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Medical Policy Manual

Topic: Hematopoietic Stem-Cell Transplantation for Autoimmune Diseases

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IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

DESCRIPTION

Autoimmune Diseases

Autoimmune diseases represent a heterogeneous group of immune-mediated disorders, with some of the most common types being multiple sclerosis (MS), rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), and systemic sclerosis/scleroderma.

The pathogenesis of autoimmune diseases is not well understood but appears to involve underlying genetic susceptibility and environmental factors that lead to loss of self-tolerance, culminating in tissue damage by the patient's own immune system (T cells).

Immune suppression is a common treatment strategy for many of these diseases, particularly the rheumatic diseases (e.g., RA, SLE, and scleroderma). Most patients with autoimmune disorders respond to conventional therapies, which consist of anti-inflammatory agents, immunosuppressants, and immunomodulating drugs. However, these drugs are not curative, and a proportion of patients will have severe, recalcitrant, or rapidly progressive disease. It is in this group of patients with severe autoimmune disease that alternative therapies have been sought, including hematopoietic stem-cell transplantation (HSCT).

HSCT in autoimmune disorders raises the question of whether ablating and "resetting" the immune system can alter the disease process and sustain remission and possibly lead to cure.[1] Certain hematologic malignancies, aplastic anemia, and inborn errors of metabolism are treated with HSCT.[1] However, its usage in autoimmune diseases has only been performed in approximately 1,000 patients in the last decade.[1]

The rationale for HSCT for autoimmune disease is based on studies in experimental animal models, and on observations of remissions of autoimmune disease in patients who received HSCT for hematologic malignancies.[2]

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 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 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 "naïve" and thus are associated with a lower incidence of rejection or graft-versus-host disease (GVHD).

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 of human leukocyte antigens (HLA) using cellular, serologic, or molecular techniques. HLA refers to the tissue type expressed at the Class I and Class II loci on chromosome 6. Depending on the disease being treated, an acceptable donor will match the patient at all or most of the HLA loci (with the exception of umbilical cord blood).

Autologous Stem-Cell Transplantation for Autoimmune Diseases

The goal of autologous HSCT in patients with autoimmune diseases is to eliminate self-reactive lymphocytes (lymphoablative) and generate new self-tolerant lymphocytes.[3] This approach is in contrast to destroying the entire hematopoietic bone marrow (myeloablative), as is often performed in autologous HSCT for hematologic malignancies.[3] However, there is currently no standard conditioning regimen for autoimmune diseases and both lymphoablative and myeloablative regimens are used.[1] The efficacy of the different conditioning regimens has not been compared in clinical trials.[1]

Currently, for autoimmune diseases, autologous transplant is preferred over allogeneic, in part because of the lower toxicity of autotransplant relative to allogeneic, the GVHD associated with allogeneic transplant, and the need to administer post-transplant immunosuppression after an allogeneic transplant.[1]

Allogeneic Stem-Cell Transplantation for Autoimmune Diseases

The experience of using allogeneic HSCT for autoimmune diseases is currently limited,[1] but has two potential advantages over autologous transplant. First, the use of donor cells from a genetically different individual could possibly eliminate genetic susceptibility to the autoimmune disease and potentially result in a cure. Second, there exists a possible graft-versus-autoimmune effect, in which the donor T

cells attack the transplant recipient's autoreactive immune cells.[1]

MEDICAL POLICY CRITERIA

I. Autologous HSCT

Autologous hematopoietic stem-cell transplantation is considered **investigational** as a treatment of autoimmune diseases, including, but not limited to:

A. Autoimmune hepatitis and cryptogenic cirrhosis

B. Behçet's disease

C. Chronic inflammatory demyelinating polyneuropathy (CIDP)

D. Crohn's Disease

E. Diabetes mellitus, type I

F. GI autoimmune diseases including Crohn's disease, ulcerative colitis, and celiac disease

G. Immune cytopenias including but not limited to: autoimmune hemolytic anemia, Evans' s syndrome, immune thrombocytopenia, pure red cell or white cell aplasia, and thrombotic thrombocytopenia purpura

H. Immune vasculitis

I. Juvenile idiopathic arthritis

J. Multiple sclerosis (MS)

K. Neuromyelitis optica

L. Relapsing polychondritis

M. Rheumatoid arthritis (RA)

N. Systemic lupus erythematosus (SLE)

O. Systemic sclerosis (i.e., scleroderma)

II. Allogeneic HSCT

Allogeneic hematopoietic stem-cell transplantation is considered **investigational** as a treatment of autoimmune diseases, including, but not limited to:

