Molina Clinical Policy
Omisirge (omidubicel-onlv)
Policy No. 435

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DISCLAIMER

This Molina Clinical Policy (MCP) is intended to facilitate the Utilization Management process. Policies are not a supplementation or recommendation for treatment; Providers are solely responsible for the diagnosis, treatment, and clinical recommendations for the Member. It expresses Molina's determination as to whether certain services or supplies are medically necessary, experimental, investigational, or cosmetic for purposes of determining appropriateness of payment. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered (e.g., will be paid for by Molina) for a particular Member. The Member's benefit plan determines coverage – each benefit plan defines which services are covered, which are excluded, and which are subject to dollar caps or other limits. Members and their Providers will need to consult the Member's benefit plan to determine if there are any exclusion(s) or other benefit limitations applicable to this service or supply. If there is a discrepancy between this policy and a Member's plan of benefits, the benefits plan will govern. In addition, coverage may be mandated by applicable legal requirements of a State, the Federal government or CMS for Medicare and Medicaid Members. CMS's Coverage Database can be found on the CMS website. The coverage directive(s) and criteria from an existing National Coverage Determination (NCD) or Local Coverage Determination (LCD) will supersede the contents of this MCP and provide the directive for all Medicare members. References included were accurate at the time of policy approval and publication.

OVERVIEW

This policy addresses the use of Omisirge for individuals with hematologic malignancies or aplastic anemia undergoing allogeneic hematopoietic stem cell transplantation (HSCT). Omisirge is an ex vivo–expanded, cord blood–derived allogeneic stem cell therapy indicated for use following myeloablative conditioning. Omisirge serves as an alternative donor source for those who lack a suitably matched donor and are eligible for umbilical cord blood transplantation. Eligible conditions include, but are not limited to, acute lymphoblastic leukemia, acute myeloid leukemia, chronic myeloid leukemia, myelodysplastic syndromes, Hodgkin lymphoma, and severe aplastic anemia.

Acute Lymphocytic Leukemia (ALL)

Acute leukemias comprise a heterogeneous group of neoplastic disorders arising from malignant transformation of hematopoietic stem cells. Malignant transformation typically involves chromosomal rearrangements (translocations), deletions, or additions, which disturb normal control of cell division, allowing affected cells to multiply without restraint. ALL is believed to arise from malignant transformation of B- or T-cell progenitor cells. The disease is characterized by the accumulation of lymphoblasts in the marrow or in various extramedullary sites. Clones, or leukemic cells, arising from such transformation influence development of white blood cells or leukocytes, and rapidly proliferate in bone marrow, replacing normal cells and causing anemia, thrombocytopenia, and granulocytopenia. Without treatment, ALL usually progresses quickly (Stock & Estrov 2025; [1-2] DynaMed 2024).

The World Health Organization (2022) classifies ALL as either B lymphoblastic leukemia or T lymphoblastic leukemia. B lymphoblastic leukemia is subdivided by the presence or absence of specific recurrent genetic abnormalities [t(9;22)], MLL rearrangement, t(12;21), hyperdiploidy, hypodiploidy, t(5;14), and t(1;19). Current treatment decisions rely on the immunophenotype (early-pre-B ALL, pre-B ALL, B-cell ALL, or T-cell ALL) and cytogenetics of affected cells ([1] NCI 2025; [2] NCI 2025).

Chronic Myeloid Leukemia (CML)

Chronic Myelogenous Leukemia (CML or chronic granulocytic leukemia or chronic myeloid leukemia) is a disease of both bone marrow and blood. It is classified as a myeloproliferative neoplasm. It most often occurs in middle-aged adults. In CML, too many granulocytes (neutrophils, eosinophils, and basophils), and not enough red blood cells and platelets develop from bone marrow myeloid stem cells. This can lead to anemia, infection, and problems with hemostasis. Signs and symptoms of CML may include night sweats, fever, exhaustion, and weight loss. It is thought that CML is due to an acquired genetic mutation called the Philadelphia chromosome (Ph) on chromosome 22. The Philadelphia chromosome (Ph) results in tyrosine kinase overactivity in the bone marrow, and it is this enzyme that causes too many of the myeloid stem cells to take the path of converting into granulocytes, rather than red blood cells or platelets. CML can occur at any age, however it most often appears in adults with a median age of 60-65 years. There are three phases of the disease that consist of an initial (indolent) chronic phase, lasting a median of 3 years, which typically transforms into an accelerated phase, followed by a blast phase or "blast crisis," which is usually the terminal event. Conventional-dose regimens used for chronic-phase disease can induce multiple remissions and delay the onset of blast crisis to a median of 4–6 years. However, successive remissions are invariably shorter and more difficult to achieve than their predecessors ([3] NCI 2025; [4] NCI 2025; [1] NMPD date unknown).

