PREMERA HMO

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PHARMACY / MEDICAL POLICY – 5.01.638

Omisirge (omidubicel)

BCBSA Ref. Policy:	8.01.68	
Effective Date:	Mar. 1, 2026	RELATED MEDICAL POLICIES:
Last Revised:	Feb. 10, 2026	N/A
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 and may be considered medically necessary for the treatment of hematologic malignancies when ALL the following criteria are met:**
	• The individual is aged 12 years or older
	AND
	• Has a diagnosis of a hematologic malignancy 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
	
	Omisirge (omidubicel-onlv) is a nicotinamide modified allogeneic hematopoietic progenitor cell therapy derived from cord blood and may be considered medically necessary for the treatment of severe aplastic anemia when ALL the following criteria are met:

Drug	Medical Necessity
	• The individual is aged 6 years or older **AND** • Has a diagnosis of severe aplastic anemia **AND** • Does not have a human leukocyte antigen-identical donor available **AND** • Omisirge (omidubicel-onlv) will be administered following reduced intensity conditioning **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.** **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.**

Length of Approval	
Approval	**Criteria**
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 hematologic malignancies should document that medical necessity criteria are met. The record should include the following:

- The individual is 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

The individual's medical records submitted for review for severe aplastic anemia should document that medical necessity criteria are met. The record should include the following:

- The individual is aged 6 years or older
- Diagnosis of severe aplastic anemia
- Does not have a human leukocyte antigen-identical donor available

Coding

Code	Description
HCPCS	
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, CF consists of a minimum of 8.0 x 10^8 total viable cells of which a minimum of 8.7% is CD34+ cells and minimum of 9.2 x 10^7 CD34+ cells, while a NF consists of a minimum of 4.0 x 10^8 total viable cells with a minimum of 2.4 x 10^7 CD3+ cells.

Dosing Limits

One intravenous infusion per lifetime

Premedication for Individuals with Hematologic Malignancies

- 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.

Premedication for Individuals with Severe Aplastic Anemia

- Administer diphenhydramine 25-50 mg PO or IV and acetaminophen 650 mg PO or weight-based dosing for pediatric patients as per institutional guidelines, approximately 30 minutes prior to OMISIRGE infusion.

Other Consideration

- Omisirge (omidubicel-onlv) label contains black-box warning for autoimmune cytopenias, 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 reconstitution.

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.

Severe Aplastic Anemia

The efficacy of OMISIRGE in individuals with severe aplastic anemia (SAA) was evaluated in study 17- H-0091 (NCT 03173937), an open-label, single center study. The study enrolled individuals with SAA who had intolerance or failure to respond to immunosuppressive therapy and availability of at least one at least 4/8 human leukocyte antigen (HLA)-matched (HLA-A, B, C and DR loci) cord blood unit. Individuals were excluded if there was availability of an HLA identical (12/12) matched related or unrelated donor. The conditioning regimen included horse anti-thymocyte globulin (ATG 40 mg/kg, D-11 to -8), cyclophosphamide (60 mg/kg, D-7 and -6), fludarabine (25 mg/m^2, D-5 to -1) and 2 Gy total body irradiation (TBI) on D-1. Graft versus host disease (GVHD) prophylaxis consisted of tacrolimus/mycophenolate mofetil (MMF). The study aimed to transplant 3-6 individuals with omidubicel combined with CD34+ selected haploidentical cells as a stem cell backup (Cohort 1), followed by the enrollment of 23 individuals receiving a single expanded UCBT (Cohort 2). The primary end point was sustained early engraftment at days 26, 42 and 100. Secondary endpoints include overall survival and standard transplant outcomes.

From August 2017 to June 2025, 18 SAA individuals (3 in Cohort 1 and 15 in Cohort 2) who failed ATG/cyclosporine/eltrombopag were transplanted. At baseline, individuals had pre-transplant ANC 440/µL (IQR 92-615), ferritin 4,265 µg/L (IQR 3,427- 6,804), 72% with HLA allo-immunization. UCB units were matched at a median of 5/8 HLA-alleles; omidubicel contained a median of 2.4 x 10^5(pre-expansion) and 95 x 10^5 (post-expansion) CD34 cells/kg, representing a median 38-fold (IQR 26-57) expansion. With a median follow-up of 2.3 years (range 35 days - 5 years), 17 (94%) achieved neutrophil recovery at a median of 8 days (IQR 7-13), 16 (89%) had platelet recovery at a median of 24 days (IQR 20-30), 17 (94%) reached full (^{3}95%) myeloid chimerism at a median of 14 days (IQR 14-15), and 14 (77%) reached full T-cell chimerism at a median of 21 days (IQR 14-27). Among 17 individuals (with 100+ days of follow-up or off-study), 15 (88%) had sustained engraftment by day 100 and transfusion independence. The cumulative incidence of grade II acute GVHD was 17%, and no occurrences of grade III-IV acute GVHD or chronic GVHD. The GVHD/relapse-free survival and overall survival rate was 94%, with one individual who died at day 62 after adenovirus infection. Immune recovery post-transplant was rapid: At day 100, median CD4 count was 123/µL [IQR 86-322] and median IgG level was 454 (IQR 351 -587); At day 180, median CD4 count was 405/µL [IQR 200-498] and median IgG level was 399 (IQR 314-690). There were 5 (28%) individuals with CMV reactivation requiring treatment and 6 (33%) with EBV reactivation requiring treatment; one individual had CMV disease and one individual had PTLD, both resolved following treatment.

The most common adverse reactions (incidence greater than 20%) are infections, hyperglycemia, skin rash, febrile neutropenia, immune thrombocytopenia, acute kidney injury, acute GvHD, hypertension, hypoxia, and infusion related reactions.

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 (v2.2025) 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 (v2.2025), acute myeloid leukemia (v2.2025), B-cell lymphomas (v2.2025), chronic myeloid leukemia (v3.2025), 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			
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 2032

NCT: national clinical trial.

2026 Update

Reviewed prescribing information for Omisirge (omidubicel-onlv). Added coverage criteria for Omisirge (omidubicel-onlv) for the treatment of adults and pediatric individuals 6 years and older with severe aplastic anemia (SAA) following reduced intensity conditioning.

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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

Date	Comments
	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 information. Clarified that non-formulary exception review authorizations for all drugs listed in this policy may be approved up to 12 months.
03/01/26	Annual Review, approved February 10, 2026. Added coverage criteria for Omisirge (omidubicel-onlv) for the treatment of adults and pediatric individuals 6 years and older with severe aplastic anemia (SAA) following reduced intensity conditioning.

Scope: Medical policies are systematically developed guidelines that serve as a resource for Company staff when determining coverage for specific medical procedures, drugs or devices. Coverage for medical services is subject to the limits and conditions of the member benefit plan. Members and their providers should consult the member benefit booklet or contact a customer service representative to determine whether there are any benefit limitations applicable to this service or supply. This medical policy does not apply to Medicare Advantage.