Corporate Medical Policy: Donislecel-jujn (Lantidra®) **"Notification"** **POLICY EFFECTIVE APRIL 1, 2026**

Restricted Product(s):

- donislecel-jujn (Lantidra®) allogeneic pancreatic islet cellular suspension for hepatic portal vein infusion for administration by a healthcare professional

FDA Approved Use:

- For the treatment of adults with Type 1 diabetes who are unable to approach target HbA1c because of current repeated episodes of severe hypoglycemia despite intensive diabetes management and education. Use is in conjunction with concomitant immunosuppression.
- Limitations of Use:
  - When considering the risks associated with the infusion procedure and long-term immunosuppression, there is no evidence to show a benefit of administration of this therapy in patients whose diabetes is well-controlled with insulin therapy or patients with hypoglycemic unawareness who are able to prevent current repeated severe hypoglycemic events (neuroglycopenia requiring active intervention from a third party) using intensive diabetes management (including insulin, devices, and education)
  - Repeated intraportal islet infusions are not recommended in patients who have experienced prior portal thrombosis, unless the thrombosis was limited to second- or third-order portal vein branches
  - There is no evidence to support the safe and effective use of this therapy in patients with liver disease, renal failure, or who have received a renal transplant
  - There are no data regarding safety or effectiveness for patients receiving more than three infusions

Criteria for Medical Necessity:

The restricted product(s) may be considered medically necessary when the following criteria are met:

Initial Criteria for Approval:

1. The patient is 18 years of age or older; **AND**
2. The patient has a confirmed diagnosis of Type 1 diabetes mellitus (DM) for a duration of more than 5 years **[medical record documentation required]**; **AND**
3. The patient is unable to achieve target HbA1c despite BOTH of the following **[medical record documentation required]**:
   a. Intensive insulin management efforts that include coordination of meals/diet and activity with physiologic insulin replacement [i.e., continuous subcutaneous insulin infusion (insulin pump) or multiple daily injections of basal and mealtime (prandial) insulin]; **AND**
   b. Intensive blood glucose monitoring with either use of a continuous glucose monitor (CGM) or insulin pump; **AND**
4. The patient has a history of current repeated episodes of severe hypoglycemia, as defined by BOTH of the following **[medical record documentation required]**:

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   a. At least one episode of severe hypoglycemia in the past 3 years which required assistance from another person and was associated with either a blood glucose level less than 50 mg/dL (2.8 mmol/L) or prompt recovery after oral carbohydrate, intravenous glucose, or glucagon administration; **AND**
   b. Reduced awareness of hypoglycemia, defined by the absence of adequate autonomic symptoms at capillary glucose levels less than 54 mg/dL (3 mmol/L); **AND**
5. The patient will be receiving the requested agent in conjunction with concomitant immunosuppression [e.g., non-depleting monoclonal anti-interleukin-2 (anti-IL-2) receptor antibodies, polyclonal T-cell-depleting antibodies, calcineurin inhibitors, mammalian target of rapamycin (mTOR) inhibitors, tumor necrosis factor (TNF) blockers] **[medical record documentation required]**; **AND**
6. The patient has a negative T- and B-cell crossmatch assay between recipient serum and donor lymphocytes **[medical record documentation required]**; **AND**
7. The patient does NOT have <u>any</u> of the following conditions **[medical record documentation required]**:
   a. Previous transplant recipient or Panel Reactive Antibody (PRA) reactivity greater than 80% indicating high-risk for transplant rejection; **OR**
   b. C-peptide response to glucagon stimulation, any C-peptide greater than 0.3 ng/mL; **OR**
   c. Insulin requirement greater than 0.7 IU/kg/day and HbA1c greater than 12%; **OR**
   d. Body mass index (BMI) greater than 27 kg/m^2; **OR**
   e. Diagnosis of co-existing cardiac disease, to include any one of the following:
      i. Myocardial infarction or stroke within the past 6 months; **OR**
      ii. Angiographic evidence of non-correctable coronary artery disease; **OR**
      iii. Ischemia on functional cardiac exam; **OR**
      iv. Heart failure (New York Heart Association classification greater than II); **OR**
   f. Abnormal kidney or liver function, and/or history of liver disease or renal failure, as defined by any one of the following:
      i. Creatinine clearance less than 80 mL/min/1.73 m^2; **OR**
      ii. Serum creatinine greater than 1.5 mg/dL; **OR**
      iii. Macroalbuminuria (urinary albumin excretion rate greater than 300 mg/24 hours); **OR**
      iv. Baseline liver function tests with any value greater than 1.5 times the upper limit of normal; **OR**
   g. Increased bleeding risk, as defined by any one of the following:
      i. Hemoglobin less than 12 g/dL in women or less than 13 g/dL in men; **OR**
      ii. Use of warfarin or other antiplatelet or anticoagulant therapy; **OR**
      iii. Prothrombin time international normalized ratio (PT-INR) greater than 1.5; **OR**
      iv. History of Factor V deficiency; **OR**
   h. Infection including hepatitis C, hepatitis B, HIV and/or tuberculosis; **OR**
   i. History of malignancy, with the exception of adequately treated basal or squamous cell skin cancer; **OR**

