Hematopoietic Stem-Cell Transplantation for Hodgkin Lymphoma
Background

**Hematopoietic Stem-Cell Transplantation**

Hematopoietic stem-cell transplantation (HSCT) refers to 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 radiation therapy. Hematopoietic stem cells may be obtained from the transplant recipient (autologous HSCT) or from a donor (allogeneic HSCT). 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 “naïve” and thus are associated with a lower incidence of rejection or graft-versus-host disease (GVHD). Cord blood is discussed in greater detail in a separate policy. (See Related Policies)

Immunologic compatibility between infused hematopoietic stem cells and the recipient is not an issue in autologous HSCT. However, immunologic compatibility between donor and patient is a critical factor for achieving a good outcome of allogeneic HSCT. Compatibility is established by typing HLA using cellular, serologic, or molecular techniques. HLA 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.

**Conventional Preparative Conditioning for HSCT**

The conventional (“classical”) practice of allogeneic HSCT 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 patient’s bone marrow space. While the slower GVM 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 allogeneic HSCT, immune suppressant drugs are required to minimize graft rejection and GVHD, which also increases susceptibility of the patient to opportunistic infections.

The success of autologous HSCT 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 prior to undergoing bone marrow ablation. As a consequence, autologous HSCT is typically performed as consolidation therapy when the patient’s disease is in complete remission. Patients who undergo autologous HSCT are susceptible to chemotherapy-related toxicities and opportunistic infections prior to engraftment, but not GVHD.

Reduced-Intensity Conditioning for Allogeneic HSCT

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 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 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 HSCT 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 the purposes of this policy, the term reduced-intensity conditioning will refer to all conditioning regimens intended to be nonmyeloablative, as opposed to fully myeloablative (conventional) regimens.

Primary Systemic 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 exhibit a pathognomonic red-green birefringence when stained with Congo red dye and examined under polarized light. These diseases are classified on the basis of the type of amyloidogenic protein involved, as well as 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 protein is produced at the site of deposition. Light-chain amyloidosis (AL), the most common type of systemic amyloidosis, has an incidence similar to that of Hodgkin’s lymphoma or chronic myelogenous leukemia, estimated at 5 to 12 people per million annually. The median age at diagnosis is approximately 60 years. The amyloidogenic protein in AL amyloidosis is an immunoglobulin light chain or light-chain fragment that is produced by a clonal population of plasma cells in the bone marrow. While the plasma cell burden in AL 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 AL amyloidogenic proteins causes organ dysfunction, most frequently in the kidneys, heart, and liver, although the central nervous system and brain may be affected.

Historically, this disease has had a poor prognosis, with a median survival from diagnosis of approximately 12 months, although outcomes have improved with the advent of combination chemotherapy with alkylating agents and autologous HSCT. Emerging approaches include the use of immunomodulating drugs such as thalidomide or lenalidomide, and the proteasome inhibitor bortezomib. Regardless of the approach chosen, treatment of AL amyloidosis is aimed 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.
Medical policies are systematically developed guidelines that serve as a resource for Company staff when determining coverage for specific medical procedures, drugs or devices. Coverage for medical services is subject to the limits and conditions of the member benefit plan. Members and their providers should consult the member benefit booklet or contact a customer service representative to determine whether there are any benefit limitations applicable to this service or supply. This medical policy does not apply to Medicare Advantage.

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<th>Rationale</th>
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| This policy was originally created in 2003 and updated regularly with searches of the MEDLINE and EMBASE databases. The most recent literature search was performed for the period January 11, 2013, through December 2, 2014. Following is a summary of key literature to date.

Conventional therapy for primary systemic amyloidosis usually combines oral melphalan with prednisone (MP), which has been shown to yield higher response rates and longer survival than colchicine or prior therapies. (1-3) Median survival after oral melphalan with prednisone (approximately 18 months) is longer than for untreated patients or those given older therapies (10-14 months), but more effective regimens have been sought. Combination therapy with vincristine, doxorubicin, and dexamethasone (VAD), a well-established regimen for myeloma, has been investigated. (1, 2) However, because of its toxicity, VAD therapy usually is 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 autologous HSCT was investigated for this disease.

