Policy Statement

Autologous hematopoietic cell transplantation may be considered **medically necessary** as a salvage therapy of chemosensitive Waldenström macroglobulinemia.

Allogeneic hematopoietic cell transplantation is considered **investigational** to treat Waldenström macroglobulinemia.

Policy Guidelines

CPT centralized codes describing autologous and allogeneic hematopoietic cell transplantation services to the hematology section (38204-38242). Not all codes are applicable for each stem cell transplant procedure. The following range of codes describes services associated with cryopreservation, storage, and thawing of cells.

### Cryopreservation and storage of cells:
- **38207**: Transplant preparation of hematopoietic progenitor cells; cryopreservation and storage

### Thawing and washing of cryopreserved cells:
- **38208**: Transplant preparation of hematopoietic progenitor cells; thawing of previously frozen harvest, without washing, per donor
- **38209**: Transplant preparation of hematopoietic progenitor cells; thawing of previously frozen harvest, with washing, per donor

### Types of cells being depleted:
- **38210**: Transplant preparation of hematopoietic progenitor cells; specific cell depletion within harvest, T-cell depletion
- **38211**: Transplant preparation of hematopoietic progenitor cells; tumor cell depletion
- **38212**: Transplant preparation of hematopoietic progenitor cells; red blood cell removal
- **38213**: Transplant preparation of hematopoietic progenitor cells; platelet depletion
- **38214**: Transplant preparation of hematopoietic progenitor cells; plasma (volume) depletion

### Plasma cell concentration:
- **38215**: Transplant preparation of hematopoietic progenitor cells; cell concentration in plasma, mononuclear, or buffy coat layer

Description

Hematopoietic cell transplantation (HCT) refers to a procedure in which hematopoietic stem cells are infused to restore bone marrow function in patients who receive bone marrow-toxic doses of drugs with or without whole body radiotherapy. Hematopoietic stem cells may be obtained from the transplant recipient (autologous HCT) or from a donor (allogeneic HCT). They can be harvested from bone marrow, peripheral blood, or umbilical cord blood shortly after delivery of neonates. Although cord blood is an allogeneic source, the stem cells in it are antigenically “naive” and thus are associated with a lower incidence of rejection or graft-versus-host disease.
Related Policies

- Hematopoietic Cell Transplantation for Non-Hodgkin Lymphomas
- Placental and Umbilical Cord Blood as a Source of Stem Cells

Benefit Application

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

Some state or federal mandates [e.g., Federal Employee Program (FEP)] prohibits plans from denying Food and Drug Administration (FDA)-approved technologies as investigational. In these instances, plans may have to consider the coverage eligibility of FDA-approved technologies on the basis of medical necessity alone.

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, title 21, parts 1270 and 1271. Hematopoietic stem cells are included in these regulations.

Rationale

Background

Waldenström Macroglobulinemia

Waldenström macroglobulinemia (WM) is a clonal disorder of B lymphocytes that accounts for 1% to 2% of hematologic malignancies, with an estimated 1500 new cases annually in the United States. Symptoms include weakness, headaches, stroke-like symptoms (confusion, loss of coordination), vision problems, excessive bleeding, unexplained weight loss, and frequent infections. The median age of WM patients is 63 to 68 years, with men comprising 55% to 70% of cases. Median survival of WM ranges from 5 to 10 years, with age, hemoglobin concentration, serum albumin level, and β2-microglobulin level as predictors of outcome.

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

Treatment

The goal of therapy for patients with WM is to achieve symptomatic relief and reduce organ damage without compromising quality of life. Treatment of WM is indicated only in symptomatic patients and should not be initiated solely on the basis of serum IgM concentration. Clinical and laboratory findings that indicate the need for therapy of diagnosed WM include a hemoglobin concentration less than 10 g/dL; platelet count less than 100,000/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 patients that 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 effect that develops after engraftment of allogeneic stem cells within patients’ bone marrow space. While the slower graft-versus-malignancy effect is considered the potentially curative component, it may be overwhelmed by extant disease without the use of pretransplant conditioning. However, intense conditioning regimens are limited to patients who are sufficiently fit medically to tolerate substantial adverse events that include preengraftment opportunistic infections secondary to loss of endogenous bone marrow function and organ damage and failure caused by the cytotoxic drugs. Furthermore, in any allogeneic HCT, immune suppressant drugs are required to minimize graft rejection and graft-versus-host disease, which also increases susceptibility of the patient to opportunistic infections.