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   j. Presence of any other concomitant disease or condition (including pregnancy) that contraindicates the transplant infusion procedure or immunosuppression; **OR**
   k. Inability to adhere to the treatment regimen necessary to preserve the transplant; **AND**
8. The prescriber is a specialist in the area of the patient's diagnosis (e.g., endocrinologist, transplant surgeon) or has consulted with a specialist in the area of the patient's diagnosis **[medical record documentation required]**; **AND**
9. The patient will be treated with a minimum of 5,000 equivalent islet number (EIN) per kg patient body weight for the initial infusion **[documentation of planned dosage required]**; **AND**
10. The patient will NOT be treated with more than 1 x 10^6 EIN per infusion **[documentation of planned dosage required]**; **AND**
11. The patient will NOT receive more than three transplant infusions total during a patient's lifetime **[medical record documentation required]**; **AND**
12. The requested dose is within FDA labeled dosing for the requested indication, and the requested quantity does NOT exceed the maximum units allowed for the duration of approval (see table below) **[medical record documentation required]**.

Duration of Approval: 365 days (One transplant infusion per authorization; Total maximum of 3 transplant infusions per lifetime)

Continuation Criteria for Approval:

1. The patient was approved through Blue Cross NC initial criteria for approval; **OR**
2. The patient would have met initial criteria for approval at the time they started therapy; **AND**
3. The patient has failed to achieve independence from exogenous insulin within one year of the previous infusion OR within one year after losing independence from exogenous insulin after the previous infusion **[medical record documentation required]**; **AND**
4. The patient does NOT have any unacceptable toxicities to prior transplant infusions with the requested agent (e.g., severe infections including opportunistic infections, malignancy and severe anemia, procedural complications including liver laceration and hemorrhage, islet graft rejection, panel reactive antibodies, portal vein thrombosis, portal hypertension) **[medical record documentation required]**; **AND**
5. At least one year has passed since the patient received the prior transplant infusion with the requested agent **[medical record documentation required]**; **AND**
6. The patient continues to use the requested agent in conjunction with concomitant immunosuppression [e.g., non-depleting monoclonal anti-interleukin-2 (anti-IL-2) receptor antibodies, polyclonal T-cell-depleting antibodies, calcineurin inhibitors, mammalian target of rapamycin (mTOR) inhibitors, tumor necrosis factor (TNF) blockers] **[medical record documentation required]**; **AND**
7. The patient has a negative T- and B-cell crossmatch assay between recipient serum and donor lymphocytes **[medical record documentation required]**; **AND**
8. The patient does NOT have any of the following conditions **[medical record documentation required]**:

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a. Previous transplant recipient (except islet transplant) or Panel Reactive Antibody (PRA) reactivity greater than 80% indicating high-risk for transplant rejection; **OR**
b. C-peptide response to glucagon stimulation, any C-peptide greater than 0.3 ng/mL; **OR**
c. Insulin requirement greater than 0.7 IU/kg/day and HbA1c greater than 12%; **OR**
d. Body mass index (BMI) greater than 27 kg/m^2; **OR**
e. Diagnosis of co-existing cardiac disease, to include any one of the following:
    i. Myocardial infarction or stroke within the past 6 months; **OR**
    ii. Angiographic evidence of non-correctable coronary artery disease; **OR**
    iii. Ischemia on functional cardiac exam; **OR**
    iv. Heart failure (New York Heart Association classification greater than II); **OR**
f. Abnormal kidney or liver function, and/or history of liver disease or renal failure, as defined by any one of the following:
    i. Creatinine clearance less than 80 mL/min/1.73 m^2; **OR**
    ii. Serum creatinine greater than 1.5 mg/dL; **OR**
    iii. Macroalbuminuria (urinary albumin excretion rate greater than 300 mg/24 hours); **OR**
    iv. Baseline liver function tests with any value greater than 1.5 times the upper limit of normal; **OR**
g. Increased bleeding risk, as defined by any one of the following:
    i. Hemoglobin less than 12 g/dL in women or less than 13 g/dL in men; **OR**
    ii. Use of warfarin or other antiplatelet or anticoagulant therapy; **OR**
    iii. Prothrombin time international normalized ratio (PT-INR) greater than 1.5; **OR**
    iv. History of Factor V deficiency; **OR**
h. Infection including hepatitis C, hepatitis B, HIV and/or tuberculosis; **OR**
i. History of malignancy, with the exception of adequately treated basal or squamous cell skin cancer; **OR**
j. Presence of any other concomitant disease or condition (including pregnancy) that contraindicates the transplant infusion procedure or immunosuppression; **OR**
k. Inability to adhere to the treatment regimen necessary to preserve the transplant; **AND**

