Preemptive policy: This is a P&T approved policy and can be used after the drug is FDA approved until it is superseded by an updated policy

CENTENE® Corporation

Clinical Policy: Donislecel (Lantidra)

Reference Number: CP.PHAR.569
Effective Date: FDA Approval Date
Last Review Date: 02.22
Line of Business: Commercial, HIM, Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Donislecel (Lantidra™) is an allogenic islet cell transplant.*

** It is the policy of health plans affiliated with Centene Corporation that requests for allogenic islet cell transplantation other than Lantidra are considered experimental/investigational.*

FDA Approved Indication(s) [Pending]

Lantidra is indicated for the treatment of brittle type 1 diabetes mellitus (labile diabetes) in adults whose symptoms are not well controlled despite intensive insulin therapy.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Lantidra is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria*

**Criteria will mirror the clinical information from the prescribing information once FDA-approved*

A. Type 1 Diabetes – Islet Cell Transplantation (must meet all)**:**

1. Diagnosis of type 1 diabetes mellitus for ≥ 5 years;*
2. Prescribed by or in consultation with an endocrinologist;
3. Age ≥ 18 years;*
4. Documentation of intensive insulin management efforts that include coordination of meals/diet and activity with physiologic insulin replacement (multiple daily injections of prandial and basal insulin, or continuous subcutaneous insulin infusion), guided by frequent monitoring of blood glucose levels, use of a continuous glucose monitor (CGM) and/or insulin pump;
5. Member has a history of at least one of the following despite intensive insulin management efforts (a or b):
   a. Uncontrolled hypoglycemia with both of the following (i and ii):
      i. Reduced awareness of hypoglycemia, defined by the absence of adequate autonomic symptoms (see *Appendix C*) at capillary glucose levels of < 54 mg/dL (3 mmol/L);

ii. At least 1 episode of severe hypoglycemia in the past 3 years, defined as an event with symptoms compatible with hypoglycemia that required the assistance of another person, and which was associated with either a blood glucose level < 50 mg/dL (2.8 mmol/L) or prompt recovery after oral carbohydrate, intravenous glucose, or glucagon administration;

b. Uncontrolled hyperglycemia with both of the following (i and ii):
   i. Two or more hospital visits for diabetic ketoacidosis over the last year;
   ii. Progressive secondary complications of diabetes (i.e., retinopathy, nephropathy, neuropathy) despite efforts at optimal glucose control;

6. Member does not have a medical history of any of the following (a-p):
   a. Previous transplant (e.g., pancreas, kidney);
   b. Recent (within the last 30 days) liver function test panel with any value > 1.5 times normal upper limits;
   c. Recent (within the last 30 days) creatinine clearance < 80 mL/min/1.73 m^2 by 24-hour urine collection;
   d. Macroalbuminuria defined as a urinary albumin excretion rate > 300 mg/24 hours;
   e. Recent (within the last 30 days) glycated hemoglobin (HbA1c) > 12%;
   f. Recent (within the last 30 days) hemoglobin (Hb) < 12 gm/dL in women or < 13 gm/dL in men;
   g. Stroke within the past 6 months;
   h. Co-existing cardiac disease characterized by any of the following conditions (i-iv):
      i. Recent (within past six months) myocardial infarction;
      ii. Angiographic evidence of non-correctable coronary artery disease;
      iii. Evidence of ischemia on functional cardiac exam (with a stress echo test for members with a history of ischemic disease);
      iv. Heart failure with New York Heart Association (NYHA) II;
   i. Malignancies except squamous* or basal* skin cancer;
      **Must have lesion(s) removed prior to transplant*
   j. Untreatable significant dysfunction of another major organ system, unless combined organ transplantation can be performed;
   k. Acute medical instability, including, but not limited to, acute sepsis or myocardial infarction;
   l. Uncorrectable bleeding diathesis, use of coumadin or other antiplatelet or anticoagulant therapy, or subject with prothrombin time (PT) international normalized ratio (INR) > 1.5;
   m. Chronic infection with highly virulent and/or resistant microbes that are poorly controlled pre-transplant (e.g., active infection including hepatitis C, hepatitis B, HIV);
   n. Inability to adhere to the regimen necessary to preserve the transplant, even with caregiver support;
   o. Absence of an adequate or reliable social support system;
   p. Substance abuse or dependence (including tobacco and alcohol) without convincing evidence of risk reduction behaviors, such as meaningful and/or long-term participation in therapy for substance abuse and/or dependence;*
      **Serial blood and urine testing may be used to verify abstinence from substances that are of concern*

