Policy Number	**SUR703.047**
Policy Effective Date	**07/15/2024**
Policy End Date	**12/31/2025**

Hematopoietic Cell Transplantation for Acquired Immunodeficiency Syndrome (AIDS)

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Related Policies (if applicable)
SUR703.002: Hematopoietic Cell Transplantation (HCT) or Additional Infusion Following Preparative Regimens (General Donor and Recipient Information)

Disclaimer

Carefully check state regulations and/or the member contract.
Each benefit plan, summary plan description or contract defines which services are covered, which services are excluded, and which services are subject to dollar caps or other limitations, conditions or exclusions. Members and their providers have the responsibility for consulting the member's benefit plan, summary plan description or contract to determine if there are any exclusions or other benefit limitations applicable to this service or supply. **If there is a discrepancy between a Medical Policy and a member's benefit plan, summary plan description or contract, the benefit plan, summary plan description or contract will govern.**

Coverage

This medical policy has become inactive as of the end date above. There is no current active version and this policy is not to be used for current claims adjudication or business purposes.

Hematopoietic cell transplantation **is considered experimental, investigational and/or unproven** as a treatment of acquired immunodeficiency syndrome (AIDS) or human immunodeficiency virus (HIV) infection.

Policy Guidelines

None.

Description

Hematopoietic Cell Transplantation
Hematopoietic cell transplantation (HCT) 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. 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 "naïve" and thus are associated with a lower incidence of rejection or graft-versus-host disease (GVHD).

Immunologic compatibility between infused hematopoietic stem cells and the recipient is not an issue in autologous HCT. However, immunologic compatibility between donor and patient is a critical factor for achieving a good outcome of allogeneic HCT. 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).

Acquired Immunodeficiency Syndrome (AIDS)/Human Immunodeficiency Virus (HIV)
AIDS is a secondary immunodeficiency syndrome resulting from a HIV infection, characterized by opportunistic infections, malignancies, neurologic dysfunction, and a variety of other conditions.

HIV is an infection caused by several retroviruses that become incorporated into a host cell and result in a wide range of conditions varying from asymptomatic carrier-states to severe debilitating and fatal disorders.

Regulatory Status
The U.S. Food and Drug Administration (FDA) regulates human cells and tissues intended for implantation, transplantation, or infusion through the Center for Biologics Evaluation and Research (CBER), under the Code of Federal Regulation (CFR) title 21, parts 1270 and 1271. Hematopoietic stem cells are included in these regulations.

Rationale

The literature search of the PubMed database for this medical policy was updated through May 29, 2024. The following is a summary of the key literature.

High-dose chemotherapy (HDC) followed by hematopoietic cell transplant (HCT) (i.e., blood or marrow) is an effective treatment modality for many patients with certain malignancies and non-malignancies. The rationale of this treatment approach is to provide a very dose-intensive treatment in order to eradicate malignant/non-malignant cells followed by rescue with peripheral blood, bone marrow, or umbilical cord blood stem cells.

In 1990, Lenarsky and Parkman reported the initial attempts to treat patients with acquired immunodeficiency syndrome (AIDS) due to the lack of effective concomitant anti-viral therapy. They concluded that HCT would continue to be in the forefront of human bone marrow transplantation. (1) Fasth reported the outcome of HCT was strongly dependent on the patient's age, clinical status at transplantation and the type of immune-deficiency. This review article generally described primary immunodeficiencies, not human immunodeficiency virus (HIV) or AIDS specifically. (2)

Published anecdotally-reported literature has primarily centered around treatment using HCT for HIV-related diseases, not actively treating AIDS/HIV directly with HCT. These related diseases include lymphoma and adaptive responses to rebound simian-HIV (SHIV) viremia, primate studies when viruses enter the bloodstream. (3, 4) Few human clinical trials have been published to treat AIDS/HIV using HCT. Therefore, studies continue with animal models of autoimmune diseases to provide the stimulus for further research in treating a variety of immune diseases, using autologous HCT for humans. (5)