A. Autoimmune hepatitis and cryptogenic cirrhosis

B. Behçet's disease

C. Chronic inflammatory demyelinating polyneuropathy (CIDP)

D. Crohn's Disease

E. Diabetes mellitus, type I

F. GI autoimmune diseases including Crohn's disease, ulcerative colitis, and celiac disease

G. Immune cytopenias including but not limited to: autoimmune hemolytic anemia, Evans' s syndrome, immune thrombocytopenia, pure red cell or white cell aplasia, and thrombotic thrombocytopenia purpura

H. Immune vasculitis

I. Juvenile idiopathic arthritis

J. Multiple sclerosis (MS)

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O. Systemic sclerosis (i.e., scleroderma)

SCIENTIFIC EVIDENCE

Ideally, for autologous and/or allogeneic hematopoietic stem cell transplant (HSCT) to be considered as treatment for autoimmune disease, head-to-head comparisons of transplantation versus standard of care are needed, preferably in well-designed randomized controlled trials (RCTs). Further, for chronic conditions such as many types of autoimmune disease, comparative trials with long-term follow-up are necessary in order to determine the durability of any beneficial treatment effects, and to establish guidelines regarding the timing of hematopoietic stem cell transplant. In order to establish guidelines for conditioning regimens, clinical trials that compare these therapies are also needed.

Technology Assessments. Reviews, and Registry Reports

- Two Blue Cross Blue Shield Association (BCBSA) Technology Evaluation Center (TEC) assessments have addressed the issue of high-dose lymphoablative therapy and stem-cell rescue in autoimmune diseases.[4,5] Both concluded that available evidence is insufficient to determine whether use of hematopoietic stem-cell transplantation (HSCT) results in improved health outcomes in patients with autoimmune disease.

- A systematic review prepared by the BCBSA TEC Evidence-based Practice Center for the Agency for Healthcare Research and Quality (AHRQ) evaluated the use of HSCT among pediatric patients (age 21 or younger) with various medical conditions (cancer, metabolic disease or autoimmune disease).[6] Despite the lack of consistency in reported health outcomes and the rarity of randomized controlled trials, the review found that moderate-level evidence existed to support the association between single autologous HSCT and "extended periods of drug-free clinical remission" among patients

with newly diagnosed type I juvenile diabetes, and severe, refractory juvenile idiopathic arthritis, systemic lupus, systemic sclerosis, and Crohn's disease. Nevertheless, the review concluded:

> The overall body of evidence is insufficient to draw conclusions about the comparative benefits (e.g., increased overall survival) or harms (treatment-related mortality, secondary malignancies) of single autologous or allogeneic HSCT versus conventional therapy or disease natural history in patients with newly diagnosed type 1 diabetes mellitus, or those with severe, refractory, poor prognosis autoimmune diseases, including: systemic lupus erythematosus, juvenile idiopathic arthritis, systemic sclerosis, malignant multiple sclerosis, Crohn's disease, myasthenia gravis, overlap syndrome, diffuse cutaneous cutis, Evans syndrome, autoimmune hemolytic anemia, and autoimmune cytopenia.

The review recommended that additional controlled trials of adequate duration are required to evaluate the net benefit of HSCT among pediatric patients with autoimmune disease.

- A report from the British Society of Blood and Marrow Transplantation (BSBMT) data registry reported on long-term health outcomes of patients with one or more autoimmune diseases treated with autologous or allogeneic HSCT from 1997 to 2009.[7] Data for 69 patients were reported (representing less than 1% of the total number of patients treated with HSCT in the United Kingdom in that time period). One and 5-year rates of overall survival (OS) were estimated at 85% and 78%, respectively, for patients treated with autologous transplantation, and 87% and 65%, respectively, for patients treated with allogeneic transplantation. Younger age at transplantation and lack of a connective tissue disorder (such as systemic lupus erythematosus) were associated with improved outcomes. Nevertheless, the authors caution that these results "should be viewed in the context of translational and developmental phases of this approach [HSCT] to poor prognosis and refractory autoimmune disease." They recommend the increased adoption of HSCT for individuals with autoimmune disease, but advocate that this take place in "prospective clinical studies in centres with a special interest."

