Lantidra (donislecel-jujn)

Disclaimer

Clinical guidelines are developed and adopted to establish evidence-based clinical criteria for utilization management decisions. Clinical guidelines are applicable according to policy and plan type. The Plan may delegate utilization management decisions of certain services to third parties who may develop and adopt their own clinical criteria.

Coverage of services is subject to the terms, conditions, and limitations of a member's policy, as well as applicable state and federal law. Clinical guidelines are also subject to in-force criteria such as the Centers for Medicare & Medicaid Services (CMS) national coverage determination (NCD) or local coverage determination (LCD) for Medicare Advantage plans. Please refer to the member's policy documents (e.g., Certificate/Evidence of Coverage, Schedule of Benefits, Plan Formulary) or contact the Plan to confirm coverage.

Summary

Lantidra (donislecel-jujn) is an allogeneic pancreatic islet cellular therapy that contains insulin-producing beta cells derived from donated pancreases. It is indicated for adults with Type 1 diabetes who have difficulty achieving target HbA1c levels due to recurrent severe hypoglycemic episodes, despite intensive diabetes management with insulin, devices, and education.

Lantidra (donislecel-jujn) aims to restore endogenous insulin production and normalize blood glucose levels. The treatment involves intravenous infusion of the drug, which contains immunoisolated allogeneic islets, followed by immunosuppression to prevent graft rejection.

- In clinical trials, Lantidra (donislecel-jujn) allowed some patients to achieve insulin independence for over 1 year. It is particularly beneficial for those with hypoglycemia unawareness, as it reduces reliance on exogenous insulin to control blood glucose.
- Limitations include lack of evidence showing benefit in well-controlled Type 1 diabetes, as well as potential risks from the infusion procedure and long-term immunosuppression. There is also no evidence to support use in patients with liver disease, kidney failure, or kidney transplants.

Lantidra (donislecel-jujn) was approved based on a small (n=48) phase 3 study with very strict inclusion criteria including: only adults 18-65 years of age; a diagnosis of type-1 diabetes mellitus for at least 5 years; a history of severe hypoglycemic events in the past 12 months despite medical care provided by an endocrinologist or diabetologist; an absence of stimulated c-peptide, impaired awareness of hypoglycemia, and/or marked glycemic lability; and an attestation regarding adherence to office visits, self-monitoring of blood glucose and the use of an insulin pump or administration of three or more injections of insulin daily. Because of the strict requirements for Lantidra (donislecel-jujn) administration, very few health systems in the United States have been approved to administer Lantidra (donislecel-jujn).

Definitions

"Allogeneic" refers to cells, tissues, or organs sourced from a genetically distinct individual of the same species.

"Beta Cells" are insulin-producing cells found in the pancreas that regulate blood glucose levels.

"C-peptide" is a protein fragment released during the conversion of insulin, often used as a marker of endogenous insulin production.

"Diabetic Ketoacidosis (DKA)" is a serious complication of diabetes caused by very low insulin levels leading to high blood sugar, ketone production, and acidosis.

"HbA1c (Glycated Hemoglobin)" is a measure used to determine average blood glucose levels over a period of several months.

"Hypoglycemia Unawareness" is a condition where individuals don't experience the typical symptoms of low blood sugar, which can lead to severe hypoglycemia.

"Hypoglycemia" is a condition characterized by abnormally low levels of blood sugar.

"Immunoisolated Allogeneic Islets" are pancreatic islet cells derived from a donor and shielded to reduce the risk of immune rejection when transplanted.

"Immunosuppression" is the act of reducing or inhibiting the body's immune response, often to prevent rejection of transplanted organs or cells.

"Intraportal Islet Cell Infusion" is the process of introducing isolated islet cells directly into the portal vein of the liver, a common site for islet transplantation.

"Pancreatic Islet Cellular Therapy" is a treatment approach where insulin-producing cells from the pancreas are transplanted into a patient to replace deficient or non-functioning cells.

