Blue Cross Blue Shield Blue Care Network of Michigan

Nonprofit corporations and independent licensees of the Blue Cross and Blue Shield Association

Medical benefit drug policies are a source for BCBSM and BCN medical policy information only. These documents are not to be used to determine benefits or reimbursement. Please reference the appropriate certificate or contract for benefit information. This policy may be updated and therefore subject to change.

Effective Date: 06/06/2024

Omisirge® (omidubicel-onlv)

HCPCS: J3590

Policy:

Requests must be supported by submission of chart notes and patient specific documentation.

A. Coverage of the requested drug is provided when all the following are met:
   a. FDA approved indication
   b. FDA approved age
   c. Must have an approval for stem cell transplant on file through the BCBSM/BCN's Human Organ Transplant Program (HOTP)
   d. Umbilical cord blood (UCB) unit human leukocyte antigen (HLA)-matched at 4 or more loci
   e. Must not have any of the following:
      i. A matched sibling or matched unrelated adult donor
      ii. A prior allogenic hematopoietic stem cell transplant (HSCT)
      iii. Marked or 3+ bone marrow (BM) fibrosis
      iv. Chronic lymphocytic leukemia (CLL)
   f. Must not have received prior treatment with Omisirge or any other modified allogeneic hematopoietic progenitor cell therapy derived from cord blood for the treatment of hematologic malignancies
   g. Trial and failure, contraindication, OR intolerance to the preferred drugs as listed in BCBSM/BCN's utilization management medical drug list

B. Quantity Limitations, Authorization Period and Renewal Criteria
   a. Quantity Limits: Align with FDA recommended dosing
   b. Authorization Period: 3 months
   c. Renewal Criteria: Not applicable as no further authorization will be provided

***Note: Coverage and approval duration may differ for Medicare Part B members based on any applicable criteria outlined in Local Coverage Determinations (LCD) or National Coverage Determinations (NCD) as determined by Center for Medicare and Medicaid Services (CMS). See the CMS website at http://www.cms.hhs.gov/. Determination of coverage of Part B drugs is based on medically accepted indications which have supported citations included or approved for inclusion determined by CMS approved compendia.

Background Information:

- Blood cancers are a form of cancer caused by uncontrolled growth of cells in the blood disrupting the ability of blood cells to perform their normal functions. This abnormal cell growth often begins in the bone marrow, which is made up of stem cells that form into different types of blood cells with specific functions in the body. Blood cancers represent about 10% of all cases of cancer each year in the U.S. They can be fatal, with varying survival rates based on multiple factors including the specific type of cancer diagnosed.

- HSCT is potentially curative for patients with certain types of hematological malignancies, such as, acute lymphoblastic leukemia, acute myeloid leukemia, and myelodysplastic syndrome. Based on the origin of hematologic cells, HSCTs are classified as autologous when the patient's own cells are used or allogeneic when the cells are from an HLA-compatible related or unrelated donor.

- The cells used in allogenic transplants can come from three sources: peripheral blood, bone marrow, and UCB. Currently, peripheral blood is the most common source for HSCT. Peripheral blood stem cells are acquired through apheresis from a donor's peripheral vein. Bone marrow stem cells come from the liquid center of the bone and are removed via surgical procedure on a donor's hip bone. Cord blood stem cells are collected from the umbilical cord and placenta after a baby is born. Unlike peripheral blood and bone marrow sources which require a living HLA-matched donor, UCB is donated to a cord blood bank upon birth, frozen, and stored for future use.

- For certain patients, there may be advantages to using cord blood stem cells instead of peripheral blood or bone marrow stem cells. Some potential advantages are increased availability compared to finding an HLA-matched donor; the ability to use a less closely matched HLA-donor compared to those using a peripheral or bone marrow donor; a decreased risk of developing graft-versus-host disease (GVHD); the ease of finding a donor for minority populations who traditionally are less likely to find a living HLA-matched donor; and less risk of transmission of blood-borne illnesses. Some of the disadvantages to using cord blood include a longer time to engraftment compared to bone marrow or peripheral blood due to the number of stem cells per unit of UCB being much smaller; umbilical cord blood transplant (UCBT) is a relatively new procedure in comparison to transplantation of peripheral blood or marrow stem cells; and the lack of knowledge as to how long UCB can be stored until it loses its effectiveness.

