

## PHARMACY / MEDICAL POLICY – 5.01.638

## Omisirge (Omidubicel)

Effective Date: Sept. 1, 2023

Last Revised: Aug. 8, 2023

Replaces: N/A

RELATED MEDICAL POLICIES:

None

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## Introduction

Hematologic malignancies are an umbrella term that talks about cancer in the blood-forming tissue, such as bone marrow, or the cells of the immune system. Different types of hematologic malignancies include lymphoma, leukemia, and multiple myeloma. The treatment regimens of hematologic malignancies include radiation therapy, blood transfusions, chimeric antigen receptor (CAR) T-cell therapies and Omisirge (omidubicel-only). The U.S. Food and Drug Administration has recently approved Omisirge (omidubicel-only), a nicotinamide modified allogeneic hematopoietic progenitor cell therapy derived from cord blood. This policy described when Omisirge (omidubicel-only) may be considered medically necessary.

**Note:** The Introduction section is for your general knowledge and is not to be taken as policy coverage criteria. The rest of the policy uses specific words and concepts familiar to medical professionals. It is intended for providers. A provider can be a person, such as a doctor, nurse, psychologist, or dentist. A provider also can be a place where medical care is given, like a hospital, clinic, or lab. This policy informs them about when a service may be covered.

## Policy Coverage Criteria

Drug	Medical Necessity
<b>Omisirge (omidubicel-only)</b>	<p><b>Omisirge (omidubicel-only) is a nicotinamide modified allogeneic hematopoietic progenitor cell therapy derived from cord blood may be considered medically necessary when the following criteria are met:</b></p> <ul style="list-style-type: none"> <li>Individual is at least 12 years of age and older</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>Individual has a diagnosis of hematologic malignancies who are planned for umbilical cord blood transplantation following myeloablative conditioning to reduce both: <ul style="list-style-type: none"> <li>Time to neutrophil recovery</li> <li>The incidence of infection</li> </ul> </li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>Individual is candidate for myeloablative allogeneic hematopoietic stem cell transplantation (HSCT)</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>Individual does not have any of the following: <ul style="list-style-type: none"> <li>Availability of human leukocyte antigen-identical or human leukocyte antigen-matched donor or human leukocyte antigen-haploidentical donor</li> <li>History of receiving prior allogeneic hematopoietic stem cell transplant</li> <li>Other malignancy or significant immunodeficiency disorder</li> <li>Active, uncontrolled HCV or HBV infection</li> </ul> </li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>The medication is being prescribed by or in consultation with hematologist/oncologist</li> </ul>

Drug	Investigational
<b>Omisirge (omidubicel-only)</b>	<b>All other uses of Omisirge (omidubicel-only) for conditions not outlined in this policy are considered investigational.</b>

Length of Approval	
Approval	Criteria
<b>Initial authorization</b>	<b>Omisirge (omidubicel-only) may be approved as a one-time infusion.</b>

Length of Approval	
Approval	Criteria
Re-authorization criteria	Future re-authorization of Omisirge (omidubicel-only) is considered investigational.

Documentation Requirements
<p><b>The individual's medical records submitted for review for all conditions should document that medical necessity criteria are met. The record should include the following:</b></p> <ul style="list-style-type: none"> <li>• Individuals is 12 years of age and older</li> <li>• Diagnosis of hematologic malignancies</li> <li>• Individual does not have: <ul style="list-style-type: none"> <li>○ Availability of human leukocyte antigen-identical or human leukocyte antigen-matched donor or human leukocyte antigen-haploidentical donor</li> <li>○ History of receiving prior gene therapy or allogenic hematopoietic stem cell transplant.</li> <li>○ Other malignancy or significant immunodeficiency disorder</li> <li>○ Active, uncontrolled HCV or HBV infection</li> </ul> </li> </ul>

## Coding

Code	Description
<b>HCPCS</b>	
C9399	Unclassified drugs or biologicals (used to code Omisirge)
J3590	Unclassified biologics (used to code Omisirge)

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## Related Information

### Recommended Dose

The single dose of Omisirge consists of a Cultured Fraction (CF) and a Non-cultured Fraction (NF). In each single dose of Omisirge, cultured Fraction consists of a minimum of  $8.0 \times 10^8$  total



viable cells of which a minimum of 8.7% is CD34+ cells and minimum of  $9.2 \times 10^7$  CD34+ cells, while a non-cultured fraction consists of a minimum of  $4.0 \times 10^8$  total viable cells with a minimum of  $2.4 \times 10^7$  CD3+ cells

## Dosing Limits

One intravenous infusion per lifetime

## Other Consideration

- Premedicate patients with diphenhydramine 50mg IV (or 0.5 mg/kg up to a maximum of 50mg) or dexchlorpheniramine 10 mg IV, hydrocortisone 50 mg IV (or 0.5 mg/kg up to a maximum of 50 mg) and acetaminophen 650 mg PO (or 10 mg/kg up to a maximum of 650 mg) approximately 30 to 60 minutes prior to Omisirge infusion
- Do not use methylprednisolone prophylactic in conjunction with Omisirge
- Omisirge (omidubicel-only) label contains black-box warning for infusion reactions, graft versus host disease, engraftment syndrome and graft failure.
- Omisirge usage is contraindicated in individuals with known sensitivity to dimethyl sulfoxide (DMSO), Dextran 40, gentamicin, human serum albumin or bovine material.
- Avoid using a leukodepleting filter.
- Omisirge administration should be under the supervision of a healthcare provider with experience in the treatment of hematologic malignancies.

## Benefit Application

Omisirge (Omidubicel -only) is managed through medical benefit.

