Clinical Policy: Allogeneic Hematopoietic Progenitor Cell Therapy

Reference Number: MC.CP.MP.249
Last Review Date: 05/25

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

This policy describes the medical necessity criteria for allogeneic hematopoietic progenitor cell therapies, which include Omisirge® (omidubicel) and RegenCyte™ (HPC Cord Blood).

The criteria below are taken from the Omisirge and RegeneCyte package inserts, which include safety information derived from published data and studies completed to evaluate the efficacy of these products.[1,9] The approval of Omisirge and RegeneCyte from the United States Food and Drug Administration (FDA) is based off examination of the risks and benefits of transplantation with Omisirge or RegeneCyte as evidenced by the results of the published data and studies completed for both products.[2,10] Current evidence for Omisirge is based on a phase three multicenter randomized controlled trial (RCT) that evaluated the efficacy of Omisirge compared with standard umbilical cord blood transplantation (UCBT).[1] The results of this phase three RCT indicate that transplantation with Omisirge is an effective stem cell therapy that reduces the time to neutrophil recovery, reduces the risk of infection, and results in less time in the hospital, thus improving quality of life and overall survival.[3] Current evidence for RegeneCyte is based on data from a prospective, single-arm study conducted by the Cord Blood Transplantation (COBLT) study (Study 1), a retrospective review of data from literature and observational studies (Study 2), and retrospective reviews of data from an observational database for RegeneCyte using information from the Center for International Blood and Marrow Transplant Research (Study 3).[9] The results of these three studies indicate that transplantation with RegeneCyte is an effective stem cell therapy that reduces time to neutrophil recovery, erythrocyte recovery, and platelet recovery, and reduces the risk of infection through hematopoietic and immunologic reconstitution.[9] The results of the studies and safety data for Omisirge and RegeneCyte demonstrate that the benefits of receiving Omisirge or RegeneCyte, when meeting the criteria below, outweigh the potential risk of adverse outcomes.

Note: *For criteria applicable to non-Medicare plans, please see CP.MP.249 Allogeneic Hematopoietic Progenitor Cell Therapy.*

Policy/Criteria

I. It is the policy of Medicare health plans affiliated with Centene Corporation® that Omisirge® (omidubicel) is **medically necessary** when all of the following criteria are met[1,2,3]:
- A. Member/enrollee is ≥ 12 years of age;
- B. Diagnosis of hematologic malignancies;
- C. Member/enrollee is planned for an umbilical cord blood transplantation following myeloablative conditioning to reduce the time to neutrophil recovery and the incidence of infection;
- D. Request is for one administration post-myeloablative conditioning.

II. It is the policy of Medicare health plans affiliated with Centene Corporation that RegeneCyte™ is **medically necessary** when all of the following criteria are met:
- A. Member/enrollee is planned for an unrelated donor hematopoietic progenitor cell

transplantation procedure;

B. An appropriate preparative regimen for hematopoietic and immunologic reconstitution will be used in conjunction with the transplantation procedure;
C. Member/ enrollee has a disorder affecting the hematopoietic system that is inherited, acquired, or a result from myeloablative treatment.

Background

Allogeneic hematopoietic cell transplantation (HCT) has been used as a treatment for cancer and diseases of the blood system for decades. For this treatment, stem cells are collected from either related or unrelated healthy donors instead of from the patients themselves.[4] During the conditioning phase, high doses of chemotherapy (HDC), with or without radiation therapy, are used to eradicate the disease, and this is followed by infusion of stem cells to rescue bone marrow and restore normal immune function. Major limitations of this technique include the increased risk of high morbidity and mortality related to increased age, relapsed or refractory disease or disease with an elevated risk of relapse following HCT, a history of aggressive chemotherapy, and comorbidities.[5] All stem cell transplant (SCT) preparative regimens have the potential for extensive toxicity. Loss of appetite and energy, alopecia, and nausea/vomiting occur frequently and contribute to poor physical and emotional tolerance of the transplant procedure. In addition, mucositis, diarrhea, and transient pancytopenia are inevitable side effects of most preparative regimens, and these complications are synergistic in dramatically increasing the risk of infections during and post-transplant.[6] Any decrease in toxicity, without concomitant loss of efficacy, would be desirable.