Medical Necessity Criteria for Initial Clinical Review

Initial Indication-Specific Criteria

Type 1 Diabetes Mellitus

The Plan considers Lantidra (donislecel-jujn) medically necessary when ALL of the following criteria are met:

1. Prescribed by or in consultation with an endocrinologist experienced in the management of type 1 diabetes and familiar with the risks and monitoring requirements of Lantidra therapy; *AND*
2. Administered by a healthcare provider experienced in performing intraportal islet cell infusion (e.g., interventional radiologists and surgeons); *AND*
3. The member is 18 years of age or older; *AND*
4. The member has a confirmed diagnosis of type 1 diabetes for at least 5 years; *AND*
5. The member has evidence of intensive diabetes management, defined as:
    a. Self-monitoring of glucose values at least 3 times per day on average; *and*
    b. Using insulin pump therapy or at least 3 insulin injections per day; *and*
    c. Under the care of a diabetes specialist with at least 3 evaluations in the past 12 months; *AND*
6. The member is exhibiting ONE (1) of the following, despite intensive insulin management efforts:
    a. Hypoglycemic unawareness, as defined by inability to sense hypoglycemia until the blood glucose falls to less than 54 mg/dL; *or*
    b. TWO (2) or more episodes of severe hypoglycemia, defined as an event with symptoms consistent with hypoglycemia in which the member requires the assistance of another person and which is associated with a blood glucose below 54 mg/dL; *or*
    c. TWO (2) or more hospital visits for diabetic ketoacidosis over the last year; *or*
7. The member has not achieved HbA1c target goals set by their diabetes care team with current treatment regimens; *AND*
8. The member is willing and able to adhere to required monitoring and immunosuppression post-infusion; *AND*

9. The member meets ALL of the following:
    a. No active infection including hepatitis C, hepatitis B, HIV; *and*
    b. No concomitant diseases or conditions, including pregnancy, that contraindicate the procedure for Lantidra (donislecel-jujn) infusion or immunosuppression; *and*
    c. C-peptide response to glucagon stimulation less than (<) 0.3 ng/mL; *and*
    d. No history of non-adherence to prescribed regimens; *and*
    e. No liver disease, renal failure, or who have received a renal transplant; *and*
    f. No previous islet or pancreas transplant; *and*
    g. No severe coexisting cardiac disease, characterized by any ONE (1) of the following conditions:
        i. Recent myocardial infarction within the past 6 months; *or*
        ii. angiographic evidence of non-correctable coronary artery disease; *or*
        iii. Evidence of ischemia on a functional cardiac exam; *or*
        iv. Left ventricular ejection fraction less than 30%; *and*
10. Initial authorization is for no more than ONE (1) infusion.

If the above prior authorization criteria are met, Lantidra (donislecel-jujn) will be authorized for one infusion.

Continued Care

Medical Necessity Criteria for Subsequent Clinical Review

Subsequent Indication-Specific Criteria

Type 1 Diabetes Mellitus

The Plan considers Lantidra (donislecel-jujn) medically necessary when ALL of the following criteria are met:

1. The member continues to meet all applicable Initial Criteria; *AND*
2. The member requires a second or third infusion due to loss of islet graft function; *AND*
3. The member responded to the prior infusion with sustained C-peptide production and/or periods of exogenous insulin independence; *AND*
4. Additional authorization is for no more than one infusion, with a lifetime limit of 3 total infusions.

If the above reauthorization criteria are met, the requested product will be authorized for up to one additional infusion (up to a lifetime limit of 3 total infusions)

Experimental or Investigational / Not Medically Necessary

Lantidra (donislecel-jujn) for any other indication or use is considered not medically necessary by the Plan, as it is deemed to be experimental, investigational, or unproven. Non-covered indications include, but are not limited to, the following:

- Complications of diabetes like diabetic neuropathy, nephropathy, and retinopathy
- In pediatric members with type 1 diabetes
- More than three infusions of Lantidra (donislecel-jujn)
- Pancreatic cancer, i.e. managing diabetes resulting after pancreatectomy for pancreatic tumors
- Members whose diabetes is well-controlled with insulin therapy
- Members with hypoglycemic unawareness who can prevent repeated severe hypoglycemic events using intensive diabetes management,
- Members with liver disease, renal failure, or history of kidney transplantation
- Members without diabetes who have hypoglycemia due to other conditions
- Type 2 diabetes.