The success of autologous HCT is predicated on the ability of cytotoxic chemotherapy with or without radiotherapy to eradicate cancerous cells from the blood and bone marrow. This permits subsequent engraftment and repopulation of bone marrow space with presumably normal hematopoietic stem cells obtained from the patient before undergoing bone marrow ablation. As a consequence, autologous HCT is typically performed as consolidation therapy when the patient’s disease is in complete remission. Patients who undergo autologous HCT are susceptible to chemotherapy-related toxicities and opportunistic infections prior to engraftment, but not graft-versus-host disease.

**Reduced-Intensity Conditioning for Allogeneic HCT**

Reduced-intensity conditioning (RIC) refers to the pretransplant use of lower doses or less intense regimens of cytotoxic drugs or radiotherapy than are used in conventional full-dose myeloablative conditioning treatments. The goal of RIC is to reduce disease burden but also to minimize as much as possible associated treatment-related morbidity and nonrelapse mortality in the period during which the beneficial graft-versus-malignancy effect of allogeneic transplantation develops. Although the definition of RIC remains arbitrary, with numerous versions employed, all seek to balance the competing effects of nonrelapse mortality and relapse due to residual disease. RIC regimens can be viewed as a continuum in effects, from nearly totally myeloablative to minimally myeloablative with lymphoablation, with intensity tailored to specific diseases and patient condition. Patients who undergo RIC with allogeneic HCT initially demonstrate donor cell engraftment and bone marrow mixed chimerism. Most will subsequently convert to full-donor chimerism, which may be supplemented with donor lymphocyte infusions to eradicate residual malignant cells. For this evidence review, the term reduced-intensity conditioning will refer to all conditioning regimens intended to be nonmyeloablative, as opposed to fully myeloablative (conventional) regimens.

**Literature Review**

Evidence reviews assess the clinical evidence to determine whether the use of a technology improves the net health outcome. Broadly defined, health outcomes are length of life, quality of life, and ability to function—including benefits and harms. Every clinical condition has specific outcomes that are important to patients and to managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.
To assess whether the evidence is sufficient to draw conclusions about the net health outcome of a technology, 2 domains are examined: the relevance and the quality and credibility. To be relevant, studies must represent one or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. Randomized controlled trials are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

**Hematopoietic Cell Transplantation for Waldenström Macroglobulinemia**

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

**Autologous HCT**

Kyriakou et al (2010) evaluated 158 adults with WM reported to the European Group for Blood and Marrow Transplantation between 1991 and 2005. Median time from diagnosis to autologous HCT was 1.7 years (range, 0.3-20.3 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, 0.5-14.8 years). Nonrelapse mortality 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 concluded that autologous HCT is a feasible procedure in young patients with advanced WM but that it should not be offered to patients with chemoresistant disease or to those who have received more than 3 lines of therapy.

**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. OS rates were 74% at 1 year and 52% at 5 years. Patients with chemosensitive disease had significantly better 1- and 5-year OS rates compared with patients who had chemoresistant 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 patients who had allogeneic HCT for WM. Patients underwent MAC (n=37) or RIC (n=49) regimens. Median age was 49 years (range, 23-64 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 rate 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.
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.

Summary of Evidence

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

Supplemental Information

Clinical Input from Physician Specialty Societies and Academic Medical Centers

While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process, through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted.

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

Practice Guidelines and Position Statements

National Comprehensive Cancer Network

National Comprehensive Cancer Network guidelines on Waldenström macroglobulinemia (WM) and lymphoplasmacytic lymphoma (v.1.2017) indicate that, for patients with previously treated WM, stem cell transplantation may be appropriate in selected cases with either: high-dose therapy with autologous stem cell rescue or allogeneic cell transplant (myeloablative or nonmyeloablative). The Network noted that allogeneic cell transplantation “should ideally be undertaken in the context of a clinical trial.” For potential autologous cell transplantation candidates, the guidelines also provide suggested treatment regimens considered non-stem-cell toxic and possibly 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 2016, consensus recommendations from the Eighth International Workshop on Waldenström’s Macroglobulinemia were published. The panel concluded that autologous HCT is a treatment option for high-risk WM patients who are eligible for transplant. It further stated that autologous HCT should be offered at early relapses and is not as beneficial once patients have been exposed to more than 3 lines of therapy or in those with chemotherapy-refractory disease.

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Regarding allogeneic HCT, it stated that this treatment, “when appropriate, should preferably be considered in the context of clinical trials.”

**Myeloma Foundation of Australia**

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

**U.S. Preventive Services Task Force Recommendations**

Not applicable.