Myelodysplastic Syndrome

Myelodysplastic syndromes (MDS) consist of a heterogeneous group of malignant hematopoietic stem cell disorders characterized by dysplastic and ineffective blood cell production and a varying risk of transformation to acute leukemia. Patients with MDS have reduced production of red blood cells, platelets, and mature granulocytes – abnormalities often result in anemia, bleeding, and increased risk of infection. MDS occurs predominantly in older patients (≥ 60 years). The median age at diagnosis is 70 years; however, patients as young as 2 years have been reported. Older men are more commonly affected by MDS. The isolated chromosome 5q deletion subtype (del5q) is more common in women. Signs and symptoms at presentation of MDS are nonspecific. Many patients are asymptomatic at diagnosis and only come to the provider's attention based upon abnormalities found on routine blood counts (e.g., anemia, neutropenia, and thrombocytopenia). Others present with symptoms or complications resulting from a previously unrecognized cytopenia (e.g., infection, fatigue). MDS is diagnosed based on an evaluation of the bone marrow and peripheral smear. The revised International Prognostic Scoring System (IPSS-R) should be used to incorporate information on bone marrow blast percentage, karyotype, and cytopenias for the purpose of stratifying the MDS into risk groups to guide management. Patients with a very low (≤1.5 points) or low (>1.5 to 3 points) IPSS-R score are primarily treated with supportive care or low intensity therapies such as azacitidine, decitabine, or immunosuppressive therapy. Patients with a high (>4.5 to 6 points) or very high (>6 points) IPSS-R score with a good performance status are primarily treated with combination chemotherapy or allogeneic hematopoietic cell transplantation (HCT) to alter the disease course. Treatment options for patients with an intermediate-risk (>3 to 4.5 points) IPSS-R score include those therapies used for patients with low- or very low-risk IPSS-R scores, and the more intensive therapies typically used for patients with high- or very high-risk IPSS-R scores (Chao 2025; Holmberg & Sandmaier 2024; Negrin 2025; Sekeres & Platzbecker 2024; Aster & Stone 2024; Negrin 2025; NLM 2016; [3] DynaMed 2024; MSF date unknown).

Acute Myeloid Leukemia (AML)

AML arises when a normal precursor cell transforms into a malignant cell by a complex, multistep process involving an accumulation of genetic mutations that alter normal growth and cell behavior. This transformed myeloid cell and the subsequent clonal expansion of abnormal cells continue to proliferate without differentiating (maturing) into mature blood cells. After release into the blood stream, leukemic cells can infiltrate any organ or site and often spread to the liver, spleen, lymph nodes, CNS. Acute myeloid leukemia (AML) is also called acute myeloblastic leukemia, acute myelogenous leukemia, and acute nonlymphocytic leukemia (ANLL). AML is an aggressive disease in which too many myeloblasts or immature white blood cells are found in the bone marrow and blood. Two methods are commonly used to classify AML. The French American British (FAB) Cooperative Group classification is based on morphological-histochemical cell characteristics and identifies eight subtypes of AML and categorized as M0 - M7 ([2-7] NMDP, date unknown).

The World Health Organization (WHO 2022) Classification System incorporates clinical, morphologic, immunophenotypic, cytogenetic and molecular markers that can be used to direct treatment that include five major subcategories of AML:

1. AML with recurrent genetic abnormalities
2. AML with multilineage dysplasia
3. Therapy-related AML and MDS
4. AML not otherwise categorized
5. Acute leukemia of ambiguous lineage

