

Protocol

Hematopoietic Stem Cell Transplantation for Autoimmune Diseases

(80125)

Medical Benefit		Effective Date: 04/01/14	Next Review Date: 11/17
Preauthorization	Yes	Review Dates: 04/07, 05/08, 01/10, 01/11, 01/12, 01/13, 01/14, 11/14, 11/15, 11/16	

Preauthorization is required and must be obtained through Case Management.

The following Protocol contains medical necessity criteria that apply for this service. The criteria are also applicable to services provided in the local Medicare Advantage operating area for those members, unless separate Medicare Advantage criteria are indicated. If the criteria are not met, reimbursement will be denied and the patient cannot be billed. Please note that payment for covered services is subject to eligibility and the limitations noted in the patient's contract at the time the services are rendered.

Populations	Interventions	Comparators	Outcomes
Individuals: • With multiple sclerosis	Interventions of interest are: • Hematopoietic stem cell transplantation	Comparators of interest are: • Conventional medication therapy	Relevant outcomes include: • Overall survival • Health status measures • Quality of life • Treatment-related mortality • Treatment-related morbidity
Individuals: • With juvenile idiopathic and rheumatoid arthritis	Interventions of interest are: • Hematopoietic stem cell transplantation	Comparators of interest are: • Conventional medication therapy • Biologic therapy	Relevant outcomes include: • Symptoms • Quality of life • Medication use • Treatment-related mortality • Treatment-related morbidity
Individuals: • With systemic lupus erythematosus	Interventions of interest are: • Hematopoietic stem cell transplantation	Comparators of interest are: • Conventional medication therapy	Relevant outcomes include: • Overall survival • Symptoms • Quality of life • Treatment-related mortality • Treatment-related morbidity
Individuals: • With systemic sclerosis/scleroderma	Interventions of interest are: • Hematopoietic stem cell transplantation	Comparators of interest are: • Conventional medication therapy	Relevant outcomes include: • Overall survival • Symptoms • Health status measures • Quality of life • Treatment-related mortality • Treatment-related morbidity
Individuals: • With type 1 diabetes mellitus	Interventions of interest are: • Hematopoietic stem cell transplantation	Comparators of interest are: • Conventional medication therapy	Relevant outcomes include: • Overall survival • Symptoms • Health status measures • Quality of life • Treatment-related mortality • Treatment-related morbidity

Populations	Interventions	Comparators	Outcomes
Individuals: <ul style="list-style-type: none"> • With chronic inflammatory demyelinating polyneuropathy 	Interventions of interest are: <ul style="list-style-type: none"> • Hematopoietic stem cell transplantation 	Comparators of interest are: <ul style="list-style-type: none"> • Conventional medication therapy 	Relevant outcomes include: <ul style="list-style-type: none"> • Overall survival • Symptoms • Health status measures • Quality of life • Treatment-related mortality • Treatment-related morbidity

Description

Most patients with autoimmune disorders respond to conventional therapies. 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).

Summary of Evidence

The evidence for HSCT in individuals who have multiple sclerosis includes one randomized controlled trial (RCT) and case series. Relevant outcomes are overall survival, health status measures, quality of life, treatment-related mortality and treatment-related morbidity. The phase 2 RCT reported intermediate outcomes (number of new T2 magnetic resonance imaging lesions); the group randomized to HSCT developed significantly fewer lesions than the group receiving conventional therapy. Findings of case series report include improvements in clinical parameters following HSCT. Controlled trials that report on clinical outcomes are needed to demonstrate efficacy. The evidence is insufficient to determine the effects of the technology on health outcomes.

The evidence for HSCT in individuals who have juvenile idiopathic and rheumatoid arthritis includes a registry study. Relevant outcomes are symptoms, quality of life, medication use, treatment-related mortality, and treatment-related morbidity. The registry study included 50 patients and the overall drug-free remission rate was approximately 50%. Additional data are needed from controlled studies to demonstrate efficacy. The evidence is insufficient to determine the effects of the technology on health outcomes.

