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PHARMACY / MEDICAL POLICY – 5.01.638

Omisirge (omidubicel)

BCBSA Ref. Policy: 8.01.68

Effective Date:	May 1, 2025	RELATED MEDICAL POLICIES:
Last Revised:	Apr. 21, 2025	None
Replaces:	N/A	

Select a hyperlink below to be directed to that section.

Clicking this icon returns you to the hyperlinks menu above.

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-onlv). The US Food and Drug Administration has recently approved Omisirge (omidubicel-onlv), a nicotinamide modified allogeneic hematopoietic progenitor cell therapy derived from cord blood. This policy described when Omisirge (omidubicel-onlv) 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

Omisirge (omidubicel-onlv)	**Omisirge (omidubicel-onlv) is a nicotinamide modified allogeneic hematopoietic progenitor cell therapy derived from cord blood may be considered medically necessary when the following criteria are met:**
	• The individual is aged 12 years or older
	AND
	• Has a diagnosis of hematologic malignancies who are planned for umbilical cord blood transplantation following myeloablative conditioning to reduce both time to neutrophil recovery and the incidence of infection
	AND
	• Is a candidate for myeloablative allogeneic hematopoietic stem cell transplantation (HSCT)
	AND
	• Does not have any of the following:
	  ○ Availability of human leukocyte antigen-identical, human leukocyte antigen-matched, partially human leukocyte antigen-mismatched, or human leukocyte antigen-haploidentical donor
	  ○ History of receiving prior allogenic hematopoietic stem cell transplant
	  ○ Other malignancy or significant immunodeficiency disorder
	  ○ Active, uncontrolled hepatitis C virus (HCV) or hepatitis B virus (HBV) infection
	AND
	• The medication is being prescribed by or in consultation with hematologist/oncologist
	AND
	• Omisirge (omidubicel-onlv) is administered as a one-time infusion

Drug	Investigational
Omisirge (omidubicel-onlv)	**All other uses of Omisirge (omidubicel-onlv) for conditions not outlined in this policy are considered investigational.**

Drug	Investigational
	Repeat treatment of Omisirge (omidubicel-onlv) is considered investigational. **The medications listed in this policy are subject to the product's US Food and Drug Administration (FDA) dosage and administration prescribing information.**

Length of Approval	
Approval	**Criteria**
Initial authorization	**Non-formulary exception reviews for Omisirge (omidubicel-onlv) may be approved up to 12 months.** **All other reviews for Omisirge (omidubicel-onlv) may be approved as a one-time infusion.**
Re-authorization criteria	**Re-authorization of repeat treatment with Omisirge (omidubicel-onlv) is considered investigational.**

Documentation Requirements

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:

- The individual aged 12 years and older
- Diagnosis of hematologic malignancies
- Does not have:
  - Availability of human leukocyte antigen-identical, human leukocyte antigen-matched, human leukocyte antigen-mismatched, or human leukocyte antigen-haploidentical donor
  - History of receiving prior gene therapy or allogenic hematopoietic stem cell transplant.
  - Other malignancy or significant immunodeficiency disorder
  - Active, uncontrolled hepatitis C virus (HCV) or hepatitis B virus (HBV) infection

Coding

Code	Description
HCPCS	

Code	Description
C9399	Unclassified drugs or biologicals (used to code Omisirge)
J3590	Unclassified biologics (used to code Omisirge)

Note: CPT codes, descriptions and materials are copyrighted by the American Medical Association (AMA). HCPCS codes, descriptions and materials are copyrighted by Centers for Medicare Services (CMS).

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 8.0×10^8 total viable cells of which a minimum of 8.7% is CD34+ cells and minimum of 9.2×10^7 CD34+ cells, while a non-cultured fraction consists of a minimum of 4.0×10^8 total viable cells with a minimum of 2.4×10^7 CD3+ cells.

Dosing Limits

One intravenous infusion per lifetime

Other Consideration

- Premedicate individuals 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-onlv) 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-onlv) is managed through medical benefit.

Evidence Review

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 are primary 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-onlv).

Omisirge (omidubicel-onlv)

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-onlv) 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. Umibilical 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 reconstituation.

The safety and efficacy of Omisirge (omidubicel-onlv) 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 x 10^8 cells and CD34+ cell count of 5.6 X 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 individuals 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.

Practice Guidelines and Position Statements

American Academy of Pediatrics

The American Academy of Pediatrics issued a position statement in 2017 concerning cord blood banking and selection, but the statement contained no discussion of ex vivo expansion.

National Comprehensive Cancer Network

Current National Comprehensive Cancer Network (NCCN) guidelines on hematopoietic cell transplantation (v1.2025) state that if a myeloablative conditioning regimen is planned for a recipient of umbilical cord blood, omidubicel-onlv has been shown to shorten the time to engraftment and reduce the risk of some infections (Grade 2A). NCCN guidance on acute lymphoblastic leukemia (v1.2025), acute myeloid leukemia (v1.2025), B-cell lymphomas (v2.2025), chronic myeloid leukemia (v2.2025), or myelodysplastic syndromes (v2.2025), Hodgkin lymphoma (v2.2025) do not provide recommendations on the use of omidubicel or ex vivo expansion of cord blood more generally.

American Society for Transplantation and Cellular Therapy

The American Society for Transplantation and Cellular Therapy published guidelines on the indications for hematopoietic cell transplantation and immune effector cell therapy in 2020; these guidelines did not provide recommendations on the use of omidubicel or ex vivo expansion of cord blood.

Ongoing and Unpublished Clinical Trials

Some currently unpublished trials that might influence this review are listed.

Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			

NCT No.	Trial Name	Planned Enrollment	Completion Date
NCT04260698[a]	Expanded Access of Omidubicel, for Allogeneic Transplantation in Patients With Hematological Malignancies[a]	36	May 2025
NCT02730299[a]	Stem Cell Transplantation With NiCord® (Omidubicel) vs Standard UCB in Patients With Leukemia, Lymphoma, and MDS[a]	125	Feb 2025
NCT03173937	Unrelated Umbilical Cord Blood Transplantation for Severe Aplastic Anemia and Hypo-plastic MDS Using CordIn(TM), Umbilical Cord Blood-Derived Ex Vivo Expanded Stem and Progenitor Cells to Expedite Engraftment and Improve Transplant Outcome	37	Mar 2028

NCT: national clinical trial.

[a] Denotes industry-sponsored or cosponsored trial.

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History

Date	Comments
09/01/23	New policy, approved August 8, 2023. Added coverage criteria for Omisirge (omidubicel-onlv) 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.
08/09/24	Minor edit to add reference policy 8.01.68 Omidubicel as Adjunct Treatment for Hematologic Malignancies to the policy.
12/01/24	Annual Review, approved November 25, 2024. Updated coverage criteria to require that the individual does not have a partially human leukocyte antigen-mismatched donor.
05/01/25	Annual Review, approved April 21, 2025. Clarified that the medications listed in this policy are subject to the product's FDA dosage and administration prescribing

Date	Comments
	information. Clarified that non-formulary exception review authorizations for all drugs listed in this policy may be approved up to 12 months.

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). ©2025 Premera All Rights Reserved.

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