Molina Clinical Policy
Allogeneic Pancreatic Islet Cell Transplantation with Lantidra (donislecel-jujn)
Policy No. 441

Last Approval: 08/12/2026
Next Review Due By: August 2027

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

Lantidra (donislecel-jujn) is an allogeneic pancreatic islet cell therapy approved for the treatment of adults with type 1 diabetes mellitus (T1DM) who are unable to approach their target hemoglobin A1c (HbA1c) due to recurrent episodes of severe hypoglycemia that are unresponsive to intensive insulin therapy and diabetes education. Hypoglycemia is a dangerous complication of T1DM and can lead to cognitive impairment, seizures, loss of consciousness, and death when not properly managed. Recurrent, severe hypoglycemia can significantly impair quality of life and may persist even with advanced diabetes technologies, such as insulin pumps and continuous glucose monitors (Robertson & Rickels 2026).

Pancreatic islet cell transplantation has historically been utilized to preserve endogenous insulin production in select patients undergoing total or near-total pancreatectomy for chronic pancreatitis. Autologous transplantation, where the patient's own islet cells are harvested and re-implanted, has been the standard approach for chronic pancreatitis. Advancements in islet cell isolation, culture techniques, and peri-transplant care have significantly improved the safety and feasibility of these procedures (Rickels & Robertson 2019). Islet allotransplantation for select patients with T1DM may restore endogenous insulin secretion, improve glycemic control, reduce or eliminate severe hypoglycemia, and may reduce insulin requirements or provide insulin independence in some patients. While graft function and insulin outcomes may decline over time, some patients maintain sustained insulin independence (Rickels et al. 2022).

Islet cell transplantation involves enzymatic digestion of the resected pancreas to isolate the islet cells. These cells are then purified, quantified, suspended in a suitable medium, and infused into the recipient's hepatic portal vein. Transplant types include autologous (self-donor), allogeneic (human donor), and xenogeneic (animal donor). Allogeneic transplantation, using donor islets from deceased individuals, is the approach utilized in Lantidra therapy.

In allogeneic islet transplantation, islet cells harvested from a deceased donor are administered percutaneously through a catheter directed into the hepatic portal vein. While earlier immunosuppression protocols relied on steroid-based regimens, more recent approaches favor steroid-free immunosuppression, which may offer improved glycemic outcomes (Rickels 2019).

Regulatory Status

On June 28, 2023, the U.S. Food and Drug Administration approved Lantidra (donislecel-jujn) (CellTrans, Inc) via the biologics license application (BLA) pathway. Lantidra is a suspension of purified allogeneic pancreatic islets in buffered transplant media containing human serum albumin. Each dose is manufactured from the pancreas of a single deceased donor and is provided in a cell suspension for percutaneous intraportal infusion. Donor pancreas allocation to the intended recipient occurs through the United Network for Organ Sharing (UNOS) and organ procurement is handled by an organ procurement organization (OPO) and the transplant center. The therapeutic effect of Lantidra is primarily attributed to insulin secretion by the transplanted beta cells. The safety and effectiveness of Lantidra has not been established in pediatric patients with T1DM. Clinical studies of Lantidra did not include sufficient numbers of patients aged 65 and over.

RELATED POLICIES

MCP-459: Pre-Transplant and Transplant Evaluation
MCP-017: Pancreas Transplantation
MCP-440: Autologous Pancreatic Islet Cell Transplantation

COVERAGE POLICY

All transplants require prior authorization from the Corporate Transplant Department. The Corporate Senior Medical Director or qualified clinical designee will review solid organ transplant requests. 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 Evaluation for pre-transplant criteria and transplant evaluation criteria that must be met prior to solid organ transplant

Allogeneic Pancreatic Islet Cell Transplantation

Lantidra (donislecel-jujn) may be **considered medically necessary** for the treatment of adults with type 1 diabetes who meet ALL the following indications with corresponding documentation:

1. All pre-transplant and transplant evaluation criteria are met as stipulated in *MCP-459 Pre-Transplant and Transplant Evaluation*
2. Member has a confirmed diagnosis of type 1 diabetes mellitus for a duration exceeding 5 years
3. Member is age 18 to 65
4. Member is currently on intensive insulin diabetes management (i.e., multiple daily insulin injections or continuous subcutaneous insulin infusion) and receives a daily average insulin administration of ≤ 0.7 units/kg/day
5. Documentation of intensive diabetes management education
6. Member unable to reach target HbA1c due to recurrent significant episodes of hypoglycemia despite intensive insulin management, defined as ALL the following:
    a. Hypoglycemia unawareness (i.e., absence of adequate autonomic response at capillary glucose level <54 mg/dL)
    b. Severe hypoglycemic events (e.g., loss of consciousness or altered mental status) that requires assistance of a third party, and is associated with either a documented blood glucose level < 50 mg/dL (2.8 mmol/L) or prompt recovery after glucose or glucagon administration
7. Laboratory studies:
    a. Stimulated C-peptide < 0.3 ng/mL following glucagon testing
    b. HbA1c ≤ 12%
    c. Creatinine clearance ≥ 80 mL/min/1.73 m^2 by 24-hour urine collection; if < 80 with serum creatinine < 1.2 mg/dL, nuclear GFR required

d. Serum creatinine ≤ 1.5 mg/dL
e. Negative pregnancy test for women of childbearing potential

8. In addition to the absolute and relative contraindications outlined in MCP-459, the following organ-specific **absolute** contraindications are absent:
   a. Heart failure greater than NYHA Class II
   b. Uncontrolled hyperlipidemia (fasting LDL cholesterol > 130 mg/dL or fasting triglycerides > 200 mg/dL)
   c. History of prior portal vein thrombosis, unless limited to second- or third-order portal vein branches
   d. Renal failure
   e. History of prior renal transplant
   f. Liver disease

9. Plan of care documents intent of concomitant immunosuppression with Lantidra

Continuation of Therapy
Coverage of Lantidra is limited to an initial infusion of 5,000 equivalent islet number per kg (EIN/kg) given via infusion via the hepatic portal vein. Maximum of 1 x 10^6 EIN (10ml) per infusion. Infusion should be terminated if portal pressure remains >22 mm Hg for longer than 10 minutes

Repeat second dose of 4,500 EIN/kg may be administered if independence from exogenous insulin is not achieved within 1 year of initial infusion or within 1 year after losing independence from exogenous insulin after a previous infusion. A third infusion may be administered using the same dose and criteria as the second dose if needed

Repeat administration beyond three infusions is considered **experimental, investigational, or unproven** based on insufficient evidence in the peer-reviewed medical literature to establish long-term safety, efficacy, and effect on net health outcomes

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

Non-Randomized Studies, Retrospective Reviews and Other Evidence
Gangemi (2008) conducted a prospective Phase 1/2 safety and reproducibility trial in which seven patients with type 1 diabetes mellitus (T1DM), severe hypoglycemia, and metabolic instability underwent allogeneic islet cell transplantation at a single center. This study established the foundation for what is now known as the University of Illinois protocol, a steroid-free immunosuppressive regimen designed to improve graft survival and reduce treatment-related toxicity. The results demonstrated a significant reduction in hypoglycemia severity across all participants, as measured by the HYPO score, a validated index used to assess the frequency and intensity of hypoglycemia in individuals with T1DM following islet transplantation. The combined treatment with etanercept and exenatide appeared to enhance graft function and contributed to increased rates of insulin independence.