- The National Comprehensive Cancer Network (NCCN) Hematopoietic Cell Transplantation (HCT) guidelines include peripheral blood, bone marrow, or UCB as options for allogenic HSCT. Recommendations for choice of hematopoietic source are based on patient-specific factors, such as, disease type, disease stage, urgency of transplant, and patient comorbidities.

- Omisirge is a nicotinamide modified allogeneic hematopoietic progenitor cell therapy derived from cord blood indicated for use in adults and pediatric patients 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.

- Safety and efficacy of Omisirge were evaluated in study P0501, a Phase III, open-label, multicenter, randomized trial of 125 subjects with high-risk hematologic malignancies, who were candidates for myeloablative allogenic-hematopoietic stem cell transplant (HSCT), and had no readily available matched sibling or matched unrelated adult donor. Patients who had a prior allogenic HSCT, marked or 3+ bone marrow fibrosis, or chronic lymphocytic leukemia (CLL) were excluded from the trial. Subjects were randomly assigned 1:1 to Omisirge vs standard UCBT and received myeloablative conditioning and prophylaxis with a calcineurin inhibitor and mycophenolate mofetil for GVHD. Granulocyte-colony stimulating factor (G-CSF) was given once per day starting on day +1 after transplantation until the absolute neutrophil count (ANC) exceeded 1000 cells/μL. Patients in the Omisirge arm had to have UCB HLA-matched at 4 or more loci with a total nucleated cell (TNC) count ≥ 1.8 × 109, a TNC dose of ≥ 1.5 × 107 cells/kg, and CD34+ cell count of ≥ 8 × 106. The primary endpoint was time to neutrophil engraftment. Secondary endpoints were platelet engraftment by 42 days, incidence of grade 2 to 3 bacterial or invasive fungal

infection during the first 100 days, and days alive and out of the hospital for the first 100 days after transplantation. Median time to neutrophil engraftment was 12 days (95% CI: 10, 14) for the Omisirge arm and 22 days (95% CI: 19, 25) for the control arm (p-value < 0.001). The cumulative incidence of neutrophil engraftment was 96% for patients receiving Omisirge and 89% for patients receiving control transplants. The Omisirge arm had faster platelet recovery (55% vs 35% recovery by 42 days; p-value = 0.028), had a lower incidence of first grade 2 to 3 bacterial or invasive fungal infection (37% vs 57%; p-value = 0.027), and spent more time out of hospital during the first 100 days after transplant (median, 61 vs 48 days; p-value = 0.005) than controls. Differences in GVHD and survival between the 2 arms were not statistically significant.

- BCBSM/BCN's Human Organ Transplant Program (HOTP) is responsible for approval of all HSCTs prior to the start of treatment. Approval of the patient's HSCT must be on file prior to determination of Omisirge's use in any patient.

- There are no studies to support use of Omisirge following failure or after treatment with another modified allogeneic hematopoietic progenitor cell therapy derived from cord blood for the treatment of hematologic malignancies.

References:

1. Omisirge [prescribing information]. Boston, MA: Gamida Cell Inc.; February 2024.
2. 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 Oct 21; 138 (16): 1429 - 40.
3. National Comprehensive Cancer Network. Hematopoietic Cell Transplantation (HCT) (Version 3.2023). 2023 Oct 9. Available at: https://www.nccn.org/professionals/physician_gls/pdf/hct.pdf. Accessed on April 18, 2024.
4. Leukemia and Lymphoma Society. Cord blood stem cell transplantation facts. 2016 May. Available at: https://www.lls.org/sites/default/files/2021-05/FS2_Cord_Blood_Transplantation_6_16FINAL.pdf. Accessed on April 26, 2023.