The evidence for HSCT in individuals who have systemic lupus erythematosus includes case series. Relevant outcomes are overall survival, symptoms, quality of life, treatment-related mortality, and treatment-related morbidity. Several case series have been published. The largest (N=50 patients) found an overall five-year survival rate of 84% and the probability of disease-free survival was 50%. Additional data are needed from controlled studies to demonstrate efficacy. The evidence is insufficient to determine the effects of the technology on health outcomes.

The evidence for HSCT in individuals who have systemic sclerosis/scleroderma includes RCTs and observational studies. Relevant outcomes are overall survival, symptoms, health status measures, quality of life, treatment-related mortality, and treatment-related morbidity. The results of the ASTIS trial suggest high-dose chemotherapy with autologous HSCT may improve survival among patients with diffuse cutaneous systemic sclerosis compared with pulsed intravenous cyclophosphamide. However, analysis of the internal validity of the trial using U.S. Preventive Services Task Force criteria showed fatal flaws and a poor study rating due to attrition in the control group that could have skewed the survival curve to show better survival for HSCT recipients than for controls. A smaller RCT (N=19) found that the rate of improvement at 12 months was significantly higher in the HSCT group than in the conventional therapy group. Data from these studies are inconclusive; additional studies are needed to confirm safety and efficacy. The evidence is insufficient to determine the effects of the technology on health outcomes.

The evidence for HSCT in individuals who have type 1 diabetes mellitus includes case series. Relevant outcomes are overall survival, symptoms, health status measures, quality of life, treatment-related mortality, and treatment-related morbidity. Several case series evaluated autologous HSCT in patients with new-onset type 1 diabetes; there were no published comparative studies. In the series, although a substantial proportion of patients tended to become insulin free after HSCT, remission rates were high. The evidence is insufficient to determine the effects of the technology on health outcomes.

The evidence for HSCT in individuals who have chronic inflammatory demyelinating polyneuropathy includes case reports. Relevant outcomes are overall survival, symptoms, health status measures, quality of life, treatment-related mortality, and treatment-related morbidity. Additional data are needed from controlled studies to demonstrate efficacy. The evidence is insufficient to determine the effects of the technology on health outcomes.

Policy

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

- multiple sclerosis
- juvenile idiopathic and rheumatoid arthritis
- systemic lupus erythematosus
- systemic sclerosis/scleroderma
- type 1 diabetes mellitus
- chronic inflammatory demyelinating polyneuropathy.

Medicare Advantage

If a transplant is needed, we arrange to have the transplant center review and decide whether the patient is an appropriate candidate for the transplant.

Background

Autoimmune Diseases

Autoimmune diseases represent a heterogeneous group of immune-mediated disorders, including multiple sclerosis, rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), systemic sclerosis/scleroderma, and chronic immune demyelinating polyneuropathy. The National Institutes of Health estimates that 5% to 8% of Americans have an autoimmune disorder.

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, 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 HSCT. The primary concept underlying use of HSCT for these diseases is that ablating and “resetting” the immune system can alter the disease process, first inducing a sustained remission that possibly leads to cure.¹

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 radiotherapy. 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 “naive” and, thus, are associated with a lower incidence of rejection or graft-versus-host disease (GVHD). Cord blood is discussed in greater detail in the Placental and Umbilical Cord Blood as a Source of Stem Cells Protocol.

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 (lymphoablation) and generate new self-tolerant lymphocytes.² This approach is in contrast to destroying the entire hematopoietic bone marrow (myeloablation), as is often performed in autologous HSCT for hematologic malignancies.² However, no standard conditioning regimen exists 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 posttransplant immunosuppression after an allogeneic transplant.¹

Allogeneic Stem Cell Transplantation for Autoimmune Diseases

The experience of using allogeneic HSCT for autoimmune diseases is currently limited¹ 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

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.

Related Protocol

Plasma Exchange

Services that are the subject of a clinical trial do not meet our Technology Assessment Protocol criteria and are considered investigational. *For explanation of experimental and investigational, please refer to the Technology Assessment Protocol.*

It is expected that only appropriate and medically necessary services will be rendered. We reserve the right to conduct prepayment and postpayment reviews to assess the medical appropriateness of the above-referenced procedures. **Some of this Protocol may not pertain to the patients you provide care to, as it may relate to products that are not available in your geographic area.**

References

We are not responsible for the continuing viability of web site addresses that may be listed in any references below.

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