Autologous Stem Cell Transplantation
Clinical Coverage Criteria

Overview

Autologous stem cell transplants are typically used in people who need to undergo high-dose chemotherapy or a combination of chemotherapy and radiation to cure their diseases. These treatments are likely to damage the bone marrow. Hematopoietic stem cells are collected from the patient in advance of the treatments and are frozen. Two sources of hematopoietic stem cells that can be used in autologous stem cell transplants are peripheral blood stem cells and bone marrow stem cells. After the patient undergoes treatment, the stem cells are returned to the body. The goal of an autologous stem cell transplant is to restore the body's ability to make normal blood cells. Most people have a single autologous transplant. Some may have a tandem transplant. A tandem transplant involves a planned second autologous stem cell transplant after the first autologous transplant).

Policy

This Policy applies to the following Fallon Health products:

☒ Commercial
☒ Medicare Advantage
☒ MassHealth ACO
☒ NaviCare
☒ PACE

Fallon Health uses guidance from the Centers for Medicare and Medicaid Services (CMS) for coverage determinations for Medicare Advantage, NaviCare and PACE plan members. National Coverage Determinations (NCDs), Local Coverage Determinations (LCDs) and guidance in the Medicare manuals are the basis for coverage determinations. When there is no NCD, LCD or manual guidance, Fallon Health Clinical Coverage Criteria are used for coverage determinations.

See Part II. below for covered indications for Autologous Stem Cell Transplantation for Medicare Advantage, NaviCare and PACE plan members.

Prior authorization is required.

Part I. Commercial and MassHealth ACO plan members
Autologous stem cell transplantation is considered medically necessary for the following indications when all criteria are met.

Acute Lymphoblastic Leukemia (ALL), Pediatric

- In first complete remission with any of the following:
  - Poor treatment response to induction therapy at 6 weeks with high risk having ≥1% minimal residual disease measured by flow cytometry,
  - Children with t- cell phenotype
  - Patients with either the t (9;22) or t (4;11) regardless of early response measures.
- In second or greater remission or refractory ALL

Acute Lymphoblastic Leukemia (ALL), Adult

- In first complete remission with any of the following:
  - Age older than 35 years

- Leukocytosis at presentation of greater than 30,000/ìl (b-cell lineage) or greater than 100,000/ìl (t-cell lineage)
- "poor prognosis" genetic abnormalities like the philadelphia chromosome (t[9;22]),
- Extramedullary disease,
- Time to attain complete remission longer than 4 weeks

Acute myeloid leukemia (AML)
- In remission or relapsed if responsive to intensified chemotherapy

Amyloidosis, primary systemic

Embryonal tumors of the central nervous system
- Previously untreated that show partial or complete response to induction chemotherapy,
- Recurrent disease
- Stable disease after induction therapy
- Tandem, either as salvage therapy or with platinum-refractory disease

Ewing sarcoma
- Initial treatment for high risk cases
- Recurrent of refractory

Germ cell tumors
- Salvage
  - With favorable prognostic factors that have failed a previous course of conventional-dose salvage chemotherapy, or
  - With unfavorable prognostic factors as initial treatment of first relapse and in patients with platinum-refractory disease
- Tandem, for testicular tumors either as salvage therapy or with platinum-refractory disease

Hodgkin's Lymphoma
- Primary refractory or relapsed
- Tandem, for primary refractory or in patients with relapsed disease with poor risk features who do not attain a complete remission to cytoreductive chemotherapy

Multiple Myeloma
- Primary or salvage
- Tandem (autologous-autologous) who fail to achieve at least a near-complete or very good partial response after the first transplant

Neuroblastoma
- Initial treatment for high risk cases, including tandem transplants
- Recurrent of refractory