The National Cancer Institute ([5] NCI, 2025) notes that certain gene and cytogenetic abnormalities have been identified as high-risk for a poor prognosis with chemotherapy. These include internal tandem duplication of the FLT3 (FMS-related tyrosine kinase 3) gene, mutation of the tp53 gene, deletions of the long arms or monosomies of chromosomes 5 or 7; translocations or inversions of chromosome 3, t(6;9), t(9;22) and abnormalities of chromosome 11q23, t(10;11) translocation, t(1;22)(p13;q13) translocation, trisomy 8, and certain antigens/glycoproteins. Most children and adults with newly diagnosed AML undergo systemic multiagent chemotherapy designed to induce disease remission (induction therapy). These aggressive treatment approaches produce severe bone marrow aplasia and suppression of the hematopoietic system, which may lead to morbidity and mortality from infection or hemorrhage. Therefore, therapy is combined with appropriate supportive care involving early recognition and treatment of infection and, when necessary, red blood cell and platelet transfusions. With effective anticancer agents and appropriate supportive care, complete remission (CR) occurs in 75% to 90% of the children and 60% to 70% of the adults with AML. Even with treatment most patients relapse and die from leukemia. Among those who achieve first CR (CR1), disease-free survival has averaged only 40% at 5 years in children and overall survival with or without disease has averaged only 25% at ≥ 3 years in adults.

Since undetected minimal residual disease is a major cause of relapse, patients in CR usually undergo a second phase and, often, a third phase of multiagent chemotherapy known as consolidation therapy and intensification therapy, respectively, which frequently employ different agents and/or higher doses than used in induction therapy to eradicate residual disease. High-dose chemotherapy may be administered for this purpose but also ablates normal marrow (myeloablation), thereby destroying the hematopoietic system.

Hodgkin Lymphoma

Lymphomas are neoplasms of the lymphatic system, a network of blood-filtering tissues that help fight infection and disease found in the lymph nodes, spleen, thymus gland, adenoids, tonsils, and bone marrow. Lymphomas affect lymphocytes which are specialized white blood cells responsible for immunity. Hodgkin lymphoma spreads in an orderly manner, typically from one group of lymph nodes to another. Symptoms include swollen lymph nodes (particularly where the lymphoma originates), fever, night sweats, fatigue, and weight loss ([6,7] NCI 2025; CDC 2017).

Hodgkin lymphoma is marked by the presence of Reed-Sternberg cells which are large, abnormal lymphocytes (a type of white blood cell) that can contain more than one nucleus. The two types of Hodgkin lymphoma are classical and nodular lymphocyte-predominant Hodgkin lymphoma (NLPHL). Most cases are the classical type which includes four subtypes: nodular sclerosing; mixed cellularity; lymphocyte-depleted; lymphocyte-rich classic. Among non-classical types, NLPHL is rare and typically grows slower than classic Hodgkin lymphoma. This type presents as a swollen lymph node in the neck, chest, armpit, or groin; many have no additional signs or symptoms of cancer at diagnosis. Treatment typically differs from classic Hodgkin lymphoma ([6,7] NCI 2025).

Risk factors for adult Hodkin lymphoma include early or late adulthood, male sex, past Epstein-Barr (EBV) infection, and a family history of Hodgkin lymphoma. Among children and adolescents diagnosed with Hodgkin lymphoma, the nodular-sclerosing type is often diagnosed in older children and adolescents and typically presents as a chest mass at diagnosis. Mixed cellularity Hodgkin lymphoma is typically diagnosed in those age 10 and under; it presents as lymph nodes in the neck and there is a connection to EBV infection. Lymphocyte-rich classic Hodgkin lymphoma is rare in children; upon viewing under a microscope, tissue samples include Reed-Sternberg cells as well as normal lymphocytes and other blood cells. Lymphocyte-depleted Hodgkin lymphoma is also rare in children and is typically found in adults and adults with HIV/AIDS. Microscope analysis shows large, oddly shaped cancer cells and few normal lymphocytes and other blood cells ([6,7] NCI 2025).

This form is usually curable in some patients who receive prompt treatment. In 2021, there were 8,830 new cases diagnosed in the United States; this accounts for 0.5% of all new cancer cases. An estimated 960 people died in 2021 (0.2% of all cancer deaths). The five-year relative survival rate for Hodgkin lymphoma is 88.3%. ([6,7] NCI, 2025). Rates of new diagnoses of Hodgkin lymphoma (per 100,000 people) are slightly higher in males (2.8) than females (2.3). By age, rates are highest in those ages 80-84 (4.1), ages 20-24 (4.0), ages 25-29 (3.8), ages 75-79 (3.8), ages 70-74 (3.6). By race and ethnicity, new diagnoses are highest in White (2.6), Black (2.5), and Hispanic (2.2) populations (CDC, 2017).