**Autologous HSCT**

Initial results of autologous HSCT in uncontrolled patient series were published in 1998. (4, 5) Clinical response rates (50%-60%) were nearly twice those reported for conventional therapy, and 2-year survival reportedly ranged from 56% to 68%.(2, 6) However, procedure-related mortality rates of 15% to 43% were substantially higher than those observed in myeloma patients, usually in cases that involved more than 2 organ systems or had symptomatic cardiac involvement. (5, 7, 8)

A subsequent retrospective study analyzed outcomes of conventional therapy for primary amyloidosis in patients who would have been eligible for autologous HSCT. (6) Inclusion required age younger than 70 years, cardiac interventricular septal thickness less than 15, left-ventricular ejection fraction (LVEF) more than 55%, serum creatinine less than 2 mg/dL, and direct bilirubin less than 2.0 mg/dL. Patients eligible for transplantation but managed conventionally reportedly had median survival of 42 months after conventional treatment, compared with median survival of only 18 months for all patients with primary amyloidosis. Survival of conventionally managed patients (n=229) at 24 months was 61%, which was similar to 56% to 65% survival at 24 months after autologous HSCT.

In the same report, survival of 39 patients given autologous HSCT at their institution was compared with survival of a matched cohorts (n=78; 2 controls for each case) selected from their database of conventionally treated amyloidosis patients. (6) Factors used to match patients were limited to age (within 5 years), sex, and number of involved organs. They reported similar survival of cases and controls at 6 (85% vs. 83%), 12 (77% vs. 74%), and 24 months (68% and 60%, respectively).

A follow-up report to the matched-pair analysis cited above included a larger group of cases (n=63) treated with autologous HSCT and used parameters measuring severity of organ involvement to select matched controls (n=63). (9) Factors used for matching were age, sex, time to presentation, LVEF, serum creatinine, cardiac septal thickness, nerve involvement, 24-hour urinary protein excretion, and serum alkaline phosphatase. At a median
follow-up of 3.5 years from diagnosis for each group, 16 transplanted patients and 44 controls had died. Kaplan-Meier analysis showed significantly greater overall survival (OS) for those given autotransplants (p=0.004). The survival rates for the high dose and standard treatment groups at 1, 2, and 4 years were 89% and 71%; 81% and 55%; and 71% and 41%, respectively.

In addition to longer survival, evidence suggests improvement in symptoms for amyloidosis patients treated with autologous HSCT. In a large retrospective series of amyloidosis patients eligible for transplant (n=394), 63 patients declined treatment and 19 lost eligibility when they progressed before treatment started. (10) Estimated median survival for 312 patients who initiated stem-cell mobilization was 4.6 years, but median follow-up was not reported. Of 181 evaluable patients (alive and followed-up for 1 year or more), 40% achieved complete hematologic response, defined as no evidence of plasma cell dyscrasia at 1 year after transplant. The authors reported functional improvement in at least 1 affected organ for 44% of evaluable patients: 66% of 73 patients with complete hematologic response, and 30% of 108 patients with an incomplete or no hematologic response. Among 277 patients who completed the transplant protocol, 36 (13%) died of treatment-related toxicity before day 100 post-transplant, 21 (8%) died between day 100 and 1 year, and 39 were alive but had not reached 1 year since transplant. This series included all patients transplanted between July 1994 and June 2002, of which one-half (n=196) had 3 or more organs involved and 43% had some cardiac involvement. Median survival for those without cardiac involvement (n=137) was significantly shorter (1.6 vs. 6.4 years, respectively; p<0.001) than for those with cardiac involvement (n=175).

A subsequent report based on the dataset from the large retrospective series outlined in the preceding paragraph provided an analysis of outcomes of risk-adjusted myeloablative melphalan and autologous HSCT in patients aged 65 years and older versus outcomes in those younger than 65 years, with up to 10 years of follow-up. (11) Patients younger than 65 years with LVEF of 45% or greater and adequate stem-cell yield (n=280; median age, 55 years; range, 29-64 years) received melphalan 200 mg/m²; those aged 65 years and older, those with reduced LVEF (40%-45%), or those with lower stem-cell yield (n=65; median age, 68 years; range, 65-79 years) received risk-adjusted melphalan 140 mg/m². No difference was observed in early treatment-related mortality (10.3% in patients 65 years or older vs. 13.4% in those younger than 65 years, p=0.665). A trend toward a lower rate of hematologic complete response (CR, defined as the absence of clonal plasma cells in the bone marrow by immunohistochemical staining and of monoclonal gammopathy by immunofixation electrophoresis of serum and urine) was observed in older patients (27.6% for patients ≥65 years) versus 13.4% in those younger than 65 years (p=0.882). However, the median survival after autologous HSCT did not differ according to age (4.0 years for patients aged ≥65 years vs. 4.85 years for those <65 years; log-rank p=0.28).

