I. DESCRIPTION/BACKGROUND

Hematopoietic Stem Cell Transplantation

Hematopoietic stem-cell transplantation (SCT) 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. Bone-marrow stem cells may be obtained from the transplant recipient (autologous SCT) or from a donor (allogeneic SCT). They can be harvested from bone marrow, peripheral blood, or umbilical cord blood and placenta 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.

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

Reduced-Intensity Conditioning for Allogeneic Stem-Cell Transplantation

Reduced-intensity conditioning (RIC) refers to chemotherapy regimens that seek to reduce adverse effects secondary to bone marrow toxicity while retaining the beneficial graft-versus-malignancy effect of allogeneic transplantation. These regimens do not eradicate the patient’s hematopoietic ability, thereby allowing for relatively prompt hematopoietic recovery (e.g., 28 days or less) even without a transplant. Patients who undergo RIC with allogeneic SCT 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. A number of different cytotoxic regimens, with or without radiotherapy, may be used for RIC allotransplantation. They represent a continuum in their effects, from nearly totally myeloablative, to minimally myeloablative with lymphoablation.
Primary 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 lymphoma or chronic myelogenous leukemia, estimated at 5 to 12 people per million annually. The median age at diagnosis is around 60 years. The amyloidogenic protein in AL amyloidosis is an immunoglobulin (Ig) 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 5-10%, this disease also may occur in association with multiple myeloma in 10-15% of patients. Deposition of AL amyloidogenic proteins causes organ dysfunction, most frequently in the kidneys, heart and liver, although the CNS and brain may be affected.

Historically, this disease has had a poor prognosis, with a median survival from diagnosis of about 12 months, although outcomes have improved with the advent of combination chemotherapy with alkylating agents and auto-SCT. 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.

Waldenstrom’s Macroglobulinemia

Waldenstrom macroglobulinemia (WM) is a B-cell malignancy that accounts for 1-2% of hematologic malignancies, with an estimated 1,500 new cases annually in the U.S. The median age of WM patients at presentation is 63-68 years, with males comprising 55-70% of cases. Median survival of WM ranges from 5 to 10 years, with age, hemoglobin concentration, serum albumin, and beta-2 microglobulin level as predictors of outcome. The Revised European American Lymphoma (REAL) and World Health Organization (WHO) classification, and a consensus group formed at the Second International Workshop on WM, recognize WM primarily as a lymphoplasmacytic lymphoma (LPL) with an associated immunoglobulin M (IgM) monoclonal gammopathy. The definition also
requires the presence of a characteristic pattern of bone marrow infiltration with small lymphocytes demonstrating plasmacytic differentiation with variable cell surface antigen expression. The Second International Workshop indicated no minimum serum concentration of IgM is necessary for a diagnosis of WM.

Treatment 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 hemoglobin concentration <100 g/L; platelet count <100 x 10⁹/L; 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 have included alkylating agents (chlorambucil, cyclophosphamide, melphalan), purine analogues (cladribine, fludarabine), and monoclonal antibody agents (rituximab), alone or in various combinations. Plasma exchange is indicated for acute treatment of symptomatic hyperviscosity.

II. **Definitions**

**Ablation** refers to the removal of a part, pathway, or function by surgery, chemical destruction, electrocautery or radiofrequency.

**Antigenic** is the provoking of an immune response or acting with antibodies.

**Allogeneic** refers to having a different genetic constitution but belonging to the same species, i.e., involves a donor and a recipient.

**Apheresis** is a procedure in which blood is temporarily withdrawn, one or more components are selectively removed, and the rest of the blood is reinfused into the donor.

**AutoLOGOUS** refers to originating within an individual, i.e., self-donation.

**Bone Marrow** is the soft tissue in the marrow cavities of long bones (yellow marrow) and in the spaces between trabeculae of spongy bone in the sternum and other flat and irregular bones (red marrow). Yellow marrow is mostly fat and stored energy. Red marrow produces all types of blood cells.

**Plasmapheresis** is the removal of plasma from withdrawn blood by centrifugation, the reconstitution of the cellular elements in an isotonic solution, and the reinfusion of this solution into the donor.

**Syngeneic** hematopoietic stem cells are those harvested from an identical twin. Their use is limited by the rarity of identical twins.
III. Policy

Autologous stem-cell support may be considered medically necessary to treat primary systemic amyloidosis.

Cross-reference

MP-9.001 Cord Blood as a Source for Stem Cells
MP-4.024 Pheresis and Apheresis Therapy
MP-2.110 Biological Therapy (Immunotherapy) with Monoclonal Antibodies

IV. Exclusions

Hematopoietic stem-cell support is considered investigational to treat Waldenström’s macroglobulinemia, as there is insufficient evidence to support a conclusion concerning the health outcomes or benefits associated with this procedure.

Allogeneic stem-cell transplantation is considered investigational to treat primary systemic amyloidosis. There is insufficient evidence to support a conclusion concerning the health outcomes or benefits associated with this procedure.

V. Benefit Variations

The existence of this medical policy does not mean that this service is a covered benefit under the member’s contract. Benefit determinations should be based in all cases on the applicable contract language. Medical policies do not constitute a description of benefits. A member’s individual or group customer benefits govern which services are covered, which are excluded, and which are subject to benefit limits and which require preauthorization. Members and providers should consult the member’s benefit information or contact Capital for benefit information.

VI. Disclaimer

Capital’s medical policies are developed to assist in administering a member’s benefits, do not constitute medical advice and are subject to change. Treating providers are solely responsible for medical advice and treatment of members. Members should discuss any medical policy related to their coverage or condition with their provider and consult their benefit information to determine if the service is covered. If there is a discrepancy between this medical policy and a member’s benefit information, the benefit information will govern. Capital considers the information contained in this medical policy to be proprietary and it may only be disseminated as permitted by law.

VII. References

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Taber’s Cyclopedic Medical Dictionary, 19th edition.


MEDICAL POLICY

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VIII. PRODUCT VARIATIONS

[N] = No product variation, policy applies as stated
[Y] = Standard product coverage varies from application of this policy, see below

[N] CHIP POS  [N] Indemnity
[N] PPO  [N] SpecialCare
[N] HMO  [N] POS
[N] CHIP HMO  [Y] FEP HMO*
[N] SeniorBlue  [Y] FEP PPO*
[N] SeniorBlue PPO

*Allogeneic stem-cell transplantation for the treatment of amyloidosis is a covered benefit.

IX. CODING INFORMATION

Note: This list of codes may not be all-inclusive, and codes are subject to change at any time. The identification of a code in this section does not denote coverage as coverage is determined by the terms of member benefit information. In addition, not all covered services are eligible for separate reimbursement.

38204 38207 38209 38211 38213 38215 38221 38241 Q0084 S2150
38206 38208 38210 38212 38214 38220 38230 Q0083 Q0085

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# Medical Policy

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## X. Policy History

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