<table>
<tr><th colspan="3">Policy History</th></tr>
<tr><th>#</th><th>Date</th><th>Change Description</th></tr>
<tr><td>1.2</td><td>Effective Date: 06/06/2024</td><td>Annual review of criteria was performed, no changes were made</td></tr>
<tr><td>1.1</td><td>Effective Date: 02/01/2024</td><td>UM medical management system update for MAPPO and BCNA
<table><tr><th>Line of Business</th><th>PA Required in Medical Management System (Yes/No)</th></tr><tr><td>BCBS</td><td>Yes</td></tr><tr><td>BCN</td><td>Yes</td></tr><tr><td>MAPPO</td><td>Yes</td></tr><tr><td>BCNA</td><td>Yes</td></tr></table></td></tr>
<tr><td>1.0</td><td>Effective Date: 06/08/2023</td><td>New policy. UM medical management system update for BCBS and BCN
<table><tr><th>Line of Business</th><th>PA Required in Medical Management System (Yes/No)</th></tr><tr><td>BCBS</td><td>Yes</td></tr><tr><td>BCN</td><td>Yes</td></tr><tr><td>MAPPO</td><td>No</td></tr><tr><td>BCNA</td><td>No</td></tr></table></td></tr>
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** The prescribing information for a drug is subject to change. To ensure you are reading the most current information it is advised that you reference the most updated prescribing information by visiting the drug or manufacturer website or http://dailymed.nlm.nih.gov/dailymed/index.cfm.*

Blue Cross Blue Shield/Blue Care Network of Michigan
Medication Authorization Request Form

Blue Cross Blue Shield Blue Care Network of Michigan

Nonprofit corporations and independent licensees of the Blue Cross and Blue Shield Association

This form is to be used by participating physicians to obtain coverage for **drugs covered under the medical benefit**. For commercial members only, please complete this form and submit via fax to 1-877-325-5979. If you have any questions regarding this process, please contact BCBSM Provider Relations and Servicing or the Medical Drug Helpdesk at 1-800-437-3803 for assistance.

PATIENT INFORMATION	PHYSICIAN INFORMATION
Name	**Name**
ID Number	**Specialty**
D.O.B. ☐Male ☐Female	**Address**
Diagnosis	**City /State/Zip**
Drug Name	**Phone/Fax: P**: ( ) - **F**: ( ) -
Dose and Quantity	**NPI**
Directions	**Contact Person**
Date of Service(s)	**Contact Person Phone / Ext.**

STEP 1: DISEASE STATE INFORMATION

1. Is this request for: ☐ Initiation ☐ Continuation *Date patient started therapy:* _____
2. Administered by patient or a medical professional? ☐ patient (self) ☐ health care professional (physician, nurse, etc.)
3. Site of administration? ☐ Provider office/Home infusion ☐ Other: _____
   ☐ Hospital outpatient facility (go to #4) *Reason for Hospital Outpatient administration:* _____
   ☐ Hospital inpatient facility for Car-T therapy only (for example: Kymriah, Yescarta, or Tecartus) (go to #5)
4. Please specify location of administration if hospital outpatient infusion: _____
5. Please specify location of administration if hospital inpatient infusion: _____
6. Please provide the NPI number for the place of administration: _____
7. **Initiation AND Continuation of therapy:**
   a. What is the patient's diagnosis? _____
   b. What other medication has the patient received for their condition? Please list_____
      i. Please describe the response to previous therapies:
      _____
   c. Will the patient be receiving any other treatment for the listed condition while on this medication? Please list:
      _____
   d. Please list any labs values important for diagnosing or monitoring this patient's condition:
      _____
8. **Continuation of therapy:**
   a. Has the patient progressed while on this medication? ☐ yes ☐ no
   b. How has the patient's condition changed while on this medication?
      ☐ Improved: Please describe: _____
      ☐ Stable: please describe: _____
      ☐ Worsened; Please describe: _____
      ☐ Other; Please describe: _____

Chart notes are required for the processing of all requests. Please add any other supporting medical information necessary for our review **(required)**

Coverage will not be provided if the prescribing physician's signature and date are not reflected on this document.

☐ Request for expedited review: I certify that applying the standard review time frame may seriously jeopardize the life or health of the member or the member's ability to regain maximum function

Physician's Name **Physician Signature** **Date**

Step 2: Checklist	☐ Form Completely Filled Out ☐ Provide chart notes	☐ Attach test results
Step 3: Submit	**By Fax: BCBSM Specialty Pharmacy Mailbox 1-877-325-5979**	**By Mail: BCBSM Specialty Pharmacy Program P.O. Box 312320, Detroit, MI 48231-2320**

7/26/2018, 9/18/2018; 1/31/2020; 3/17/2020; 8/9/2021