Multiple Sclerosis (MS)

According to a 2010 report by the Center for International Blood and Marrow Transplant Research (CIBMTR) and the European Group for Blood and Marrow Transplantation (EBMT)
MS is the most common autoimmune disease for which autologous HSCT is being studied.[8] Noting that advances in study design and clinical management have decreased transplant-related mortality in recent studies, the group concludes that long-term follow-up (multiple years) and sufficiently large sample sizes are needed to definitively assess impact of transplantation on net health outcomes.

Systematic Review

A 2011 systematic review evaluated the safety and efficacy of autologous HSCT in patients with progressive MS refractory to conventional medical treatment.[9] Eight small case series which monitored progression-free survival (PFS) with a median follow-up of at least 2 years were included. An additional 6 studies were included for a summary of mortality and morbidity. There was substantial heterogeneity across the 8 case series. The majority of patients (77%) had secondary progressive MS, although studies also included those with primary progressive, progressive-relapsing, and relapse-remitting disease. Numbers of patients across studies ranged between 14 and 26. The studies differed in the types and intensities of conditioning regimens used prior to HSCT, with 5 studies using an intermediate-intensity regimen, while the other 3 used high-intensity regimens. All of the studies were rated of moderate

quality. The estimated rate of long-term PFS of patients receiving intermediate-intensity conditioning regimen was 79.4% (95% confidence interval [CI] 69.9-86.5%) with a median follow-up of 39 months, while the estimate for patients who received a high-dose regimen was 44.6% (95% CI 26.5-64.5%) at a median follow-up of 24 months. Of the 14 studies that reported on adverse events, 13 were case series; from these, a total of 7 treatment-related deaths were recorded; 6 non-treatment-related deaths occurred, 5 associated with disease progression.

Non-Randomized Studies

- In an observational study of 48 patients, Burman et al. evaluated the safety and side effects association with HCST treatment for MS.[10] At 5 years, relapse-free survival was 87%; MRI event-free survival was 85%; expanded disability status scale (EDSS) score progression-free survival was 77%; and disease-free survival (no relapses, no new MRI lesions and no EDSS progression) was 68%. Presence of gadolinium-enhancing lesions prior to HSCT was associated with a favorable outcome (disease-free survival 79% vs 46%, p=0.028). There was no mortality. The most common long-term side effects were herpes zoster reactivation (15%) and thyroid disease (8.4%).

- Burt and colleagues have transplanted 21 patients with relapsing-remitting MS with ongoing relapses during treatment with interferon.[11] The conditioning regimen was nonmyeloablative. With a median follow-up of 37 months, 16 patients remained free of relapse, whereas 17 of the 21 patients had a 1-point or greater improvement in their EDSS score.

- Guimaraes et al studied quality of life in 34 MS patients. At one year post transplantation, 27 (79%) patients showed stabilization or neurological improvement and statistically significant improvement in all domains of health-related quality of life.[12]

- The EBMT autoimmune diseases working party database published results on a retrospective study of 178 patients with MS who underwent autologous HSCT.[13] After median follow-up of 42 months, the disease remained stable or improved in 63% of the group. In sub-group analysis, autologous HSCT was found to be associated with significantly better progression-free survival in younger patients (i.e., younger than 40 years of age) with severe, progressive MS diagnosis compared to those older than 40 years. However, the authors caution that the role of autologous SCT in the treatment of refractory MS needs to be established through prospective randomized, controlled trials. Several editorials concur with the view that the role of autologous HSCT is not established in MS or other autoimmune diseases.[14-16]

- Fassas and colleagues reported the long-term results of a Phase I/II study conducted in a single center that investigated the effect of HSCT in the treatment of MS.[17] The authors reported on the clinical and MRI outcomes of 35 patients with aggressive MS treated with HSCT after a median follow-up period of 11 (range 2-15) years. Disease PFS at 15 years was 44% for patients with active central nervous system (CNS) disease and 10% for those without (p=0.01); median time to progression was 11 years (95% CI: 0-22) and 2 years (0-6). Improvements by 0.5-5.5 (median 1) Expanded Disability Status Scale (EDSS) points were observed in 16 cases lasting for a median of 2 years. In 9 of these patients, EDSS scores did not progress above baseline scores. Two patients died, at 2 months and 2.5 years, from transplant-related complications. Gadolinium-enhancing lesions were significantly reduced after mobilization but were maximally and persistently diminished post-HSCT. The authors concluded that HSCT should be reserved for aggressive cases of MS, still in the inflammatory phase of the disease, and for the malignant form, in which it can be life-saving, and that HSCT can result in PFS rates of 25% and can have an impressive and

sustained effect in suppressing disease activity on MRI.