Applicable Billing Codes

Table 1	
CPT/HCPCS codes for type 1 diabetes mellitus considered medically necessary if criteria are met:	
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
C9399	Unclassified drugs or biologicals
J3590	Unclassified biologics
G0341	Percutaneous islet cell transplant, includes portal vein catheterization and infusion

Table 2	
ICD-10 diagnosis codes considered medically necessary for type 1 diabetes mellitus with Table 1if criteria are met:	
Code	*Description*
E10.649	Type 1 diabetes mellitus with hypoglycemia without coma
E10.8	Type 1 diabetes mellitus with unspecified complications
E10.9	Type 1 diabetes mellitus without complications

References

1. Alam S, Khan SJ, Lee CYF, Zaidi SAT, Murtaza SF. Type 1 Diabetes Mellitus Management and Islet Cell Therapy: A New Chapter in Patient Care. Cureus. 2023 Oct 12;15(10):e46912. doi: 10.7759/cureus.46912.
2. American Diabetes Association Professional Practice Committee. 9. Pharmacologic Approaches to Glycemic Treatment: Standards of Care in Diabetes-2025. Diabetes Care. 2025 Jan 1;48(1 Suppl 1):S181-S206. doi: 10.2337/dc25-S009. PMID: 39651989; PMCID: PMC11635045.
3. Anazawa T, Marubashi S, Kodama S, et al. Efficacy and Safety of Allogeneic Islet Transplantation Demonstrated by a Multicenter Clinical Trial in Japan. Transplant Direct. 2025 Feb 7;11(3):e1765. doi: 10.1097/TXD.0000000000001765.
4. Canadian Diabetes Association Clinical Practice Guidelines Expert Committee; Paty BW, Koh A, Senior P. Pancreas and islet transplantation. Can J Diabetes. 2013 Apr;37 Suppl 1:S94-6. doi: 10.1016/j.jcjd.2013.01.028. Epub 2013 Mar 26.
5. Erbasan E, Aliciaslan M, Erendor F, Dandin O, Sanlioglu S. Lantidra (donislecel) in type 1 diabetes: An in-depth analysis of pharmacology, clinical effectiveness, safety, and the therapeutic role of the first FDA-approved allogeneic islet cell therapy. Diabet Med. 2025 Nov 11:e70168. doi: 10.1111/dme.70168. Epub ahead of print.
6. Food and Drug Administration (FDA) News Release. FDA approves first cellular therapy to treat patients with type 1 diabetes. Jun 28, 2023. Available at: https://www.fda.gov/news-events/press-announcements/fda-approves-first-cellular-therapy-treat-patients-type-1-diabetes#.
7. Foster ED, Bridges ND, Feurer ID, et al. Improved Health-Related Quality of Life in a Phase 3 Islet Transplantation Trial in Type 1 Diabetes Complicated by Severe Hypoglycemia. Diabetes Care. 2018 May;41(5):1001-1008. doi: 10.2337/dc17-1779. Epub 2018 Mar 21.
8. Gangemi A, Salehi P, Hatipoglu B, et al. Islet transplantation for brittle type 1 diabetes: the UIC protocol. Am J Transplant. 2008 Jun;8(6):1250-61. doi: 10.1111/j.1600-6143.2008.02234.x. Epub 2008 Apr 29.
9. Harris E. FDA greenlights first cell therapy for adults with type 1 diabetes. JAMA. 2023 Jul 12; doi: 10.1001/jama.2023.12542.
10. Health Quality Ontario. Pancreas Islet Transplantation for Patients With Type 1 Diabetes Mellitus: A Clinical Evidence Review. Ont Health Technol Assess Ser. 2015 Sep 1;15(16):1-84.
11. Hering, B. J., Clarke, W. R., Bridges, N. D., et al. (2016). Phase 3 Trial of Transplantation of Human Islets in Type 1 Diabetes Complicated by Severe Hypoglycemia. Diabetes Care, 39(7), 1230-40.
12. Hering BJ, Rickels MR, Bellin MD, et al. Advances in Cell Replacement Therapies for Diabetes. Diabetes. 2025 Jul 1;74(7):1068-1077. doi: 10.2337/db25-0037.
13. Holt RIG, DeVries JH, Hess-Fischl A, et al. The management of type 1 diabetes in adults. A consensus report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). Diabetologia. 2021 Dec;64(12):2609-2652. doi: 10.1007/s00125-021-05568-3. Erratum in: Diabetologia. 2022 Jan;65(1):255. doi: 10.1007/s00125-021-05600-6.
14. Lantidra (donislecel) [prescribing information]. Chicago, IL: CellTrans Inc; November 2024.
15. Luu, Q. F., Villareal, C. J., Fritschi, C., Monson, R. S., Oberholzer, J., & Danielson, K. K. (2018). Concerns and hopes of patients with type 1 diabetes prior to islet cell transplantation: A content analysis. J Diabetes Complications, 32(7), 677-681.
16. Mbaye EHA, Scott EA, Burke JA. From Edmonton to Lantidra and beyond: immunoengineering islet transplantation to cure type 1 diabetes. Front Transplant. 2025 Mar 20;4:1514956. doi: 10.3389/frtra.2025.1514956.
17. Piemonti L. Islet Transplantation. 2025 Sep 15. In: Feingold KR, Ahmed SF, Anawalt B, Blackman MR, Boyce A, Chrousos G, Corpas E, de Herder WW, Dhatariya K, Dungan K, Hofland J, Kalra S, Kaltsas G, Kapoor N, Koch C, Kopp P, Korbonits M, Kovacs CS, Kuohung W, Laferrère B, Levy M, McGee EA, McLachlan R, Muzumdar R, Purnell J, Rey R, Sahay R, Shah AS, Singer F, Sperling

