

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.

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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;¹⁴ *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 up to one infusion.^[5]

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 as evidenced by ONE (1) of the following:
 - a. A sustained C-peptide production; and/or
 - b. Periods of exogenous insulin independence; *and/or*
 - c. No severe hypoglycemic events, 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; *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).^[5]

Experimental or Investigational / Not Medically Necessary^[5]

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. While those with type 1 diabetes may have complications of diabetes, the intended goal of Lantidra (donislecel-jujn) was to eradicate severe hypoglycemic events with excellent glycemic control and insulin independence.
- In pediatric members with type 1 diabetes. Lantidra (donislecel-jujn) has only been studied in those 18 years of age and older.
- More than three infusions of Lantidra (donislecel-jujn). As of now, there is no data to support the safety and efficacy in those receiving more than three infusions in a lifetime.
- Pancreatic cancer, i.e. managing diabetes resulting after pancreatectomy for pancreatic tumors.
- Members whose diabetes is well-controlled with insulin therapy. Lantidra (donislecel-jujn) has only been studied in those unable to achieve glycemic control without hypoglycemia episodes, despite care with a diabetes specialist and an allowed HbA1c of greater than 7%.
- 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. There is no evidence to support the safety and efficacy of Lantidra (donislecel-jujn) in those with liver disease, renal failure, or a history of kidney transplant.
- Members without diabetes who have hypoglycemia due to other conditions. Lantidra (donislecel-jujn) is focused primarily on the mechanism of type 1 diabetes - increased secretion of insulin by infused (transplanted) beta-cells. It is unknown if Lantidra (donislecel-jujn) would be safe and effective in those without type 1 diabetes.
- Type 2 diabetes. Lantidra (donislecel-jujn) has only been studied in those with type 1 diabetes.

Applicable Billing Codes

Table 1	
CPT/HCPCS codes for type 1 diabetes mellitus considered medically necessary if criteria are met:	
<i>Code</i>	<i>Description</i>
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 1 if criteria are met:	
<i>Code</i>	<i>Description</i>
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

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