A registry analysis of 107 amyloidosis patients who received transplants between 1995 and 2001 at 48 centers included 37 (35%) patients who received a transplant for initial therapy of amyloidosis, while 27 (25%) received a transplant after 2 or more prior therapies. (12) With a median follow-up of 30 months after transplant, OS at 1 and 3 years was 66% (95% confidence interval [CI], 56 to 75%) and 56% (95% CI: 45% to 66%), respectively. For those with no or 1 organ involved at transplant, survival at 1 year was 72% (95% CI: 61% to 82%), while for those with 2 or more organs involved, survival at 1 year was 54% (95% CI: 38% to 70%). Survival at 1 year also was greater for those without (69%; 95% CI: 58% to 79%) than with (56%; 95% CI: 37–74%) cardiac involvement. Treatment-related mortality at 30 days was 18% (95% CI: 11% to 26%), mostly among patients with cardiac and/or multiple organ involvement.

Long-term survival and outcomes were evaluated in a series of 80 patients with AL amyloidosis who were treated with myeloablative full-dose or risk-adjusted melphalan according to a risk-based protocol and underwent autologous HSCT. (13) All patients had a histologic diagnosis of amyloidosis with evidence of plasma cell dyscrasia and met eligibility criteria for autologous HSCT in clinical protocols. Patients (median age, 56 years; range, 29-71 years) received risk-adjusted melphalan 100 mg/m² (n=37) or full-dose melphalan 200 mg/m² (n=43) followed by autologous HSCT 24 to 72 hours after completion of the conditioning regimen. Treatment-related mortality was reported in 11 (14%) cases, 6 of whom had received risk-adjusted melphalan, while 5 received the full-dose regimen. Median survival for all 80 patients was 57 months; 18 (23%) were alive 10 or more years after undergoing autologous HSCT. Hematologic CR was assessed in 63 (79%) surviving patients at 1 year following treatment. Thirty-two of those patients (51%) achieved a hematologic CR; among those, median survival had not been reached at the time the report was prepared for publication. In contrast, the median survival for patients who failed to achieve a CR was 50 months, with a 6% estimated probability of survival at 10 years (p<0.001 vs. patients with complete response).

In a series of 282 consecutive patients with light-chain AL who underwent autologous HSCT, investigators sought to determine whether a hematologic CR, as determined by normalization of serum and urine monoclonal protein
levels, provides an adequate surrogate marker for OS. (14) All patients had AL histologically verified with Congo red tissue stain, and received risk-adjusted melphalan conditioning based on the presence of numbers of organs involved, creatinine level, age, and cardiac involvement. One-third (n=93) of the patients received risk-adjusted melphalan (100 or 140 mg/m2) and 67% (n=189) received full-dose melphalan (200 mg/m2). The mortality at day 100 was 11%, with 28% of the cohort dead by the time this report was prepared. Ninety-three (33%) patients achieved a CR, 108 (38%) had a partial response (PR), and 36 (13%) had no response (NR) to autologous HSCT. Kaplan-Meier analysis showed that median survival was reached only in the NR group, compared with the CR and PR groups after more than 80 months of follow-up (log-rank p<0.001 for NR vs. CR and PR). An analysis (landmark analysis) focused on patients who survived for at least 6 months after autologous HSCT included 86 patients in the CR group, 91 who had PR, and 36 NR patients. This analysis showed that the survival curve differences remained significant between response groups as in the overall cohort, with a median survival of 40 months reached only in the NR group.