The Phase 3 clinical trial (NCT00679042) sponsored by CellTrans, *Islet Transplantation in Type 1 Diabetic Patients Using the University of Illinois at Chicago Protocol* provided additional data. This open-label, non-randomized interventional study aimed to broaden access to biological therapy for individuals with brittle T1DM. A second Phase 3 trial (NCT03791567), also reviewed by the FDA, employed the same protocol to generate additional efficacy and safety data. A total of 21 participants with T1DM enrolled in the trial, ranging in age from 21 to 67 years with a median age of 47 years. The study population consisted of 15 females (71.4%) and 6 males (28.6%). All participants received up to three infusions of allogenic human islets and were treated with an immunosuppressive regimen that included basiliximab, tacrolimus, sirolimus, etanercept, and exenatide. During the first year of follow-up, two participants withdrew, and 19 completed the 12-month assessment. At five years, five participants had completed

long-term follow-up, six were still being followed, one had died, and seven were lost to follow-up. The co-primary efficacy endpoints were achieving a hemoglobin A1c (HbA1c) level below 6.5% at one year after transplantation and avoiding any severe hypoglycemic episodes between day 28 and one year following both the first and last islet infusions. At one year following the initial transplant, 8 participants (38.1%) met the co-primary efficacy endpoint. When measured one year after the final transplant, this number increased to 11 participants (52.4%).

Secondary endpoints included achieving insulin independence one year after infusion, maintaining fasting capillary glucose levels below 140 mg/dL on more than three days per week, fasting plasma glucose levels under 126 mg/dL, and two-hour postprandial capillary glucose levels not exceeding 180 mg/dL more than once per week. Evidence of endogenous insulin production, as defined by C-peptide levels greater than 0.5 ng/mL, was also monitored. In addition, the HYPO score (Ryan, 2004) was used to track changes in hypoglycemia frequency and severity throughout the study. At one year following the last transplant, 12 participants (57.1%) achieved insulin independence, and 11 (52.4%) demonstrated fasting plasma glucose ≤126 mg/dL. Additionally, 10 participants (47.6%) maintained fasting capillary glucose levels <140 mg/dL on more than three days per week, and 9 (42.9%) had postprandial glucose <180 mg/dL on no more than one occasion weekly. All participants demonstrated C-peptide levels ≥0.5 ng/mL, confirming endogenous insulin production. The median HYPO score decreased from 266 at baseline to 18.7 at one year after the last transplant, reflecting a 90.1% mean reduction.

Serious transplant-related adverse events occurred in 11 participants (52.4%), though none resulted in death or withdrawal from the study. Treatment-emergent adverse events (TEAEs) were observed in all participants, with 16 participants (76.2%) experiencing events rated as severe or worse. TEAEs were monitored for an average of one year after the final transplant. The most reported non-serious adverse events included vomiting (81%), fatigue (76.2%), acne (66.7%), asthenia (66.7%), diarrhea (61.9%), abnormal weight loss (61.9%), and headache (57.1%). Reported procedural complications included liver laceration, hematoma, hemorrhage, intra-abdominal bleeding, and elevated portal pressure. Infections, such as pneumonia (9.5%) and cytomegalovirus viremia (4.8%), were noted, along with one case of uterine leiomyoma (4.8%) related to immunosuppressive therapy. Despite the frequency of adverse events, no deaths or study discontinuations were attributed to these complications.

National and Specialty Organizations

The **Organ Procurement and Transplant Network (OPTN)** policy 11, *Allocation of Pancreas, Kidney-Pancreas, and Islets* (OPTN 2026), recognizes allogenic islet transplantation as a form of organ transplant. According to the policy, a transplant center may assign active status on the national waiting list to an islet transplant candidate if the individual meets at least one of the following criteria:

1. The candidate is insulin dependent
2. The candidate has an HbA1c value greater than 6.5%

The **American Diabetes Association (ADA)** published *Standards of Medical Care in Diabetes: Pharmacologic Approaches to Glycemic Treatment* (ADA 2026), acknowledging that allogenic islet cell transplantation with donislecel-jujn is FDA-approved for adults with T1DM who are unable to achieve their HbA1c goals due to repeated severe hypoglycemic episodes despite intensive diabetes management and education. The ADA highlights that in "much of the world, allogenic islet transplantation is regulated as an organ transplant," but that in the U.S., it's regulated as a cell therapy, with donislecel-jujn being the first of its kind. Additionally, alternative islet sources are currently under active investigation. The ADA states that successful islet transplantation can normalize glucose levels and mitigate microvascular complications of T1DM. However, recipients require lifelong immunosuppression to prevent graft rejection or recurrence of autoimmune islet destruction.