MA, Stratakis CA, Trence DL, Wilson DP, editors. Endotext [Internet]. South Dartmouth (MA): MDText.com, Inc.; 2000–. PMID: 25905200.
18. Qi, M., Kinzer, K., Danielson, K. K., Martellotto, J., Barbaro, B., Wang, Y., ... & Oberholzer, J. (2014). Five-year follow-up of patients with type 1 diabetes transplanted with allogeneic islets: the UIC experience. Acta Diabetol, 51(5), 833-43.
19. Rickels, M. R., Liu, C., Shlansky-Goldberg, R. D., Soleimanpour, S. A., Vivek, K., Kamoun, M., ... & Naji, A. (2013). Improvement in beta-cell secretory capacity after human islet transplantation according to the CIT07 protocol. Diabetes, 62(8), 2890-7.
20. Rickels MR, Stock PG, de Koning EJP, et al. Defining Outcomes for β-cell Replacement Therapy in the Treatment of Diabetes: A Consensus Report on the Igls Criteria From the IPITA/EPITA Opinion Leaders Workshop. Transplantation. 2018 Sep;102(9):1479-1486. doi: 10.1097/TP.0000000000002158.
21. Ricordi C, Goldstein JS, Balamurugan AN, et al. National Institutes of Health-Sponsored Clinical Islet Transplantation Consortium Phase 3 Trial: Manufacture of a Complex Cellular Product at Eight Processing Facilities. Diabetes. 2016 Nov;65(11):3418-3428. doi: 10.2337/db16-0234. Epub 2016 Jul 27. Erratum in: Diabetes. 2017 Sep;66(9):2531. doi: 10.2337/db17-er09a.
22. Shapiro, A. M., Ricordi, C., Hering, B. J., Auchincloss, H., Lindblad, R., Robertson, R. P., ... & Lakey, J. R. (2006). International trial of the Edmonton protocol for islet transplantation. N Engl J Med, 355(13), 1318-30.
23. Wang Y, Chen Y, McGarrigle J, et al. Cell Therapy for T1D Beyond BLA: Gearing Up Toward Clinical Practice. Diabetes Ther. 2025 Jun;16(6):1125-1138. doi: 10.1007/s13300-025-01732-9. Epub 2025 Apr 11.
24. Wang Y, McGarrigle J, Cook J, et al. The future of islet transplantation beyond the BLA approval: challenges and opportunities. Front Transplant. 2025 Mar 7;4:1522409. doi: 10.3389/frtra.2025.1522409.
25. Witkowski, P., Anteby, R., Olaitan, O. K., et al. (2021). Pancreatic islets quality and potency cannot be verified as required for drugs: Reflection on the FDA review of a biological license application for human islets. Transplantation, 105(12), e409–e10.

Clinical Guideline Revision / History Information

Original Date: 9/21/2023

Reviewed/Revised: 12/19/2024, 05/01/2026