- Shevchenko and colleagues reported the results of a prospective Phase II open-label single-center study which analyzed the safety and efficacy of autologous HSCT with reduced-intensity conditioning regimen in 95 patients with different types of MS.[18] The patients underwent early, conventional, and salvage/late transplantation. The efficacy was evaluated based on clinical and quality-of-life outcomes. No transplantation-related deaths were observed. All of the patients, except one, responded to the treatment. At long-term follow-up (mean 46 months), the overall clinical response in terms of disease improvement or stabilization was 80%. The estimated PFS at 5 years was 92% in the group after early transplant versus 73% in the group after conventional/salvage transplant ($p=0.01$). No active, new, or enlarging lesions in MRI were registered in patients without disease progression. All patients who did not have disease progression were off therapy throughout the post-transplantation period. HSCT was accompanied by a significant improvement in quality of life with statistically significant changes in the majority of quality-of-life parameters ($p<0.05$).

- Mancardi and colleagues reported their experience with 74 consecutive patients with MS treated with autologous HSCT with an intermediate intensity conditioning regimen in the period from 1996 to 2008.[19] Clinical and MRI outcomes were reported. The median follow-up period was 48.3 months (range=0.8-126). Two patients (2.7%) died from transplant-related causes. After 5 years, 66% of patients remained stable or improved. Among patients with a follow-up longer than 1 year, 8 out of 25 subjects with a relapsing-remitting course (31%) had a 6-12 months confirmed EDSS improvement >1 point after HSCT, as compared with 1 out of 36 (3%) patients with a secondary progressive disease course ($p=0.009$). Among the 18 cases with a follow-up longer than 7 years, 8 (44%) remained stable or had a sustained improvement, while 10 (56%), after an initial period of stabilization or improvement with a median duration of 3.5 years, showed a slow disability progression.

- Bowen and colleagues reported the long-term safety and effectiveness of high-dose immunosuppressive therapy followed by autologous HSCT in advanced MS.[20] Neurologic examinations, brain MRI and cerebrospinal fluid (CSF) for oligoclonal bands (OCB) were serially evaluated. There were 26 patients with a mean EDSS of 7.0; 17 with secondary progressive MS, 8 with primary progressive, and 1 with relapsing/remitting. Median follow up was 48 months after HSCT. The 72-month probability of worsening $\geq$1.0 EDSS point was 0.52 (95% CI: 0.30-0.75). Five patients had an EDSS at baseline of $\leq$6.0; 4 of them had not failed treatment at last study visit. OCB in CSF persisted with minor changes in the banding pattern. Four new or enhancing lesions were seen on MRI, all within 13 months of treatment. In this population with high baseline EDSS, a significant proportion of patients with advanced MS remained stable for as long as 7 years after transplant. Non-inflammatory events may have contributed to neurologic worsening after treatment. HSCT may be more effective in patients with less advanced relapsing/remitting MS.

Systemic Lupus Erythematosus (SLE)

Burt and colleagues recently published the results of a prospective case series on the use of autologous HSCT as salvage treatment in 50 patients (mean age 30; 43 women, 7 men) with SLE refractory to standard care.[21] Patients underwent autologous SCT following a lymphoablative conditioning regimen and primary outcomes consisted of overall survival (OS) and disease-free survival. Treatment-related mortality was 4% (2/50) and after a mean follow-up of 29 months (range, 6 months to 7.5 years), estimated 5-year survival was 84%, and the estimated probability of disease-free survival at 5 years was

50%. The investigators suggest these results justify a randomized trial comparing immunosuppression plus autologous HSCT versus continued standard of care.

An editorial by Petri and Brodsky that accompanied the article by Burt and colleagues concurred that randomized clinical trials are needed to determine whether this treatment approach improves outcomes when compared with conventional therapies.[22]

A report from the EBMT Autoimmune Disease Working Party on the variables associated with development of a secondary autoimmune disease following autologous HSCT in a group of 347 patients (with various primary autoimmune diseases) identified SLE as a risk factor for this complication (using multivariate analysis).[23] This finding points to the need for prospective, randomized, controlled trials to identify factors pre-disposing patients, specifically those with SLE, to development of a secondary autoimmune disease.