9. The prescriber is a specialist in the area of the patient's diagnosis (e.g., endocrinologist, transplant surgeon) or has consulted with a specialist in the area of the patient's diagnosis **[medical record documentation required]**; **AND**
10. The patient will be treated with a minimum of 4,500 equivalent islet number (EIN) per kg patient body weight for each subsequent infusion in the same recipient **[documentation of planned dosage required]**; **AND**
11. The patient will NOT be treated with more than 1 x 10^6 EIN per infusion **[documentation of planned dosage required]**; **AND**
12. The patient will NOT receive more than three transplant infusions total during a patient's lifetime **[medical record documentation required]**; **AND**
13. The requested dose is within FDA labeled dosing for the requested indication, and the requested quantity does NOT exceed the maximum units allowed for the duration of approval (see table below) **[medical record documentation required]**.

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Duration of Approval: 365 days (One transplant infusion per authorization; Total maximum of 3 transplant infusions per lifetime)

Please note, for certain identified gene and cellular therapies such as donislecel-jujn (Lantidra®), when coverage is available and the individual meets medically necessary criteria, distribution from a specialty pharmacy provider due to cost (distribution channel restriction) may be required in order for coverage to be provided. **Please contact Blue Cross NC to coordinate this therapy.

FDA Label Reference				
Medication	**Indication**	**Dosing**	**HCPCS**	**Maximum Units***
donislecel-jujn (Lantidra®) allogeneic pancreatic islet cellular suspension hepatic portal vein infusion	Type 1 diabetes in adults who are unable to approach target HbA1c because of current repeated episodes of severe hypoglycemia despite intensive diabetes management and education	Initial infusion (transplant): Minimum dose of 5,000 equivalent islet number (EIN) per kg patient body weight Subsequent infusions (up to a maximum of 2 additional infusions): Minimum dose of 4,500 EIN/kg in the same recipient Administer cells through the hepatic portal vein. Estimated tissue volume not to exceed 10 cc per transplant infusion, and up to a maximum of 1 x 10^6 EIN per infusion bag. A second or third infusion may be performed for patients not achieving independence from exogenous insulin within 1 year of infusion or within 1 year after losing independence from exogenous insulin after a previous infusion.	C9399** J3490** J3590**	**1**

***Maximum units allowed for duration of approval**
****Non-specific assigned HCPCS codes, must submit requested product NDC**

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Other revenue codes that may be applicable to this policy: 0891, 0892

References: all information referenced is from FDA package insert unless otherwise noted below.

1. Luu QF, Villareal CJ, Fritschi C, et al. Concerns and hopes of patients with type 1 diabetes prior to islet cell transplantation: A content analysis. *J Diabetes Complications*. 2018 Jul;32(7):677-681.
2. Qi M, Kinzer K, Danielson KK, et al. Five-year follow-up of patients with type 1 diabetes transplanted with allogeneic islets: the UIC experience. *Acta Diabetol*. 2014 Oct;51(5):833-43.
3. Williams J, Jacus N, Kavalackal K, et al. Over ten-year insulin independence following single allogeneic islet transplant without T-cell depleting antibody induction. *Islets*. 2018;10(4):168-174.

Policy Implementation/Update Information: Criteria and treatment protocols are reviewed annually by the Blue Cross NC P&T Committee, regardless of change. This policy is reviewed in Q1 annually.

April 2026: Coding change: Added the following applicable revenue codes associated with policy HCPCS code(s): 0891 (Special Processed Drugs – FDA Approved Cell Therapy) and 0892 (Special Processed Drugs – FDA Approved Gene Therapy). **Policy notification given 2/1/2026 for effective date 4/1/2026**.
October 2025: Criteria update: Minor updates made to formatting throughout policy for clarity.
October 2023: Original medical policy criteria issued.

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