## Evidence Review

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## Description

Hematologic malignancies are an umbrella term that talks about cancer in the blood-forming tissue, such as bone marrow, or the cells of the immune system. Different types of hematologic malignancies include lymphoma, leukemia, and multiple myeloma. Leukemia is a type of blood cancer in the blood and bone marrow, where the abnormal white blood cells grow rapidly. Lymphoma is a type of blood cancer in the lymphatic system, where abnormal lymphocytes grow rapidly impairing the immune system. Myeloma is a type of cancer, where abnormal plasma cells grow rapidly. It is estimated that more than 553,000 people in the United States might be suffering from various hematologic malignancies.

Hematologic malignancies is primarily a disease of older adults, with a median age of diagnosis at 65 years or older.

The treatment regimens of hematologic malignancies include radiation therapy, blood transfusions, chimeric antigen receptor (CAR) T-cell therapies and Omisirge (omidubicel-only).

## Omisirge (omidubicel-only)

Omisirge is a nicotinamide modified allogeneic hematopoietic progenitor cell therapy derived from umbilical cord blood indicated for use in individuals 12 years and older with hematologic malignancies who are planned for umbilical cord blood transplantation following myeloablative conditioning to reduce the time to neutrophil recovery and the incidence of infection.

Omisirge (omidubicel-only) contains the allogeneic hematopoietic stem cells from umbilical cord blood (UCB) that are processed and cultured with nicotinamide. Omisirge is manufactured by the proprietary NAM based technology producing enriched HPCs. Umbilical cord blood derived HPCs in presence of NAM leads to the preservation of their stemness, and retained engraftment capacity as shown by rapid neutrophil engraftment and multi lineage immune reconstitution.

The safety and efficacy of Omisirge (omidubicel-only) was studied in a phase 3, open-label, multicenter, randomized clinical trial (P0501) where 125 individuals were randomized to receive Omisirge (n = 62) or umbilical cord blood (UCB) transplantation (n = 63). The inclusion criteria required individuals to have total nucleated viable cell (TNVC) count of  $8.0 \times 10^8$  cells and CD34+ cell count of  $5.6 \times 10^7$ . The efficacy was established based on the time to neutrophil recovery after transplantation and incidence of BMT CTN Grade 2/3 bacterial or Grade 3 fungal infections through Day 100 following transplantation.



The median time to neutrophil recovery was 12 days (95% CI: 10-15 days) in the Omisirge groups versus 22 days (95% CI: 19-25 days) in the UCB group, with the absolute difference of 10 days (95% CI: 6 -14 days). The time to neutrophil recovery was defined as the time from transplantation to the earliest of 3 consecutive measurements on different days with absolute neutrophil count greater than or equal to 0.5 Gi/L assessed with 42 days of follow up. Overall, 87% of individuals in the Omisirge group and 83% in the UCB group achieved neutrophil recovery. The incidence of Grade 2/3 bacterial or Grade 3 fungal infections through 100 days following transplantation was 39% in the Omisirge group compared to 60% in the UCB group with absolute difference of 22% (95% CI: 4%-39%).

One-year post-transplantation data shows that Omisirge led to sustainable clinical benefits such as significant reduction in infectious complications, reduced non-relapse mortality, and no significant increase in the rates of relapse or GVHD.

A planned pooled analysis of 5 multicenter clinical trials worldwide with 105 patients with hematologic malignancies or sickle cell hemoglobinopathy who underwent Omisirge transplantation showed a 3-year estimated overall survival rate of 62.5% and disease-free survival rate of 54.0%. The incidence of grade 2 to 4 acute graft-vs-host disease (aGVHD) at day 100 was 62% in the Omisirge group vs 43% in the control group.

The most common adverse reactions are graft versus host disease, infusion related reactions and infections.

## References

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1. Omisirge (omidubiceL-only). [Prescribing Information]. Boston, MA; Gamida Cell Inc. Revised April 2023.
2. Mitchell H, et al. Stem Cell Transplantation With NiCord® (OmidubiceL) vs Standard UCB in Patients With Leukemia, Lymphoma, and MDS. ClinicalTrials.gov. Available at: Stem Cell Transplantation With NiCord® (OmidubiceL) vs Standard UCB in Patients With Leukemia, Lymphoma, and MDS - Full Text View - ClinicalTrials.gov. Accessed on August 3, 2023.
3. Nelson Chao. Selection of an umbilical cord blood graft for hematopoietic cell transplantation. In: UpToDate. Rosmarin, AG (Ed). UpToDate. Last updated April 7, 2022. Accessed August 3, 2023.

## History

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Date	Comments
09/01/23	New policy, approved August 8, 2023. Added coverage criteria for Omisirge (omidubicel-only) for the treatment of 12 years of age and older with hematologic malignancies who are planned for umbilical cord blood transplantation following myeloablative conditioning to reduce the time to neutrophil recovery and the incidence of infection. HCPCS codes J3590 and C9399 added for Omisirge.

**Disclaimer:** This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. The Company adopts policies after careful review of published peer-reviewed scientific literature, national guidelines and local standards of practice. Since medical technology is constantly changing, the Company reserves the right to review and update policies as appropriate. Member contracts differ in their benefits. Always consult the member benefit booklet or contact a member service representative to determine coverage for a specific medical service or supply. CPT codes, descriptions and materials are copyrighted by the American Medical Association (AMA). ©2023 Premera All Rights Reserved.

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**Washington residents:** You can also file a civil rights complaint with the Washington State Office of the Insurance Commissioner, electronically through the Office of the Insurance Commissioner Complaint Portal available at <https://www.insurance.wa.gov/file-complaint-or-check-your-complaint-status>, or by phone at 800-562-6900, 360-586-0241 (TDD). Complaint forms are available at <https://fortress.wa.gov/oic/online-services/cc/pub/complaintinformation.aspx>.

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## Language Assistance

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