Systemic Sclerosis/Scleroderma

Randomized Controlled Trial (RCT)

An open-label, randomized, controlled Phase 2 trial (ASSIST) assessed the safety and efficacy of autologous non-myeloablative HSCT compared with the standard of care for systemic sclerosis.[24] A small group of consecutively enrolled patients (n=19), all younger than 60 years of age, with diffuse systemic sclerosis were randomly allocated by use of a computer-generated sequence to receive HSCT, 200 mg/kg intravenous cyclophosphamide, and rabbit antithymocyte globulin or to 1.0 g/m2 intravenous cyclophosphamide once per month for 6 months. The primary outcome was improvement at 12 months' follow-up, defined as a decrease in mRSS (<25% for those with initial mRSS >14) or an increase in forced vital capacity by more than 10%. Patients in the control group with disease progression (>25% increase in mRSS or decrease of >10% in forced vital capacity) despite treatment with cyclophosphamide could switch to HSCT 12 months after enrollment. No deaths occurred in either group during follow-up. Patients allocated to HSCT (n=10) improved at or before 12 months' follow-up, compared with none of the 9 allocated to cyclophosphamide (p=0.00001). Treatment failure (i.e., disease progression without interval improvement), occurred in 8 of 9 controls compared with none of the 10 patients treated by HSCT (p=0.0001). After long-term follow-up (mean 2.6 years) of patients who were allocated to HSCT, all but 2 patients had sustained improvement in mRSS and forced vital capacity, with a longest follow-up of 60 months. Seven patients allocated to receive cyclophosphamide switched treatment groups at a mean of 14 months after enrollment and underwent HSCT without complication, and all improved after HSCT. Four of these patients followed for at least 1 year had a mean decrease in mRSS points from 27 (standard deviation [SD] 15.5) to 15 (SD 7.4), an increase in forced vital capacity from 65% (SD 20.6) to 76% (SD 26.5) and an increase in total lung capacity from 81% (SD 14.0) to 88% (SD 13.9%). Data for 11 patients with follow-up to 2 years after HSCT suggested that the improvements in mRSS (p<0.0001) and forced vital capacity (p<0.03) persisted.

Non-randomized Studies

- Vonk and colleagues reported the results of 28 patients with severe diffuse cutaneous systemic sclerosis who underwent autologous HSCT from 1998 to 2004.[25] There was 1 transplant-related death and 1 death due to progressive disease, leaving 26 patients for evaluation. After a median follow-up of 5.3 years (range, 1–7.5), 81% (n=21/26) of the patients demonstrated a clinically beneficial response. Estimated survival at 5 years was 96.2% (95% confidence interval [CI]: 89–100%) and 84.8% (95% CI: 70.2–100%) at 7 years. Event-free survival was 64.3% (95% CI: 47.9–

86%) at 5 years and 57.1% (95% CI: 39.3–83%) at 7 years.

- Nash and colleagues reported the long-term follow-up of 34 patients with diffuse cutaneous systemic sclerosis with significant visceral organ involvement who were enrolled in a multi-institutional pilot study between 1997 and 2005 and underwent autologous HSCT.[26] Overall and progression-free survival were both 64% at 5 years.

- Henes and colleagues reported on their experience with autologous HSCT for systemic sclerosis in 26 consecutive patients scheduled for HSCT between 1997 and 2009.[27] The major outcome variable was the response to treatment (reduction of modified Rodnan skin score [mRSS] by 25%) at 6 months. Secondary endpoints were transplant-related mortality and PFS. At 6 months, significant skin and lung function improvement of the mRSS was achieved in 78.3% of patients. The overall response rate was 91%, as some patients improved after month 6. Three patients died between mobilization and conditioning treatment, 2 due to severe disease progression and 1 whose death was considered treatment-related. Seven patients experienced a relapse during the 4.4 years of follow up. PFS was 74%. Four patients died during follow-up, and the most frequent causes of death were pulmonary and cardiac complications of systemic sclerosis. The authors concluded that autologous HSCT resulted in significant improvement in most patients with systemic sclerosis.

However, lack of a comparison group limits the ability to identify the treatment effect experienced by these groups of patients over and beyond that experienced by patients undergoing standard care for systemic sclerosis.

Juvenile Arthritis

A review article by Saccardi summarizes the experience thus far with juvenile idiopathic and rheumatoid arthritis as follows.[28] More than 50 patients with juvenile idiopathic arthritis have been reported to the EBMT Registry. The largest cohort study initially used one conditioning regimen, and thereafter, a modified protocol. Overall drug-free remission rate was approximately 50%. Some late relapses have been reported, and only partial correction of growth impairment has been seen. A new retrospective analysis is ongoing on behalf of the Autoimmune Diseases, Pediatric and Inborn Error EBMT Working Parties. The frequency of HSCT for rheumatoid arthritis has decreased significantly since 2000, due to the introduction of new biologic therapies. Most patients who have undergone HSCT have had persistence or relapse of disease activity within 6 months of transplant.

