Allogeneic Stem Cell Transplantation
Clinical Coverage Criteria

Overview

Stem cell transplantation, also known as hematopoietic stem cell transplantation, is a process in which stem cells are harvested from either a patient's (autologous) or donor's (allogeneic) bone marrow or peripheral blood for intravenous infusion.

In an allogeneic hematopoietic stem cell transplant (HSCT), stem cells are donated to the patient from another person who is a genetically matched stem cell donor. This is usually a sibling with the same tissue type as the patient. Where no sibling is available, a search is made of donor registries to find a suitably matched unrelated stem cell donor. Allogeneic HSCTs can offer the best chance of curing a number of blood and bone marrow cancers and other diseases. They are complex procedures that carry significant risks. The complexities and risks may be increased even more with a mismatched donor or volunteer unrelated donor transplant. As such, allogeneic HSCTs are usually not suitable for all patients.

There are two types of allogeneic HSCT treatment plans available: myeloablative and non-myeloablative. Before a myeloablative allogeneic HSCT, the patient receives a conditioning regimen of high-dose chemotherapy and, sometimes, radiation therapy. This conditioning regimen serves two purposes: (1) it destroys any remaining cancer cells in the body and (2) it weakens the patient's immune system to keep the body from rejecting the donated stem cells. When a transplant is successful, the donated stem cells move to the bone marrow where the they will begin to produce new blood cells, including red blood cells, platelets and white blood cells. This process is called engraftment. One of the benefits of allogeneic HSCT is that after the donated cells engraft in the patient, they create a new immune system that attacks any remaining cancer cells in the patient's body. This is called the graft-versus-tumor effect and it may be even more important than the conditioning regimen that is administered to destroy the cancer cells. This benefit can only occur in allogeneic stem cell transplantation.

One complication of allogeneic HSCT is that despite the treatment to suppress the immune system, the patient's body may reject the donated stem cells before they are able to engraft in the bone marrow. Another complication of allogeneic HSCT is that the immune cells from the donor (the graft) may attack healthy cells in the patient's body (host). This is called graft-versus-host-disease (GVHD). GVHD can be mild, moderate or severe. There are treatments for GVHD, but in some patients, GVHD does not respond to treatment and can be fatal.

Myeloablative allogeneic HSCT for patients who are older or have overall poor health are relatively uncommon. This is because the pre-transplant conditioning regimen is generally not well tolerated by such patients, especially those with poorly functioning internal organs. However, reduced intensity allogeneic stem cell transplants may be an appropriate treatment for some older or sicker patients. Reduced-intensity allogeneic transplants, sometimes called nonmyeloablative or mini-transplants, use lower, less toxic doses of chemotherapy and radiation than the conditioning regimen that is given before a standard myeloablative allogeneic HSCT. Reduced-intensity allogeneic transplants may be an option for certain patients who are older, who have organ complications or who are otherwise not healthy or strong enough to undergo standard allogeneic transplantation.

Policy

This Policy applies to the following Fallon Health products:

☒ Commercial

☒ Medicare Advantage
☒ MassHealth ACO
☒ NaviCare
☒ PACE

Prior authorization is required.

Part I. For commercial and MassHealth ACO plan members:

Allogeneic stem cell transplantation is considered medically necessary for the following indications when all criteria are met.

Acute Lymphoblastic Leukemia (ALL), Pediatric
- Relapsing ALL after a prior autologous stem cell transplant

Acute Lymphoblastic Leukemia (ALL), Adult
- In remission or relapsed or refractory
- Reduced intensity conditioning when the member is in complete marrow and extramedullary first or second remission
- Relapsing ALL after a prior autologous stem cell transplant

Acute myeloid leukemia (AML)
- In first complete remission with poor- to intermediate-risk
- Refractory/relapsed to standard chemotherapy but responsive to intensified chemotherapy
- Refractory/relapsed after autologous stem cell transplant but responsive to intensified chemotherapy
- Reduced intensity conditioning when the member is in complete marrow and extramedullary first or second remission