Severe aplastic anemia (SAA)

Severe aplastic anemia is a life-threatening bone marrow failure disorder characterized by hypocellular marrow and peripheral pancytopenia, resulting in anemia, neutropenia, and thrombocytopenia. Patients are at high risk for infection, bleeding, and fatigue-related complications. Severe aplastic anemia is defined by bone marrow hypocellularity (<25%) in combination with at least two cytopenias (ANC <500/μL, platelets <20,000/μL, or reticulocytes <60,000/μL), consistent with modified Camitta criteria (Scheinberg et al. ASH 2026).

Omisirge (Omidubicel-onlv)

Omisirge (Omidubicel-onlv) is an ex vivo expanded hematopoietic progenitor cell and non-expanded myeloid and lymphoid cell product derived from a single umbilical cord blood unit. Omidubicel-onlv utilizes the small molecule nicotinamide to inhibit differentiation and to increase the migration, bone marrow homing and engraftment efficiency of hematopoietic progenitor cells. Omidubicel-onlv is cryopreserved and composed of the cultured fraction (CF) and non-cultured fraction (NF) of the same unit of cord blood. The CF is the ex vivo expanded, umbilical cord blood derived hematopoietic CD34+ progenitor cells. For some high-risk hematologic malignancies, allogeneic hematopoietic stem cell transplantation (HSCT) is the only potential curative treatment; however, about 40% of patients do not receive transplant due to many factors, including inability to find a matched donor. For those patients able to receive HSCT, they may develop complications such as graft-versus-host disease, infection and increased early treatment-related morbidity and mortality due to delayed hematopoietic and immunologic recovery. Omidubicel addresses these

challenges by providing rapid and durable engraftment by expanding hematopoietic stem and progenitor cells leading to faster neutrophil recovery after myeloablative conditioning. There are approximately 2000-2500 patients in the United States with blood malignancies that are eligible for transplant, but unable to find a donor (Horwitz et al. 2021).

Regulatory Status
Omisirge (omidubicel-onlv) was FDA (Food and Drug Administration) approved on April 17, 2023, for adult and pediatric patients 12 years and older with hematologic malignancies (ALL, CML, AML, MDS, and Hodgkin Lymphoma) and severe aplastic anemia planned for umbilical cord blood transplantation (UCBT) following a myeloablative conditioning regimen. The advantage over umbilical cord blood is Omisirge's (Omidubicel-onlv) demonstrated ability to reduce the time to neutrophil recovery and reduction in incidence of infection. In 2025 Omisirge received approval for an additional indication, severe aplastic anemia.

RELATED POLICIES

MCP-459: Pre-Transplant and Transplant Evaluations
MCP-455: Hematopoietic Stem Cell Transplantation for Blood Cancers
MCP-456: Hematopoietic Stem Cell Transplantation for Blood Disorders

COVERAGE POLICY

All transplants require prior authorization from the Corporate Transplant Department. Solid organ transplant requests will be reviewed by the Corporate Senior Medical Director or qualified clinical designee. All other transplants will be reviewed by the Corporate Senior Medical Director or covering Medical Director. If the criteria are met using appropriate NCD and/or LCD guidelines, State regulations, and/or MCP policies the Corporate Senior Medical Director's designee can approve the requested transplant.

Office visits with participating Providers do NOT require prior authorization. Providers should see the Member in office visits as soon as possible and without delay. Failure to see the Member in office visits may be considered a serious quality of care concern.

Please see *MCP-459 Pre-Transplant and Transplant Evaluations* for additional criteria and information.

Criteria for Omisirge (Omidubicel-onlv)

Omisirge (omidubicel-onlv) may be **considered medically necessary** for members who meet criteria for umbilical cord blood transplant when ALL the following criteria are met.

1. All applicable pre-transplant criteria are met as stipulated in *MCP 459 Pre-Transplant and Transplant Evaluations*
2. Documentation of a hematologic malignancy without symptoms of CNS disease (e.g., Acute lymphocytic leukemia, Chronic myeloid leukemia, Myelodysplastic syndromes, Acute myeloid leukemia, Hodgkin lymphoma, Non-Hodgkin lymphoma, Acute lymphoblastic leukemia, Severe aplastic anemia, etc.)
3. Members with hematologic malignancies are between 12 and 65 years of age
4. Members with aplastic anemia are greater than or equal to 6 years of age
5. Member does not have an allogeneic human leukocyte antigen (HLA) matched donor OR had allogeneic hematopoietic stem cell transplantation in the past
6. Favorable Karnofsky/Lansky Performance Status
7. Member does not have an active or uncontrolled infection of any kind
8. Member does not have any other documented current active non-hematologic malignancy

9. Member does not have known hypersensitivity to dimethyl sulfoxide (DMSO), Dextran 40, gentamicin, human serum albumin, or bovine products

10. For women of child-bearing potential: Documentation or attestation that member is not pregnant or lactating

CONTINUATION OF THERAPY: Omisirge is approved for one time use.