Patients with AL amyloidosis and cardiac involvement were treated in a series from Mayo Clinic. (15) A total of 187 patients of median age 57 years received high-dose melphalan followed by autologous HSCT. The median time from diagnosis to HSCT was about 4 months, and median estimated follow-up from diagnosis was 65 months (95% CI: 61 to 74 months). The median estimated OS for all 187 patients was 66 months (95% CI: 42 to 83 months). Overall, hematologic and cardiac responses were observed in 66% and 41% of patients, respectively. Overall, 30 (16%) patients died within 100 days of treatment; 29 of those deaths were considered to be the result of therapy.

A series of 421 consecutive patients treated with high-dose melphalan and autologous HSCT at a single referral center compared outcomes for patients with and without a CR. (16) Treatment-related mortality was about 11% overall (5.6% in the last 5 years). By intention-to-treat (ITT) analysis, the CR rate was 34% and the median event-free survival (EFS) and OS were 2.6 and 6.3 years, respectively. Eighty-one patients died within the first year after HSCT and were not evaluable for hematologic and organ response. Of 340 evaluable patients, 43% achieved CR and 78% of them experienced an organ response. For CR patients, median EFS and OS were 8.3 and 13.2 years, respectively. Among the 195 patients who did not obtain CR, 52% achieved an organ response, and their median EFS and OS were 2 and 5.9 years, respectively. Thus, treatment of selected AL patients with high-dose melphalan and autologous HSCT resulted in a high organ response rate and long OS, even for those patients who did not achieve CR. These results are compatible with others previously cited.

Several additional retrospective and prospective series have been reported on the use of autologous HSCT in patients with AL. (17-21) Results from these series are consistent with others that suggest autologous HSCT is feasible and beneficial in selected patients with AL.

One randomized multicenter trial involving 8 centers from the Myelome Autogreffe and Intergroupe Francophone du Myelome Intergroup has been reported in which conventional chemotherapy with melphalan plus dexamethasone was compared with myeloablative melphalan followed by autologous HSCT in patients with AL amyloidosis. (22) Patients between 18 and 70 years of age had a histologic diagnosis of AL amyloidosis and either a complete hematologic response characterization of amyloid deposits or evidence of a monoclonal immunoglobulin protein in the serum or urine or a monoclonal staining pattern of bone marrow plasma cells and had received no more than 2 courses of any chemotherapy regimen. They were randomly allocated, stratified according to age (younger than 65 years or 65 years or older) and according to the affected organ system (cardiac, renal, neurologic, or other). Of note, approximately two-thirds of the patients had 2 or more organs affected. Patients in the melphalan plus dexamethasone group (n=50) received monthly courses of dose-adjusted (according to cytopenic status) oral melphalan, 10 mg/m² of body-surface area, on days 1 to 4 plus oral dexamethasone, 40 mg/day on days 1 to 4, for up to 18 courses if no severe adverse events occurred. In the autologous HSCT patients (n=50), hematopoietic stem cells were obtained from peripheral blood with granulocyte colony-stimulating factor mobilization. Melphalan was administered intravenously on day 0, and stem cells were infused on day 2, with the dose reduced from 200 mg/m² to 140 mg/m² for patients aged 65 years or older and for those with an LVEF less than 30%, a calculated creatinine clearance less than 30 mL/min, or severe liver disease. According to ITT analysis, the hematologic response rate did not differ between groups, with 12 CR (24%) and 14 PR (28%) in the melphalan-dexamethasone recipients versus 11 CR (22%) and 7 PR (14%) in the autologous HSCT group (p=0.11). At publication of the study, the median follow-up for the entire cohort was 24 months, and for survivors it was 36 months; 20 patients in the melphalan-dexamethasone group had died versus 31 in the autologous HSCT group. Among 65 patients who could be evaluated, the ITT median survival for patients assigned to melphalan plus dexamethasone was 56.9 months, versus 22.2 months in the autologous HSCT group (p=0.04). Survival rates and duration were significantly better in responders (CR plus PR) compared with NR (p<0.001). Analysis of patients who survived for at least 6 months and who received their assigned
treatment, showed no significant difference in survival rates in patients assigned to melphalan plus dexamethasone compared with autologous HSCT, with neither group reaching median survival after 80 months (p=0.38).