Non-Hodgkin Lymphomas
Aggressive B-cell subtypes
Myeloablative conditioning or high dose chemotherapy
- Salvage therapy for those who do not achieve complete remission after first-line treatment with a full course of standard-dose chemotherapy
- Consolidate or achieve a complete remission during responding treatment of a relapse
- In patients with diffuse large B-cell lymphoma, with an adjusted International Prognostic Index score that predicts a high- or high-intermediate risk of relapse, who are in their first complete remission

Indolent B-cell subtypes
- Salvage therapy for those who do not achieve complete remission after first-line treatment with a full course of standard-dose chemotherapy

- Consolidate or achieve a complete remission during responding treatment of a relapse

Mantle cell lymphoma
- To consolidate a first complete remission

Mature T-cell or NK-cell (peripheral T-cell) lymphoma
- To consolidate a first complete remission
- Salvage therapy

POEMS syndrome with diffuse sclerotic lesions or disseminated bone marrow involvement

Retinoblastoma with metastasis

Scleroderma/systemic sclerosis with ALL of the following:
- Adult patients <60 years of age
- Maximum duration of condition of 5 years
- Modified Rodnan Scale Scores >15
- Abnormal electrocardiogram OR diffusing capacity of carbon monoxide (dlco) <80% of predicted value OR decline of forced vital capacity (FVC) of >10% in last 12 months OR pulmonary fibrosis OR ground glass appearance on high resolution chest CT OR scleroderma-related renal disease
- History of < 6 months' treatment with cyclophosphamide
- No active gastric antral vascular ectasia
- Do not have any of the following:
  - Left ventricular ejection fraction <50%
  - Tricuspid annular plane systolic excursion <1.8 cm
  - Pulmonary artery systolic pressure >40 mm hg
  - Mean pulmonary artery pressure >25 mm hg
  - Dlco <40% of predicted value
  - Fvc <45% of predicted value
  - Creatinine clearance <40 ml/minute

Waldenstrom macroglobulinemia
- Salvage therapy if chemosensitive

Part II. Medicare Advantage, NaviCare and PACE plan members

Medicare National Coverage Determination (NCD) for Stem Cell Transplantation (110.23) describes the covered indications for autologous stem cell transplantation. Autologous stem cell transplantation is a technique for restoring stem cells using the patient's own previously stored cells. Stem cell transplantation is a process which includes mobilization, harvesting, and transplant of bone marrow or peripheral blood stem cells and the administration of high dose chemotherapy or radiotherapy prior to the actual transplant. When stem cell transplantation is covered, all necessary steps are included in coverage. When bone marrow or peripheral blood stem cell transplantation is non-covered, none of the steps are covered.

The NCD lists the following nationally covered indications for autologous stem cell transplantation for Medicare beneficiaries:
- Acute leukemia in remission who have a high probability of relapse and who have no human leucocyte antigens (HLA)-matched;

- Resistant non-Hodgkin's lymphomas or those presenting with poor prognostic features following an initial response;
- Recurrent or refractory neuroblastoma; or,
- Advanced Hodgkin's disease who have failed conventional therapy and have no HLA-matched donor.
- Single autologous stem cell transplantation is covered for Durie-Salmon Stage II or III patients that fit the following requirements:
    - Newly diagnosed or responsive multiple myeloma. This includes those patients with previously untreated disease, those with at least a partial response to prior chemotherapy (defined as a 50% decrease either in measurable paraprotein [serum and/or urine] or in bone marrow infiltration, sustained for at least 1 month), and those in responsive relapse; and
    - Adequate cardiac, renal, pulmonary, and hepatic function.
- Autologous stem cell transplantation in combination with high dose melphalan is covered for Medicare beneficiaries with primary amyloid light chain amyloidosis who meet the following criteria:
    - Amyloid deposition in 2 or fewer organs; and,
    - Cardiac left ventricular ejection fraction (EF) greater than 45%.

Autologous stem cell transplantation is considered not medically necessary and is not covered for Medicare beneficiaries for the following indications:

- Acute leukemia not in remission;
- Chronic granulocytic leukemia;
- Solid tumors (other than neuroblastoma);
- Tandem transplantation (multiple rounds of autologous stem cell transplantation) for patients with multiple myeloma; and
- Non-primary amyloid light chain amyloidosis.