DOCUMENTATION REQUIREMENTS: Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational, or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

SUMMARY OF MEDICAL EVIDENCE

Omisirge (Omidubicel-onlv) was studied in a phase 3 (NCT02730299), randomized, open label trial in patients aged 12 to 65 years with high-risk hematologic malignancies who were also candidates for myeloablative allogeneic HSCT. Patients were randomized (n=125) to receive either Omisirge (n=62) or a standard umbilical cord blood graft (n=63). All patients received myeloablative preparative regimens and graft versus host disease prophylaxis with tacrolimus or cyclosporin plus mycophenolate mofetil. The primary endpoint was time to neutrophil engraftment, Horowitz et al. (2021).

Key inclusion criteria:
Patients were 12 to 65 years of age with high-risk hematologic malignancies (AML, ALL, CML, Lymphoma, or other rare leukemias). All participants had sufficient physiologic reserve and were considered candidates for myeloablative allo-HSCT but did not have an optimal donor source of cells (HLA -Matched donor).

Key exclusion criteria:
Participants with a history of prior stem cell transplant, active central nervous system disease, active infection, other nonhematologic malignancies or pregnant / lactating females, were not allowed to participate in the study.

Both study arms had equivalent, available UCB units that were HLA–matched at four or more loci (HLA-A and -B at the antigen level, and DRB1 at the allele level) with a total nucleated cell (TNC) count ≥1.8 × 10^9. These UCB units were to be used as either a backup for the Omisirge arm or used in the UCB only arm.

Multiple conditioning regimens were used, including total body irradiation–based or chemotherapy-based options. Demographic and baseline patient characteristics in the UCB & Omisirge arms were similar. The efficacy of Omisirge was established based on time to neutrophil recovery following transplantation and the incidence of Blood and Marrow Transplant Clinical Trials Network Grade 2/3 bacterial or Grade 3 fungal infections through Day 100 following transplantation.

Efficacy
In the Omisirge (Omidubicel-onlv) group, patients had faster platelet recovery (55% vs. 35%), a lower incidence of bacterial and invasive fungal infections (37% vs. 57%) and had less in-hospital days within the first 100 days post-transplant (median, 61 vs. 48) in comparison to the control group. The cumulative incidence of neutrophil engraftment by Day 42 following transplantation in the Omisirge group (as-treated population, n = 52) was 96%, with a median time to engraftment of 10 days (95% CI, 8 to 13 days) compared with 89% for patients in the standard UCBT group (n = 56) with a median time to engraftment of 20 days (95% CI, 18 to 24 days) (P <0.001). The cumulative incidence of platelet engraftment by Day 42 for patients assigned to Omisirge was 55% compared to 35% for patients assigned to standard UCBT (P = 0.028). For the patients transplanted with Omisirge, the cumulative incidence of platelet engraftment by Day 100 was 83%, with a median time to engraftment of 37 days (95% CI, 33–42 days), compared to 73%, with a median time to engraftment of 50 days (95% CI, 42–58 days), for standard UCBT (P = 0.023). Full donor chimerism (defined as >90% in the whole blood fraction) was observed at Day 30 and Day 100 after transplantation in all but two Omisirge recipients; one experienced early relapse and the other experienced primary graft failure. Six standard UCBT recipients experienced graft failure on Day 42. The remaining evaluable standard UCBT recipients had full donor chimerism on Day 30 and Day 100 after transplantation.