Myeloablative means that the treatment kills (ablates) the stem cells in the bone marrow; the cells that produce new blood cells. Myeloablative conditioning (MAC) is a regimen that consists of a single agent or combination of agents that are anticipated to destroy the hematopoietic cells in the bone marrow.[6] Extensive pancytopenia occurs within one to three weeks after administration of a MAC regimen and is typically irreversible.[6]

Omisirge® (omidubicel)

In April 2023, the U.S. Food and Drug Administration (FDA) approved Omisirge, a nicotinamide-modified allogeneic hematopoietic progenitor cell therapy. Omisirge is derived from cord blood and quickens the recovery of neutrophils in the body and reduces the incidence of infection. The product is intended to be used in patients ≥ 12 years of age with blood malignancies who have a planned umbilical cord blood transplantation following myeloablative conditioning.[1,2]

A randomized, multicenter study with 125 enrollees comparing transplantation of Omisirge to transplantation of umbilical cord blood supports the safety and effectiveness of Omisirge.[2,3,7] The study found that 87% of subjects who received Omisirge attained neutrophil recovery in an average of 12 days after treatment. In comparison, neutrophil recovery was achieved in an average of 22 days in 83% of subjects who received umbilical cord blood transplantation.[3,7] Additionally, subjects in the study who received Omisirge had fewer bacterial or fungal infections than the group of subjects who received umbilical cord blood transplantation.[2,3,7] Further analysis of this study regarding healthcare resource utilization showed that in the first 100 days after transplantation, patients who received Omisirge had fewer days in the intensive care unit, a shorter total hospital length of stay, and fewer deaths compared to the group of patients who received umbilical cord blood transplantation.[8] These findings suggest that the use of Omisirge is associated with reduced healthcare resources due to faster hematopoietic recovery.[8]

RegeneCyte™ HPC (Hematopoietic Progenitor Cell), Cord Blood

In November 2024, the FDA approved RegeneCyte, an allogeneic hematopoietic stem cell therapy derived from human umbilical cord blood.[11] RegeneCyte is approved for unrelated donor hematopoietic progenitor cell transplantation procedures in conjunction with an appropriate preparative regimen for hematopoietic and immunologic reconstitution. The product is intended for use in patients with disorders affecting the hematopoietic system that are inherited, acquired, or result from myeloablative treatment.[9,10,11]

The FDA's decision to support the safety and effectiveness of RegeneCyte is based on data from the Cord Blood Transplantation (COBLT) study (Study 1), data in the FDA dockets and public information (Study 2), and data from the Center for International Blood and Marrow Transplant Research (Study 3).[9]

Study 1 is based on a prospective, single-arm study conducted by the COBLT study group of unrelated cord blood transplantation (CBT). The purpose of this study was to clarify the role of this stem cell source for patients requiring unrelated allogeneic transplantation. The chief aim of this study was survival at 180 days. Secondary objectives included engraftment, graft-versus-host disease, relapse, and long-term survival. The preparative regimens and graft-vs-host disease prophylaxis in this study were not standardized, and 79% (n=257) of the patients enrolled in this study were treated for hematologic malignancies.[9]

Among the 324 patients treated in this study, 76% achieved neutrophil recovery at day 42, platelet recovery (20,000/uL) (95% CI) was achieved in 57% at day 100, and 65% achieved erythrocyte recovery at day 100. The median time to neutrophil recovery was 27 days, the median time to platelet recovery (20,000/uL) was 90 days, and the median time to erythrocyte recovery was 64 days.[9]

Study 2 is based on a retrospective review of data from published literature and from observational registries, institutional databases, and multiple cord blood banks that reported to the FDA docket for HPC, Cord Blood. According to public data and information in the dockets, the preparative regimens and graft-vs-host disease prophylaxis varied, and 66% (n=862) of the 1,299 patients underwent transplantation as treatment for hematologic malignancy.[9] In this study, 77% of patients achieved neutrophil recovery at day 42, and 45% of patients achieved platelet recovery at day 100. The median time to neutrophil recovery was 25 days, and the median time to platelet recovery was 122 days.[9]