Type 1 Diabetes

Couri and colleagues reported the results of a prospective Phase I/II study of autologous HSCT in 23 patients with type 1 diabetes (age range, 13-31 years) diagnosed in the previous 6 weeks by clinical findings with hyperglycemia.[29] After a mean follow-up of just over 2 years (29.8 months; range, 7-58 months) post-transplantation , the majority of patients achieved insulin independence with good glycemic control. There was no transplant-related mortality. Nevertheless, interpretation of these results is limited by lack of long-term follow-up of primary health outcomes (morbidity and mortality related to diabetes). Additionally lack of a comparison group limits the possibility of ruling out chance as an explanatory factor,

Other Autoimmune Diseases

In 2012, Vanikar and colleagues reported the results of a small prospective study (n=11) on the use of

allogeneic HSCT for treatment of Pemphigus vulgaris (PV).[30] However, patient selection criteria, length of follow-up, and overall survival (or other primary health outcomes) were not stated. Therefore, interpretation of the treatment benefit reported in the manuscript is unclear.

No other prospective clinical trials of sufficient size were identified for the use of HSCT in other autoimmune diseases (including immune cytopenias, relapsing polychondritis, and others).

Guidelines

No evidence-based clinical practice guidelines were identified on the use of HSCT for treatment of autoimmune diseases.

Summary

Initial studies focused on use of autologous or allogeneic hematopoietic stem-cell transplantation (HSCT) as salvage therapy for end-stage treatment of refractory autoimmune diseases. More recent experience has helped to define which patients are most likely to benefit from HSCT, and the field has shifted to the use of HSCT earlier in the disease course before irreversible organ damage has occurred and to the use of safer and less intense nonmyeloablative conditioning regimens. Despite these improvements, the net treatment benefit associated with HSCT in patients with autoimmune disease has not been clearly identified in the scientific literature. It is unclear how this treatment compares with other therapies, and potential benefits relating to treatment have not clearly been weighed against risk of adverse effects associated with transplantation. Therefore, autologous or allogeneic HSCT is considered investigational for treatment of any autoimmune disease.

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CROSS REFERENCES

Donor Lymphocyte Infusion for Malignancies Treated with an Allogeneic Hematopoietic Stem-Cell Transplant, Transplant, Policy No. 45.03

Placental and Umbilical Cord Blood as a Source of Stem Cells, Transplant, Policy No. 45.16

CODES	NUMBER	DESCRIPTION
CPT	38204	Management of recipient hematopoietic cell donor search and cell acquisition
	38205	Blood-derived hematopoietic progenitor cell harvesting for transplantation, per collection, allogeneic
	38206	;autologous
	38207	Transplant preparation of hematopoietic progenitor cells; cryopreservation and storage
	38208	;thawing of previously frozen harvest, without washing, per donor
	38209	;thawing of previously frozen harvest with washing, per donor
	38210	;specific cell depletion with harvest, T cell depletion
	38211	;tumor cell depletion

CODES	NUMBER	DESCRIPTION
	38212	;red blood cell removal
	38213	;platelet depletion
	38214	;plasma (volume) depletion
	38215	;cell concentration in plasma, mononuclear, or buffy coat layer
	38220	Bone marrow; aspiration only
	38221	Bone marrow; biopsy, needle or trocar
	38230	Bone marrow harvesting for transplantation; allogeneic
	38232	Bone marrow harvesting for transplantation; autologous
	38240	Hematopoietic progenitor cell (HPC); allogeneic transplantation per donor
	38241	;autologous transplantation
	38242	Allogeneic lymphocyte infusions
HCPCS	J9000–J9999	Chemotherapy drugs code range
	Q0083–Q0085	Chemotherapy administration code range
	S2140	Cord blood harvesting for transplantation; allogeneic
	S2142	Cord blood derived stem-cell transplantation, allogeneic
	S2150	Bone marrow or blood-derived peripheral stem-cell harvesting and transplantation, allogeneic or autologous, including pheresis, high-dose chemotherapy, and the number of days of post-transplant care in the global definition (including drugs; hospitalization; medical surgical, diagnostic and emergency services)