In addition to the nationally covered indications for autologous stem cell transplantation, the following indications are covered when medically necessary in accordance with **National Government Services, Inc. Local Coverage Article: Billing and Coding: Stem Cell Transplantation (A52879)**:

- Anaplastic large cell lymphoma
- Large cell lymphoma/B-cell lymphoma
- Peripheral T-cell lymphoma
- Primary central nervous system lymphoma
- Testicular cancer
- Waldenström macroglobulinemia

Exclusions

- Autologous stem cell transplant is considered experimental and therefore is not covered for the following conditions:
    - Cancer of the bile duct
    - Cancer of the fallopian tubes
    - Cervical cancer
    - Chronic inflammatory demyelinating polyneuropathy
    - Chronic myeloid leukemia
    - Colon cancer
    - Diabetes mellitus, Type 1
    - Ependymoma
    - Esophageal cancer

- Gall bladder cancer
- Juvenile idiopathic or rheumatoid arthritis
- Lung cancer, any histology
- Malignant melanoma.
- Multiple sclerosis
- Nasopharyngeal cancer
- Neuroendocrine tumors
- Osteosarcoma
- Ovarian cancer
- Pancreas cancer
- Paranasal sinus cancer
- Prostate cancer
- Rectal cancer
- Renal cell cancer
- Retinoblastoma without metastasis
- Rhabdomyosarcoma
- Soft tissue sarcomas
- Stomach cancer
- Systemic lupus erythematosus
- Thyroid tumors
- Tumors of the thymus
- Tumors of unknown primary origin, or
- Uterine cancer
- Wilms tumor

Coding

The following codes are included below for informational purposes only; inclusion of a code does not constitute or imply coverage or reimbursement.

Code	Description
38241	Hematopoietic progenitor cell (HPC); autologous transplantation

References

1. Hatzimichael E, Tuthill M. Hematopoietic stem cell transplantation. *Stem Cells Cloning*. 2010;3:105-117.
2. Medicare National Coverage Determinations Manual., Chapter 1, Part 2, Section 110.23 - Stem Cell Transplantation (110.23). Effective January 27, 2016. Available at: https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/ncd103c1_Part2.pdf.
3. National Government Services, Inc. Local Coverage Article: Billing and Coding for Stem Cell Transplantation (A52879). Original Effective Date: October 1, 2015. Revision Effective Date: April 1, 2021. Available at: https://www.cms.gov/medicare-coverage-database/overview-and-quick-search.aspx. Accessed June 15, 2021.
4. Majhail NS, Farnia SH, Carpenter PA, et al. Indications for Autologous and Allogeneic Hematopoietic Cell Transplantation: Guidelines from the American Society for Blood and Marrow Transplantation. *Biol Blood Marrow Transplant*. 2015;21(11):1863-1869.

5. Kanate AS, Majhail NS, Savani BN, et al. Indications for Hematopoietic Cell Transplantation and Immune Effector Cell Therapy: Guidelines from the American Society for Transplantation and Cellular Therapy. *Biol Blood Marrow Transplant*. 2020;S1083-8791(20)30114-2.

Policy history

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Not all services mentioned in this policy are covered for all products or employer groups. Coverage is based upon the terms of a member's particular benefit plan which may contain its own specific provisions for coverage and exclusions regardless of medical necessity. Please consult the product's Evidence of Coverage for exclusions or other benefit limitations applicable to this service or supply. If there is any discrepancy between this policy and a member's benefit plan, the provisions of the benefit plan will govern. However, applicable state mandates take precedence with respect to fully-insured plans and self-funded non-ERISA (e.g., government, school boards, church) plans. Unless otherwise specifically excluded, federal mandates will apply to all plans. For Medicare and Medicaid members, this policy will apply unless Medicare and Medicaid policies extend coverage beyond this policy.