Study 3 is based on retrospective reviews of data from an observational database for RegeneCyte, using information from the Center for International Blood and Marrow Transplant Research. In this database, 81.5% of patients (44 of 54) underwent transplantation for a hematologic malignancy. Preparative regimens and graft-vs-host disease prophylaxis were not standardized in this study group, and the reactions were not graded. Among the 54 patients treated in this study, 91% achieved neutrophil recovery at Day 42, and 72% achieved platelet recovery (20,000/uL) (95% CI) at Day 100. The median time to neutrophil recovery was 22 days, and the median time to platelet recovery (20,000/uL) was 50 days.[9]

Overall, the effectiveness of RegeneCyte is defined by hematopoietic reconstitution, which was demonstrated in all three studies.[9]

Coding Implications

This clinical policy references Current Procedural Terminology (CPT®). CPT® is a registered trademark of the American Medical Association. All CPT codes and descriptions are copyrighted

HCPCS Codes	Description
J3590	Unclassified biologics
C9399	Unclassified drugs or biologicals

Reviews, Revisions, and Approvals	Review Date	Approval Date
Policy developed.	02/24	02/24
Annual review. Description updated with no impact on criteria. Added "Medicare" to health plans in Policy/Criteria I. Background updated with no impact on criteria. References reviewed and updated. Reviewed by external specialist.	06/24	06/24
Annual review. Removed Omisirge specific language from title of policy due to expanding policy. Updated Description of policy to include RegeneCyte and to updated title in the Note referencing the non-Medicare version of policy. Added Criteria II. to include medically necessary criteria for RegeneCyte…Background updated to include RegeneCyte information to align with updated criteria. Reviewed codes and descriptions. References reviewed and updated. Reviewed by internal specialist.	05/25	05/25

References

1. Omisirge. [package insert]. Jerusalem, Israel: Gamida Cell Ltd.; 2023.
2. U.S. Food and Drug Administration. FDA Approves Cell Therapy for Patients with Blood Cancers to Reduce Risk of Infection Following Stem Cell Transplantation. https://www.fda.gov/news-events/press-announcements/fda-approves-cell-therapy-patients-blood-cancers-reduce-risk-infection-following-stem-cell. Published April 17, 2023. Accessed March 20, 2025.
3. Horwitz ME, Stiff PJ, Cutler C, et al. Omidubicel vs standard myeloablative umbilical cord blood transplantation: results of a phase 3 randomized study. *Blood*. 2021;138(16):1429 to 1440. doi:10.1182/blood.2021011719
4. American Cancer Society. Types of Stem Cell Transplants for Cancer Treatment. https://www.cancer.org/cancer/managing-cancer/treatment-types/stem-cell-transplant/types-of-transplants.html. Published May 04, 2023. Accessed March 21, 2025.
5. Deeg HJ, Sandmaier BM. Allogeneic hematopoietic cell transplantation: Indications, eligibility, and prognosis. UpToDate. www.uptodate.com. Updated January 30, 2025. Accessed March 21, 2025.
6. Negrin RS. Early complications of hematopoietic cell transplantation. UpToDate. www.uptodate.com. Updated September 25, 2024. Accessed March 21, 2025.
7. Chao NJ. Selection of an umbilical cord blood graft for hematopoietic cell transplantation. UpToDate. www.uptodate.com. Updated March 20, 2024. Accessed March 21, 2025.
8. Majhail NS, Miller B, Dean R, et al. Hospitalization and Healthcare Resource Utilization of Omidubicel-Onlv versus Umbilical Cord Blood Transplantation for Hematologic

Malignancies: Secondary Analysis from a Pivotal Phase 3 Clinical Trial. *Transplant Cell Ther*. 2023;29(12):749.e1-749.e5. doi:10.1016/j.jtct.2023.09.004
9. RegeneCyte. [package insert]. Baldwin Park, CA: StemCyte; 2024.
10. U.S. Food and Drug Administration. REGENECYTE. https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/regenecyte. Published December 16, 2024. Accessed March 21, 2025.
11. StemCyte. U.S. FDA Approves StemCyte Biologics License Application for REGENECYTE™ Cord Blood Cell Therapy Product. https://www.stemcyte.com/usfda-approves-stemcyte-bla. Accessed March 21, 2025.

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

Note: For Medicare members, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs, and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Refer to the CMS website at http://www.cms.gov for additional information.