In 2016, Kuritzkes reviewed the experience with HCT in HIV infection. (6) Early attempts to apply HCT as an approach to immune reconstitution in patients with AIDS or as treatment for hematologic malignancies met with little success. In the absence of effective antiretroviral therapy (ART), HCT had little impact on the course of HIV disease and most patients died of progressive immunodeficiency or recurrent leukemia or lymphoma. In the early 2000s, a 40-year old male living in Berlin with a 10-year history of HIV infection and a diagnosis of acute myelogenous leukemia (AML) received a human leukocyte antigens- (HLA) matched HCT from an unrelated donor. Proviral HIV-1 DNA became undetectable in peripheral blood mononuclear cells (PBMCs) after full chimerism was achieved on posttransplant day 61. Despite relapse of AML nearly one year later, HIV-1 RNA and DNA remained undetectable. The patient underwent a second HCT from the same donor and has had sustained remission of AML and HIV-1 infection ever since. Although at the time of this review the apparent cure of HIV infection following allogeneic HCT remains a singular event, other failed attempts have provided information about the viral reservoir and the relative contributions of conditioning regiments, graft-versus-host reaction, and coreceptor usage in establishing long-term, ART-free remission.

In a 2019 case report, an adult (the London patient) infected with HIV-1 underwent allogeneic HCT for Hodgkin's lymphoma using cells from a CCR5Δ32/Δ32 donor. (7) He experienced mild gut graft-versus-host disease (GVHD). ART was interrupted 16 months after transplantation. HIV-1 remission has been maintained over 18 months. Plasma HIV-1 RNA has been undetectable at less than one copy per millilitre along with undetectable HIV-1 DNA in peripheral CD4 T lymphocytes. Although it is premature to conclude that this patient has been cured, these data suggest that a single allogeneic HCT with homozygous CCR5Δ32 donor cells may be sufficient to achieve HIV-1 remission with reduced intensity conditioning and no irradiation, and the findings provide further support for the development of HIV-1 remission strategies based on preventing CCR5 expression. Longer term data for this patient was presented by Gupta in 2020. (8) The London patient has been in HIV-1 remission for 30 months

with no detectable replication-competent virus in blood, cerebrospinal fluid, intestinal tissue, or lymphoid tissue. Donor chimerism has been maintained at 99% in peripheral T cells. Mathematical modelling suggests that the probability of remission for life (cure) is 98% in the context of 80% donor chimerism in total HIV target cells and greater than 99% probability of remission for life with 90% donor chimerism. Researchers believe these findings probably represent the second recorded HIV-1 cure after CCR5Δ32/Δ32 allo-HSCT, with evidence of residual low-level HIV-1 DNA.

Despite showing (in both the London patient and the Berlin patient) that CCR5-directed approaches can lead to long-term remission of HIV-1, several barriers remain to be overcome (e.g., gene editing efficiency and robust safety data) before CCR5 gene editing can be used as a scalable cure strategy for HIV-1.

Summary of Evidence

The evidence is insufficient to support the use of hematopoietic cell transplantation (HCT) for the treatment of acquired immunodeficiency syndrome (AIDS)/human immunodeficiency virus (HIV). This is based on the lack of published clinical trials. Therefore, the use of HCT to treat AIDS/HIV is considered experimental, investigational and/or unproven.

Practice Guidelines and Position Statements

There are no professional guidelines and position statements that would likely influence this policy.

Ongoing and Unpublished Clinical Trials

A search of ClinicalTrials.gov in May 2024 did not identify any ongoing or unpublished trials that would likely influence this medical policy. National clinical trial #02732457 (Allogeneic Hematopoietic Stem Cell Transplantation in HIV-1 Infected Patients) was terminated due to the rare patient population and ongoing COVID-19 demands on healthcare systems.

Coding

Procedure codes on Medical Policy documents are included **only** as a general reference tool for each policy. **They may not be all-inclusive.**

The presence or absence of procedure, service, supply, or device codes in a Medical Policy document has no relevance for determination of benefit coverage for members or reimbursement for providers. **Only the written coverage position in a Medical Policy should be used for such determinations.**

Benefit coverage determinations based on written Medical Policy coverage positions must include review of the member's benefit contract or Summary Plan Description (SPD) for defined coverage vs. non-coverage, benefit exclusions, and benefit limitations such as dollar or duration caps.