These randomized trial data suggest that autologous HSCT may be no more efficacious than conventional chemotherapy in prolonging survival among patients with AL amyloidosis. However, the results are limited by the size of the study, a lack of assessor blinding or allocation concealment, and a large attrition post-randomization. Thus, among 50 patients assigned to autologous HSCT, 13 (26%) did not receive the planned treatment (1 declined, 2 had insufficient stem-cell harvest, 10 died before treatment), whereas 7 of 50 (14%) assigned to melphalan plus dexamethasone did not receive planned treatment (5 died before treatment, 1 did not tolerate treatment, 1 received incorrect treatment). Therefore, even though this was a randomized trial, the results are sufficiently confounded preventing conclusion except that careful selection of transplant candidates significantly affects outcome results as has been demonstrated previously in nonrandomized studies.

**Allogeneic HSCT**

Data on the use of allogeneic HSCT to treat AL amyloidosis are sparse, with no systematic evaluation in a clinical trial. (23) Concerns about the use of allogeneic HSCT include high treatment-related mortality (more than 40%), morbidity secondary to graft-versus-host disease, and questions about the efficacy of a proposed graft-versus-malignancy effect on low-grade plasma cell dyscrasias.

**Clinical Input Received through Physician Specialty Societies and Academic Medical Centers**

In response to requests, input was received from no physician specialty societies and 5 academic medical centers, including 3 transplant centers, while this policy was under review in 2011. 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. There was support for the policy statements regarding HSCT in the treatment of amyloidosis.

**Summary**

Chemotherapy for the treatment of light-chain amyloidosis (AL) was introduced in 1972 in the form of melphalan and prednisone. (3) Median survival with this regimen was typically 12 to 18 months, with therapy remaining unchanged until the introduction of autologous hematopoietic stem-cell transplantation (HSCT). The use of autologous HSCT for AL amyloidosis may eradicate the amyloidogenic light chain produced by the clonal plasma cell populations, which is the proximal cause of pathology and subsequent death. This has extended survival rates to a reported 53% at 10 years in carefully selected patients with a complete response to treatment. (13) In selected candidates, transplant-related mortality rates have declined, from as high as 40% to 7% in current studies. (24) Therefore, autologous HSCT is an important option for selected patients who are deemed eligible, and for them it is considered medically necessary. Retrospective and small prospective trials have demonstrated the adverse prognostic importance of organ involvement in patients with AL amyloidosis undergoing HSCT [4,5,17-20]. In several series of transplanted patients, major findings were the prognostic value of the number and severity of clinical manifestations of amyloidosis at the time of transplantation [5, 20]. The criteria included creatinine clearance <30 mL/min, nephrotic syndrome, heart failure, neuropathy, or hepatomegaly associated with an alkaline phosphatase concentration >200 international units/L, serum BNP, and age [5,20,21]. Poor outcomes were due to a > 75 % incidence of toxic death with HSCT for unselected patients. Data on the use of allogeneic HSCT are sparse and it remains investigational.

**National Comprehensive Cancer Network Guidelines**

For 2014, National Comprehensive Cancer Network (NCCN) published guidelines specific for AL amyloidosis. (25) Optional treatments include autologous HSCT as primary therapy for systemic amyloidosis; however, they caution that the optimal therapy is not established and that such treatment would best be performed in a clinical trial.

**National Cancer Institute Physician Data Query (PDQ®) Database**
A search of the National Cancer Institute clinical trials PDQ database in January 2014 identified one active Phase II study (NCT00681044): High-Dose Melphalan and Stem-Cell Transplant in Treating Patients With Immunoglobulin Deposition Disease or Light-Chain Deposition Disease. The purpose of the study is:

- To assess the tolerability of high-dose melphalan and autologous stem-cell transplantation in patients with immunoglobulin deposition disease or light-chain deposition disease.
- To determine the hematologic response rate in patients treated with this regimen.
- To determine the predictability of early free light-chain response for heme response in patients treated with this regimen.
- To determine organ or clinical response in patients treated with this regimen.
- To determine overall survival of these patients.