The **American Diabetes Association (ADA)** and the **European Association for the Study of Diabetes (EASD)** issued a joint consensus report on the management of T1DM in adults, outlining the potential role of allogeneic islet cell transplantation for selected individuals. The report highlights that islet transplantation may be appropriate for patients experiencing significant glycemic variability and frequent level 3 hypoglycemia, despite receiving optimized medical therapy. This approach may also benefit individuals who are older or have comorbidities, such as coronary artery disease, which make them ineligible for whole-organ pancreas transplantation (Holt et al. 2021).

The **National Institute for Health and Care Excellence (NICE)** published guideline [NG17] on the diagnosis and management of T1DM in adults (NICE 2022). The guidelines recommend that for adults with T1DM who have recurrent severe hypoglycemia nonresponsive to other treatments, including hypoglycemia awareness and management, consider referral for islet and/or pancreas transplantation. Additionally, consider islet or pancreas transplantation for adults with T1DM with suboptimal diabetes control if they've had a renal transplant and are currently on immunosuppressive therapy.

CODING & BILLING INFORMATION

CPT (Current Procedural Terminology)

Code	Description
0584T	Islet cell transplant, includes portal vein catheterization and infusion, including all imaging, including guidance, and radiological supervision and interpretation, when performed; percutaneous
0585T	Islet cell transplant, includes portal vein catheterization and infusion, including all imaging, including guidance, and radiological supervision and interpretation, when performed; laparoscopic
0586T	Islet cell transplant, includes portal vein catheterization and infusion, including all imaging, including guidance, and radiological supervision and interpretation, when performed; open
48554	Transplantation of pancreatic allograft
48556	Removal of transplanted pancreatic allograft

HCPCS (Healthcare Common Procedure Coding System)

Code	Description
C9399	Unclassified drugs or biologicals [when specified as Lantidra (donislecel-jujn)]
J3590	Unclassified biologics [when specified as Lantidra (donislecel-jujn)]
G0341	Percutaneous islet cell transplant, includes portal vein catheterization and infusion
G0342	Laparoscopy for islet cell transplant, includes portal vein catheterization and infusion
G0343	Laparotomy for islet cell transplant, includes portal vein catheterization and infusion
S2102	Islet cell tissue transplant from pancreas; allogeneic
S2152	Solid organ(s), complete or segmental, single organ or combination of organs; deceased or living donor (s), procurement, transplantation, and related complications; including drugs; supplies; hospitalization with outpatient follow-up; medical/surgical, diagnostic, emergency, and rehabilitative services, and the number of days of pre- and post-transplant care in the global definition

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

08/12/2026	Policy revised. Changed total fasting cholesterol requirement to a fasting LDL cholesterol requirement. Changed heart failure threshold to > NYHA class II. Added requirement of meeting MCP 459 Pre-Transplant and Transplant criteria. Removed contraindications that are stipulated in MCP 459. Changed title to "Allogeneic Pancreatic Islet Cell Transplantation with Lantidra".
08/13/2025	Policy revised. Removed prescriber requirements. Updated Summary of Medical Evidence and References. IRO Peer Review on August 1, 2025, by a practicing physician board-certified in Surgery, Vascular Surgery, Surgical Critical Care.
08/14/2024	Policy reviewed, updated references, Reformatted indications, no changes to coverage criteria.
08/09/2023	New Policy. New FDA indication. IRO (Independent Review Organization) peer review by reviewer board certified in Transplant Hepatology July 2023.

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