CPT Codes	36511, 38204, 38205, 38206, 38207, 38208, 38209, 38210, 38211, 38212, 38213, 38214, 38215, 38220, 38221, 38222, 38230, 38232, 38240, 38241, 38242, 38243, 81265, 81266, 81267, 81268, 81370, 81371, 81372, 81373, 81374, 81375, 81376, 81377, 81378, 81379, 81380, 81381, 81382, 81383, 86805, 86806, 86807, 86808, 86812,

	86813, 86816, 86817, 86821, 86822, 86825, 86826, 86828, 86829, 86830, 86831, 86832, 86833, 86834, 86835, 86849, 86950, 86985, 88240, 88241
HCPCS Codes	S2140, S2142, S2150

*Current Procedural Terminology (CPT®) ©2023 American Medical Association: Chicago, IL.

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Centers for Medicare and Medicaid Services (CMS)

The information contained in this section is for informational purposes only. HCSC makes no representation as to the accuracy of this information. It is not to be used for claims adjudication for HCSC Plans.

The Centers for Medicare and Medicaid Services (CMS) does not have a national Medicare coverage position. Coverage may be subject to local carrier discretion.

A national coverage position for Medicare may have been developed since this medical policy document was written. See Medicare's National Coverage at <https://www.cms.hhs.gov>.

Policy History/Revision	
Date	**Description of Change**
12/31/2025	Document became inactive.
07/15/2024	Document updated with literature review. Coverage unchanged. No new references added.
05/01/2023	Reviewed. No changes.
12/01/2022	Document updated with literature review. Coverage unchanged. Added reference 8.
06/15/2021	Reviewed. No changes.
04/15/2020	Document updated with literature review. Coverage unchanged. Added references 6-7. Title changed from: "Hematopoietic Stem-Cell Transplantation for Acquired Immunodeficiency Syndrome (AIDS)".
06/15/2018	Reviewed. No changes.
07/15/2017	Document updated with literature review. Coverage unchanged.
07/15/2016	Reviewed. No changes.
02/15/2015	Document updated with literature review. Coverage language modified, without change to coverage position. CPT/HCPCS code(s) updated. Title changed from: Stem-Cell Transplant for Acquired Immunodeficiency Syndrome (AIDS).
10/15/2013	Document updated with literature review. The following was added: 1) Donor leukocyte infusion and hematopoietic progenitor cell boost are considered experimental, investigational and unproven; and 2) Any related services for the treatment of AIDS or HIV infection, such as short tandem repeat (STR) markers, are considered experimental, investigational and unproven. Otherwise, coverage unchanged. Rationale significantly revised.
04/01/2010	New medical document originating from: SUR703.017, Peripheral/Bone Marrow Stem-cell Transplantation (PSCT/BMT) for Non-Malignancies; SUR703.018, Peripheral/Bone Marrow Stem-cell Transplantation (PSCT/BMT) for Malignancies; SUR703.022, Cord Blood as a Source of Stem-cells (CBSC); SUR703.023, Donor Leukocyte Infusion (DLI); and SUR703.024, Tandem/Triple High-Dose Chemoradiotherapy with Stem-cell Support for Malignancies. Stem-cell transplant remains experimental, investigational and unproved when used to treat AIDS. NOTE: A link to the medical policies with the following titles can be found at the end of the medical policy SUR703.002, Stem-Cell Reinfusion or Transplantation Following Chemotherapy (General Donor and Recipient Information): • Peripheral/Bone Marrow Stem-cell Transplantation (PSCT/BMT) for Non-Malignancies; • Peripheral/Bone Marrow Stem-cell Transplantation (PSCT/BMT) for Malignancies; • Cord Blood as a Source of Stem-cells; • Donor Leukocyte Infusion (DLI); and

	Tandem/Triple High-Dose Chemoradiotherapy with Stem-cell Support for Malignancies.