References


**Coding**

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allogeneic
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38242     Allogeneic donor lymphocyte infusions

ICD-9 Procedure
41.01     Autologous bone marrow transplant without purging
41.02     Allogeneic bone marrow transplant with purging
41.03     Allogeneic bone marrow transplant without purging
41.04     Autologous hematopoietic stem-cell transplant without purging
41.05     Allogeneic hematopoietic stem-cell transplant without purging
41.07     Autologous hematopoietic stem cell transplant with purging
41.08     Allogeneic hematopoietic stem cell transplant with purging
41.09     Autologous bone marrow transplant with purging
41.91     Aspiration of bone marrow from donor for transplant
99.79     Other therapeutic apheresis (harvest) of stem cells

ICD-9 Diagnosis
277.30 – Amyloidosis code range
277.39 –

ICD-10-CM
10/01/15
E85.0-E85.9
Amyloidosis code range (this policy would exclude E85.3 secondary systemic and E85.4 organ limited as they are not primary systemic)

ICD-10-PCS
10/01/15
30243G0, 30243X0, 30243Y0
Percutaneous transfusion, central vein, bone marrow or stem cells, autologous, code list
07DQ0ZZ, 07DQ3ZZ, 07DR0ZZ, 07DR3ZZ, 07DS0ZZ, 07DS3ZZ
Surgical, lymphatic and hemic systems, extraction, bone marrow, code list

HCPCS
S2140     Cord blood harvesting for transplantation, allogeneic
S2142     Cord blood derived stem-cell transplantation, allogeneic
S2150     Bone marrow or blood-derived stem-cells (peripheral or umbilical), allogeneic or autologous, harvesting, transplantation, and related complications; including pheresis and cell preparation/storage; marrow ablative therapy; drugs, supplies, hospitalization with out-patient follow-up; medical/surgical, diagnostic, emergency, and rehabilitative services; and the number of days of pre- and post-transplant care or the global definition.

Type of Service
Therapy

Place of Service
Inpatient/Outpatient

Appendix
N/A

History
Date       Reason
05/12/14   New PR policy replacing 8.01.42. Autologous HSCT may be considered medically necessary to treat primary systemic amyloidosis in carefully selected patients with no more than 2 adverse prognostic characteristics (previously allowed with no qualifying criteria); investigational in all other situations except when enrolled in a clinical trial.
06/24/14   Update Related Policies. Remove 8.01.54 and add 8.01.531
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  • Information written in other languages

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PO Box 91102, Seattle, WA 98111
Toll free 855-332-4535, Fax 425-918-5952, TTY 800-842-5357
Email AppealsDepartmentInquiries@Premera.com

You can file a grievance in person or by mail, fax, or email. If you need help filing a grievance, the Civil Rights Coordinator is available to help you.

You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights, electronically through the Office for Civil Rights Complaint Portal, available at https://ocrportal.hhs.gov/ocr/portal/lobby.jsf, or by mail or phone at:
U.S. Department of Health and Human Services
200 Independence Avenue SW, Room 509F, HHH Building
Washington, D.C. 20201, 1-800-368-1019, 800-537-7697 (TDD)

Complaint forms are available at
200 Independence Avenue SW, Room 509F, HHH Building
U.S. Department of Health and Human Services
https://ocrportal.hhs.gov/ocr/portal/lobby.jsf, or by mail or phone at:

Getting Help in Other Languages

This Notice has Important Information. This notice may have important information about your application or coverage through Premera Blue Cross. There may be key dates in this notice. You may need to take action by certain deadlines to keep your health coverage or help with costs. You have the right to get this information and help in your language at no cost. Call 800-722-1471 (TTY: 800-842-5357).

Français (French):

Kreyòl ayisyen (Creole):
Avi si a gen anfòmasyon anpòtan ladan nan. Avi si a kapab genyen anfòmasyon enpòtan konsènan aplikasyon w lan oswa konsènan kouvèti aisers lan atravè Premera Blue Cross. Kapab genyen dat ki enpòtan nan avi si a. Ou ka gen pou pran kék aksyon avan sèten dat limit pou ka renbe kouvèti aisers sante w la oswa pou yo ka eke w avèk depans yo. Se dwa w pou resewwa enfòmasyon sa a ak asistans nan lang ou pale a, san ou pa gen pou peye pou sa. Rate nan 800-722-1471 (TTY: 800-842-5357).