Chronic Myeloid Leukemia
- Using myeloablative
- With reduced intensity, with comorbidities

Hodgkin's Lymphoma
- Primary refractory or relapsed, using either myeloablative or reduced-intensity conditioning

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 or Mature T-cell lymphoma

- Salvage therapy with myeloablative or reduced-intensity conditioning

Chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma(SLL) in patients with:

- Non-response or early relapse (within 12 months) after purine analogue containing therapy
- Relapse (within 24 months) after purine analogue combination therapy or treatment of similar efficacy (i.e., autologous stem cell transplantation)
- p53 deletion/mutation (del 17p) requiring treatment

Part II. For Medicare Advantage, NaviCare and PACE plan members:

The Medicare National Coverage Determination (NCD) for Stem Cell Transplantation (110.23) describes the covered indications for allogeneic stem cell transplants. 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 allogeneic HSCT for Medicare beneficiaries:

- Leukemia
- Leukemia in remission
- Aplastic anemia
- Severe combined immunodeficiency disease (SCID)
- Wiskott-Aldrich syndrome

In addition to the nationally covered indications for allogeneic HSCT, Medicare beneficiaries have coverage for the following indications under National Government Services, Inc. Local Coverage Article (A52879):

- Primary refractory Hodgkin's and non-Hodgkin's lymphoma; and
- Thalassemia major for patients with minimal or no portal fibrosis, hepatomegaly, or active hepatitis.

Additionally, allogeneic HSCT is covered for Medicare beneficiaries pursuant to Coverage with Evidence Development (CED) for the following indications:

- Myelodysplastic Syndromes (MDS) and participating in a CMS-approved, prospective clinical trial. For a list of CMS-approved clinical trials, go to: https://www.cms.gov/Medicare/Coverage/Coverage-with-Evidence-Development/allo-HSCT.
- Multiple myeloma only for beneficiaries with Durie-Salmon Stage II or III multiple myeloma or International Staging System (ISS) Stage II or Stage III multiple myeloma, and participating in a CMS-approved, prospective clinical trial. For a list of CMS-approved clinical trials, go to: https://www.cms.gov/Medicare/Coverage/Coverage-with-Evidence-Development/allo-MM.
- Myelofibrosis (MF) only for beneficiaries with Dynamic International Prognostic Scoring System (DIPSSplus) intermediate-2 or High primary or secondary MF, and participating in a CMS-approved, prospective clinical trial. For a list of CMS-approved clinical trials, go to: https://www.cms.gov/Medicare/Coverage/Coverage-with-Evidence-Development/allo-myelo.
- Sickle cell disease (SCD) only for beneficiaries with severe symptomatic SCD, and participating in a CMS-approved, prospective clinical trial. For a list of CMS-approved clinical trials, go to: https://www.cms.gov/Medicare/Coverage/Coverage-with-Evidence-Development/allo-scd.

CMS has determined that the evidence does not demonstrate that the use of allogeneic HSCT improves health outcomes in Medicare beneficiaries with MDS, multiple myeloma, MF or SCD. CMS does believe the available evidence shows that allogeneic HSCT for MDS, multiple myeloma, MF or SCD, as described above, is reasonable and necessary under §1862(a)(1)(E) of the Social Security Act through Coverage with Evidence Development (CED). All other requests for allogeneic HSCT for MDS, multiple myeloma, MF or SCD are not reasonable and necessary under §1862(a)(1)(A) of the Social Security Act and are not covered.

All other indications for allogeneic HSCT not otherwise noted above as covered remain at the discretion of Fallon Health.

Exclusions

- Allogeneic stem cell transplant is considered experimental and therefore is not covered for the following conditions:
    - mantle cell lymphoma to consolidate a first remission
    - Tandem transplants to treat patients with any stage, grade, or subtype of NHL
    - NK-cell lymphoma to consolidate a first remission
    - Waldenstrom macroglobulinemia

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: May 7, 2020. Available at: https://www.cms.gov/medicare-coverage-database/overview-and-quick-search.aspx. Accessed June 23, 2020.
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.