**Medicare National Coverage**

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

**Ongoing and Unpublished Clinical Trials**

Currently, unpublished trials that might influence this review are listed in Table 1.

<table>
<thead>
<tr>
<th>NCT No.</th>
<th>Trial Name</th>
<th>Planned Enrollment</th>
<th>Completion Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>NCT01251575</td>
<td>Sirolimus, Cyclosporine, and Mycophenolate Mofetil in Preventing Graft-versus-Host Disease in Treating Patients with Blood Cancer Undergoing Peripheral Blood Stem Cell Transplant</td>
<td>80</td>
<td>Nov 2018</td>
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<tr>
<td>NCT02844361</td>
<td>Comparison of ASCT and Conventional Chemotherapy in High Risk Waldenström Macroglobulinemia (BDH-WM03)</td>
<td>70</td>
<td>May 2020</td>
</tr>
</tbody>
</table>

NCT: National Clinical Trial.

**References**

Documentation for Clinical Review

Please provide the following documentation (if/when requested):

- Referring physician history and physical
- Bone marrow transplant consultation report and/or progress notes documenting:
  - Diagnosis (including disease staging) and prognosis
  - Synopsis of alternative treatments performed and results
  - Specific transplant type being requested
- Surgical consultation report and/or progress notes
- Results of completed transplant evaluation including:
  - Clinical history
  - Specific issues identified during the transplant evaluation
  - Consultation reports/letters (when applicable)
  - Correspondence from referring physicians (when applicable)
  - Identification of donor for allogeneic related bone marrow/stem cell transplant
  (when information available)
- Medical social service/social worker and/or psychiatric (if issues are noted) evaluations
  including psychosocial assessment or impression of patient’s ability to be an adequate
  candidate for transplant
- Radiology reports including:
  - Chest x-ray (CXR)
  - PET scan, CT scan, and bone survey (as appropriate)
- Cardiology procedures and pulmonary function reports:
  - EKG
  - Echocardiogram
  - Pulmonary function tests (PFTs)
- Biopsy/Pathology reports including:
  - Bone marrow biopsy
  - Lymph node biopsy (as appropriate)
- Laboratory reports

Coding

This Policy relates only to the services or supplies described herein. Benefits may vary according
to product design; therefore, contract language should be reviewed before applying the terms
of the Policy. Inclusion or exclusion of codes does not constitute or imply member coverage or
provider reimbursement.

MN/IE
The following services may be considered medically necessary in certain instances and
investigational in others. Services may be considered medically necessary when policy criteria
are met. Services may be considered investigational when the policy criteria are not met or
when the code describes application of a product in the position statement that is
investigational.

<table>
<thead>
<tr>
<th>Type</th>
<th>Code</th>
<th>Description</th>
</tr>
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<tbody>
<tr>
<td>CPT®</td>
<td>38204</td>
<td>Management of recipient hematopoietic progenitor cell donor</td>
</tr>
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</table>
<pre><code>                               |                      | search and cell acquisition                                      |
</code></pre>
### Hematopoietic Cell Transplantation for Waldenström Macroglobulinemia

**Type** | **Code** | **Description**
---|---|---
| 38205 | Blood-derived hematopoietic progenitor cell harvesting for transplantation, per collection; allogeneic
| 38206 | Blood-derived hematopoietic progenitor cell harvesting for transplantation, per collection; autologous
| 38207 | Transplant preparation of hematopoietic progenitor cells; cryopreservation and storage
| 38208 | Transplant preparation of hematopoietic progenitor cells; thawing of previously frozen harvest, without washing, per donor
| 38209 | Transplant preparation of hematopoietic progenitor cells; thawing of previously frozen harvest, with washing, per donor
| 38210 | Transplant preparation of hematopoietic progenitor cells; specific cell depletion within harvest; T-cell depletion
| 38211 | Transplant preparation of hematopoietic progenitor cells; tumor cell depletion
| 38212 | Transplant preparation of hematopoietic progenitor cells; red blood cell removal
| 38213 | Transplant preparation of hematopoietic progenitor cells; platelet depletion
| 38214 | Transplant preparation of hematopoietic progenitor cells; plasma (volume) depletion
| 38215 | Transplant preparation of hematopoietic progenitor cells; cell concentration in plasma, mononuclear, or buffy coat layer
| 38220 | Diagnostic bone marrow; aspiration(s) (**Code revision effective 1/1/2018**)
| 38221 | Diagnostic bone marrow; biopsy(ies) (**Code revision effective 1/1/2018**)
| 38222 | Diagnostic bone marrow; biopsy(ies) and aspiration(s) (**Code effective 1/1/2018**)
| 38230 | Bone marrow harvesting for transplantation; allogeneic
| 38232 | Bone marrow harvesting for transplantation; autologous
| 38240 | Hematopoietic progenitor cell (HPC); allogeneic transplantation per donor
| 38241 | Hematopoietic progenitor cell (HPC); autologous transplantation
| 38242 | Allogeneic lymphocyte infusions