Deutsche (German):

Hmoob (Hmong):

Ilokó (Illoko):
Daytoy a Pakdaak ket naglaon iti Napateg nga Impormasion. Daytoy a pakdaak mabalín nga adda ket naglaon iti napateg nga impormasion maipánggep iti aplikasyono weno coverage babaen iti Premera Blue Cross. Daytoy ket mabalín dagiti importante a pelsa iti daytoy a pakdaak. Mabalín nga adda rumbeng nga ariamendiyo nga adda sàkkay dagiti particular a naitudding nga aldaw tapno mapataligayley dée tiree ti salun-atyo weno tulong kadagiti gastos. Adda karbèngayn a mangala iti daytoy a impormasion ken tulong iti bukodyo a pagasasao nga awan ti bayadanyo. Tumawg iti numero nga 800-722-1471 (TTY: 800-842-5357).

Italiano (Italian):

中文 (Chinese):
本通知有重要的訊息。本通知可能有關於您透過Premera Blue Cross提交的申請或保險的重要資訊。本通知可能有重要日期。您可能需要在截止日期之前採取行動，以保留您的健康保險或費用補貼。您有權利免費以您的母語得到本訊息和幫助。請撥電話 800-722-1471 (TTY: 800-842-5357)。
Japanese (Japanese): この通知には重要な情報が含まれています。この通知に、Premera Blue Crossの申請または補償範囲に関する重要な情報が含まれていますが、この通知に記載されている情報は重要な日を確認ください。健康保険や無料サポートを維持するには、特定の日程を遵守することが必要です。この通知の添付された情報について、あなたの発言による情報がサポートされる技術についての詳細は、800-722-1471 (TTY: 800-842-5357) までお電話ください。

한국어 (Korean): 본 통지서에는 중요한 정보가 들어 있습니다. 즉 이 통지서는 귀하의 신청에 관한 Premera Blue Cross를 통한 커버리지에 관한 정보를 포함하고 있을 것입니다. 본 통지서는 텍스트이며 보안이 되는 매일매일일 수 있습니다. 귀하의 신청을 기록할 커버리지를 제외한 경우 또는 불편함을 위해서 일정한 마감일까지 조치를 취해야 할 필요가 있을 수 있습니다. 귀하의 이러한 정보와 관련된 귀하의 안전과 비용 부담없이 읽을 수 있는 권리가 있습니다。800-722-1471 (TTY: 800-842-5357)로 전화하십시오。


Русский (Russian): Настоящее уведомление содержит важную информацию. Это уведомление может содержать важную информацию о вашем заявлении или страховом покрытии через Premera Blue Cross. В настоящем уведомлении могут быть указаны ключевые даты. Вам, возможно, потребуется привезти к определенным предыдущим срокам для сохранения страхового покрытия или помощи с расходами. Вы имеете право на бесплатное получение этой информации и помощь на вашем языке. Звоните по телефону 800-722-1471 (TTY: 800-842-5357).

Spanish (Spanish): Este Aviso contiene información importante. Es posible que este aviso contenga información importante acerca de su solicitud o cobertura a través de Premera Blue Cross. Es posible que haya fechas claves en este aviso. Es posible que deba tomar alguna medida antes de determinadas fechas para mantener su cobertura médica o ayuda con los costos. Usted tiene derecho a recibir esta información y ayuda en su idioma sin costo alguno. Llame al 800-722-1471 (TTY: 800-842-5357).


ไทย (Thai): ประกาศนี้มีข้อมูลสำคัญ ประกาศนี้มีข้อมูลสำคัญเกี่ยวกับการขอความช่วยเหลือหรือการบริการ ของสุขภาพของ Premera Blue Cross และการขอความช่วยเหลือในกรณีที่คุณจะต้อง ดำเนินการภายในกำหนดเวลาที่ระบุแล้วจะได้รับการประสานงานของสิทธิการชดเชยที่ มีให้จ่าย คุณจะต้องได้รับข้อมูลและคำแนะนำเกี่ยวกับการดำเนินการไปที่ 800-722-1471 (TTY: 800-842-5357).

Український (Ukrainian): Це повідомлення містить важливу інформацію. Це повідомлення може містити важливу інформацію про Ваше звернення щодо страхувального покриття через Premera Blue Cross. Зверніть увагу на ключові дати, які можуть бути вказані у цьому повідомленні. Існує імовірність того, що Вам треба безпосередньо звернутися до медичної підтримки або отримати фінансову допомогу. У Вас є право на отримання цієї інформації та допомоги безкоштовно на Вашій рідній мові. Дозвоніться за номером телефону 800-722-1471 (TTY: 800-842-5357).