Clinical Policy: Omisirge (omidubicel): Nicotinamide-modified allogeneic hematopoietic progenitor cell therapy

Reference Number: MC.CP.MP.249
Last Review Date: 06/24

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 Omisirge (omidubicel), a nicotinamide-modified allogeneic hematopoietic progenitor cell therapy, to be delivered following myeloablative conditioning for hematologic malignancies.[1]

The criteria below are taken from the Omisirge package insert, which includes safety data derived from a phase three multicenter randomized controlled trial (RCT) that evaluated the efficacy of Omisirge compared with standard umbilical cord blood transplantation (UCBT).[1] The approval of Omisirge from the United States Food and Drug Administration (FDA) is based off examination of the risks and benefits of transplantation with Omisirge as evidenced by the results of this RCT.[2] Current evidence, based on the phase three RCT, indicates 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] These results demonstrate that the benefits of receiving Omisirge, 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 Omisirge (omidubicel): Nicotinamide-modified 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.

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]

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 2023, American Medical Association. All rights reserved. CPT codes and CPT descriptions are from the current manuals and those included herein are not intended to be all-inclusive and are included for informational purposes only. Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

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

References

1. Omisirge. [package insert]. Jerusalem, Israel: Gamida Cell Ltd.; 2023.
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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
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5. Deeg HJ, Sandmaier BM. Determining eligibility for allogeneic hematopoietic cell transplantation. UpToDate. www.uptodate.com. Updated February 21, 2022. Accessed April 30, 2024.
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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

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,

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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.

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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.