Among patients who received a transplant who were randomly assigned to Omisirge (n = 59) or standard UCBT (n = 58), the incidence of Grade 2 to 4 acute graft-versus-host disease (aGVHD) at Day 100 was similar, at 56% versus 43%, respectively (13% difference: 95% CI, −6% to 30%; P = 0.18). The incidence of Grade 3 or 4 aGVHD at Day 100 was also similar in the Omisirge and standard UCBT groups, at 14% versus 21%, respectively (−7% difference; 95% CI, −21% to 7%; P = 0.33). The cumulative incidence of all chronic GVHD (cGVHD) at 1 year was 35% for the Omisirge group and 29% for the controls (6% difference; 95% CI, −14% to 25%; P = 0.57). The 1-year cumulative incidence of moderate to severe cGVHD was 27% for the Omisirge group and 21% for the controls (6% difference; 95% CI, −11% to 24%; P = 0.49).

Patients in the Omisirge group spent a median of 61 days (range, 0–89 days) out of the hospital in the first 100 days following transplant. In the standard UCBT group, patients spent a median of 48 days out of the hospital in the first 100 days after transplant (range, 0–84 days) (P value for difference = 0.005). Additionally, the median time from transplant to discharge from the hospital was 27 days in the Omisirge group versus 35 days in the standard UCBT group, respectively (P = 0.005).

The cumulative incidence of first Grade 2 or 3 bacterial or invasive fungal infections was 37% and 57% for Omisirge and standard UCBT recipients, respectively (P = 0.03). The rate of first Grade 3 viral infection within the first year after transplantation was 10% among Omisirge recipients and 26% for standard UCBT recipients, respectively (P = 0.02).

The median follow-up of all patients was 10 months after transplantation (range, 1–19 months). Using ITT (intention to treat) analysis, the cumulative incidence of nonrelapse mortality (NRM) at 210 days after random assignment was 11% for the Omisirge group and 24% for the control group (P = 0.09). The cumulative incidence of disease relapse at 15 months after random assignment was 25% for the Omisirge group and 17% for the control group (P = 0.32). During the time from random assignment to transplantation, relapse was reported in four patients in the Omisirge group and four patients in the standard UCBT group. Among these, relapse prevented two patients in the Omisirge group and three patients in the standard UCBT group from receiving a transplant by Day 90.

The adjusted hazard ratio (HR) for treatment failure (relapse or death, inverse of relapse-free survival [RFS]) with Omisirge versus standard UCB was 0.79 (95% CI, 0.45–1.38; P = 0.4). The adjusted HR for mortality with Omisirge versus standard UCBT was 0.57 (95% CI, 0.3–1.1; P = 0.09). The 1-year GVHD-free RFS for the Omisirge group was 36% compared to 45% for standard UCBT (P = 0.56).

Safety

Fatal adverse reactions occurred in 17% of patients treated with Omisirge (Omidubicel-onlv), including infection (6%), acute GvHD (6%), veno-occlusive disease (VOD)/sinusoidal obstruction syndrome (SOS) (2%), thrombotic thrombocytopenic purpura (TTP)/thrombotic microangiopathy (TMA) (2%), and pulmonary hemorrhage (2%). Fatal adverse reactions occurred in 29% of subjects treated with UCB, including infection/sepsis (11%), respiratory disorders (11%), GvHD (5%), and VOD/SOS (2%). Infusion reactions occurred in 56% of patients that received Omisirge (Omidubicel-onlv) and 71% of patients that received UCB. The most common infusion reactions were hypertension, mucosal inflammation, arrythmia, and fatigue. Infections (Grades 1-3) following transplantation with Omisirge (Omidubicel-onlv) vs. UCB for viral infections were 75% versus 80%, bacterial infections 65% versus 80% and fungal infections 21% versus 27% respectively. Acute and chronic GvHD occurred following treatment with OMISIRGE. Moderate to severe chronic GvHD was reported in 23% of patients in the Omisirge (Omidubicel-onlv) arm versus 20% in the control arm. Primary graft failure (defined as failure to achieve an absolute neutrophil count greater than or equal to 0.5 Gi/L by Day 42 after transplantation) occurred in 2% of patients treated with Omisirge (omidubicel-onlv), compared to 11% of patients receiving UCB. Disease relapse occurred in 21% of patients treated with Omisirge (Omidubicel-onlv) compared to 13% of patients that received standard UCB. Other adverse reactions reported ≥ 10% incidence include pain, mucosal inflammation, hypertension, and gastrointestinal toxicity. (Horwitz, 2021; Omisirge PI, 2023).

A substudy (Szabolcs 2023) found that immune reconstitution of major immune subtypes began as early as 7 days post-transplantation. It was hypothesized that earlier reconstitution may in part explain the reduced rate of infections post-transplant.