<table>
<thead>
<tr>
<th>HCPCS</th>
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</table>
| 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 outpatient follow-up; medical/surgical, diagnostic, emergency, and rehabilitative services; and the number of days of pre and post-transplant care in the global definition

<table>
<thead>
<tr>
<th>ICD-10 Procedure</th>
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</table>
| 07DQ0ZZ | Extraction of Sternum Bone Marrow, Open Approach
| 07DQ3ZZ | Extraction of Sternum Bone Marrow, Percutaneous Approach
| 07DR0ZZ | Extraction of Iliac Bone Marrow, Open Approach
| 07DR3ZZ | Extraction of Iliac Bone Marrow, Percutaneous Approach
| 07DS0ZZ | Extraction of Vertebral Bone Marrow, Open Approach
| 07DS3ZZ | Extraction of Vertebral Bone Marrow, Percutaneous Approach
| 30243G0 | Transfusion of Autologous Bone Marrow into Central Vein, Percutaneous Approach
| 30243G2 | Transfusion of Allogeneic Related Bone Marrow into Central Vein, Percutaneous Approach
### Policy History

This section provides a chronological history of the activities, updates and changes that have occurred with this Medical Policy.

<table>
<thead>
<tr>
<th>Effective Date</th>
<th>Action</th>
<th>Reason</th>
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</thead>
<tbody>
<tr>
<td>5/29/2015</td>
<td>Policy title change from Hematopoietic Stem-Cell Transplantation for Primary Amyloidosis or Waldenström Macroglobulinemia</td>
<td>Medical Policy Committee</td>
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<tr>
<td></td>
<td>BCBSA Medical Policy adoption</td>
<td></td>
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<tr>
<td></td>
<td>Policy revision without position change</td>
<td></td>
</tr>
<tr>
<td>02/01/2017</td>
<td>Policy revision without position change</td>
<td>Medical Policy Committee</td>
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<td></td>
<td>Policy title change from Hematopoietic Stem Cell Transplantation for Waldenström Macroglobulinemia</td>
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<tr>
<td>01/01/2018</td>
<td>Coding update</td>
<td>Administrative Review</td>
</tr>
<tr>
<td>04/01/2018</td>
<td>Policy revision without position change</td>
<td>Medical Policy Committee</td>
</tr>
</tbody>
</table>

### Definitions of Decision Determinations

**Medically Necessary:** A treatment, procedure, or drug is medically necessary only when it has been established as safe and effective for the particular symptoms or diagnosis, is not investigational or experimental, is not being provided primarily for the convenience of the patient or the provider, and is provided at the most appropriate level to treat the condition.

**Investigational/Experimental:** A treatment, procedure, or drug is investigational when it has not been recognized as safe and effective for use in treating the particular condition in accordance with generally accepted professional medical standards. This includes services where approval by the federal or state governmental is required prior to use, but has not yet been granted.

**Split Evaluation:** Blue Shield of California/Blue Shield of California Life & Health Insurance Company (Blue Shield) policy review can result in a split evaluation, where a treatment, procedure, or drug will be considered to be investigational for certain indications or conditions.
but will be deemed safe and effective for other indications or conditions, and therefore potentially medically necessary in those instances.

**Prior Authorization Requirements (as applicable to your plan)**

Within five days before the actual date of service, the provider must confirm with Blue Shield that the member's health plan coverage is still in effect. Blue Shield reserves the right to revoke an authorization prior to services being rendered based on cancellation of the member's eligibility. Final determination of benefits will be made after review of the claim for limitations or exclusions.

Questions regarding the applicability of this policy should also be directed to the Transplant Case Management Department. Please call 1-800-637-2066 ext. 3507708 or visit the Provider Portal at [www.blueshieldca.com/provider](http://www.blueshieldca.com/provider).

Disclaimer: This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. Blue Shield of California may consider published peer-reviewed scientific literature, national guidelines, and local standards of practice in developing its medical policy. Federal and state law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over medical policy and must be considered first in determining covered services. Member contracts may differ in their benefits. Blue Shield reserves the right to review and update policies as appropriate.