Outcomes from trial NCT04260698 phase 3 expanded access for Omidubicel were reported by Horowitz (2025). This was an open label, single arm, expanded access study. There was no control group. The expanded access program patient cohort (EAP) demonstrated similar trends to the Omisirge treatment arm with respect to engraftment kinetics

and decreased infections as compared to umbilical cord blood. Non-relapse mortality was also lower in the EAP cohort. trial.

Omisirge was recently approved for a new indication, severe aplastic anemia. This approval is based in part on the study NCT03173937. This is an open-label, single-center study designed to look at the safety and efficacy of Omisirge in severe aplastic anemia and myelodysplastic syndrome. Data has not been published in a peer reviewed journal but abstract posters were presented at ASH and the FDA has allowed the use of this data to expand the indication of Omisirge to include aplastic anemia.

Patients enrolled in study NCT03173937 had severe aplastic anemia and were refractory or intolerant to immunosuppressive therapy and lacked a fully matched donor but had a ≥4/8 HLA-matched cord blood unit available. A total of 17 patients were treated, with 14 receiving OMISIRGE alone (included in the efficacy analysis). Patients had a median age of 17 years, significant baseline cytopenias, and a high burden of comorbidities. All underwent reduced-intensity conditioning followed by OMISIRGE infusion, with standard graft-versus-host disease prophylaxis. The primary endpoint was early and sustained neutrophil recovery (ANC ≥500/μL by Day 26 and maintained through Days 42 and 100), with secondary endpoints including time to neutrophil engraftment, red blood cell and platelet recovery, and transfusion independence. Among the 14 patients with severe aplastic anemia treated with OMISIRGE, 86% achieved early and sustained neutrophil recovery by Day 100 (95% CI: 57%–98%), with a median time to neutrophil engraftment of 11 days (range: 7–20). Red blood cell transfusion independence was achieved in 86% of patients, with a median time of 58.5 days (range: 42–446). Platelet recovery to ≥20,000/μL within one year was also observed in 86% of patients, with a median time of 31.5 days (range: 20–197). Additionally, 79% of patients achieved platelet transfusion independence, with a median time of 53 days (range: 43–93), (FDA package insert, 2026 and ASH Annual Meeting Abstract; NCT03173937).

SUPPLEMENTAL INFORMATION

Omisirge (Omidubicel-onlv) has a **black box warning** for infusion reactions, graft versus host disease (GvHD), engraftment syndrome, graft failure and autoimmune cytopenias. Infusion reactions, GvHD, engraftment syndrome and graft failure may be fatal

There is no available data regarding the use of Omisirge (Omidubicel-onlv) in pregnancy and lactation. Pregnant and lactating members were explicitly excluded from study populations. Pregnancy status of females with reproductive potential should be verified prior to starting the conditioning regimen for Omisirge (Omidubicel-onlv).

CODING & BILLING INFORMATION

CPT (Current Procedural Terminology)

Code	Description
96413	Chemotherapy administration, intravenous infusion technique; up to 1 hour, single or initial substance/drug
96415	Chemotherapy administration, intravenous infusion technique; each additional hour (List separately in addition to code for primary procedure)

HCPCS (Healthcare Common Procedure Coding System)

Code	Description
C9399	Unclassified drugs or biologicals [when specified as Omisirge (Omidubicel-onlv)]
J3590	Unclassified biologics [when specified as Omisirge (Omidubicel-onlv)]

CODING DISCLAIMER: Codes listed in this policy are for reference purposes only and may not be all-inclusive. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does not guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry standard coding practices for all submissions. When improper billing and coding is not followed, Molina has the right to reject/deny the claim and recover claim payment(s). Due to changing industry practices, Molina reserves the right to revise this policy as needed.

APPROVAL HISTORY

06/10/2026	Policy revised to include new indication for severe aplastic anemia consistent with updated FDA label. Updated medical evidence summary and references. Independent Review Organization Peer Review on June 5, 2026, by a practicing, board-certified physician with a specialty in Hematology and Medical Oncology.
06/11/2025	Updated introduction and medical summary. No changes in criteria
06/12/2024	Updated introduction, formatted criteria without Boolean, updated references, edited medical summary section.
06/14/2023	New policy. Independent Review Organization Peer Review on May 18, 2023, by a practicing, board-certified physician with a specialty in Pathology - Hematology, Internal Medicine, Medical Oncology.

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