7. Lantidra is prescribed concurrently with both of the following (a and b):
   a. Immunosuppressives (e.g., daclizumab, basiliximab, sirolimus, everolimus, cyclosporin, tacrolimus, mycophenolate mofetil, anti-human thymocyte immunoglobulin [ATG], etanercept);
   b. Glucagon-like peptide-1 (GLP-1) receptor agonist;*
8. Dose does not exceed packed cell volume of 10 mL per transplant.*

Approval duration: 3 months (one transplant)

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy*

**Criteria will mirror the clinical information from the prescribing information once FDA-approved*

A. Type 1 Diabetes – Islet Cell Transplantation (must meet all)**:**

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
2. Member is responding positively to therapy as evidenced by, including but not limited to, improvement in <u>any</u> of the following parameters:
   a. HbA1c ≤ 6.5% with no severe hypoglycemic events, composite hypoglycemic (HYPO) score of 0, or HYPO score ≤ 50% decrease compared to baseline;
   b. Insulin independence (e.g., absence of exogenous insulin requirements);
   c. Evidence of endogenous insulin production defined as fasting or stimulated C-peptide levels 0.5 ng/mL or greater;
   d. Reduction of insulin requirements ≥ 50% from baseline with a decrease in HbA1c of ≥ 0.3% compared to baseline:

3. Member had a period of insulin independence of at least 30 days following prior islet transplantation and currently demonstrates declining islet function requiring the reintroduction of exogenous insulin;
4. Member continues to be adherent to prescribed immunosuppressive therapy as evidenced by proportion of days covered (PDC) of 0.8 in the last 6 months (or since initiating therapy if less than 6 months since initial transplant);
5. Member has not received more than two Lantidra transplantations;
6. If request is for a dose increase, new dose does not exceed packed cell volume of 10 mL per transplant.*

Approval duration: 3 months (one additional transplant, up to a total of three transplants lifetime)

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

FDA: Food and Drug Administration
Hb: hemoglobin
HbA1c: glycated hemoglobin
HYPO: composite hypoglycemic score
NHYA: New York Heart Association
PDC: proportion of days covered

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings [Pending]

- Contraindication(s): pending
- Boxed warning(s): pending

Appendix D: General Information

- HYPO Score is used as an objective system to quantify the degree and severity of hypoglycemia to standardize assessment of patients undergoing solitary pancreas or islet cell transplantation. A HYPO Score ≥ 1,047 (90th percentile) indicates serious problems with hypoglycemia, scores 423 - 1,046 indicate moderate problems, and scores < 423 indicate less serious problems
- Autonomic symptoms of hypoglycemia include tremulousness, palpitations, anxiety, sweating, hunger, paresthesias, confusion, sensation of warmth, weakness or fatigue, severe cognitive failure, seizure, coma. Glycemic thresholds for symptoms of hypoglycemia shift to lower plasma glucose concentrations following recent episodes of hypoglycemia, leading to the syndrome of hypoglycemia unawareness (loss of the warning symptoms of developing hypoglycemia).
- PDC is a measure of adherence. PDC is calculated as the sum of days covered in a time frame divided by the number of days in the time frame. To achieve a PDC of 0.8, a member must have received their immunosuppressive therapy for 144 days out of the last 180 days, or approximately 5 months of the last 6 months.

V. Dosage and Administration [Pending]

Indication	Dosing Regimen	Maximum Dose
Type 1 diabetes – islet cell transplantation*	Target: minimum islet dose of 10,000 IE/kg with a packed cell volume not to exceed 10 mL per transplant administered to the portal vein via transhepatic access*	10 mL packed cell volume*

VI. Product Availability [Pending]

Pending

VII. References

1. Cellular, Tissue, and Gene Therapies Advisory Committee April 15, 2021 Meeting Briefing Document. Available at: https://www.fda.gov/media/147525/download. Accessed November 8, 2021.
2. Ryan EA, Shandro T, Green K, et al. Assessment of the Severity of Hypoglycemia and Glycemic Lability in Type 1 Diabetic Subjects Undergoing Islet Transplantation. April 2004. Diabetes; 53: 955-962.
3. 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) 51:833–843.
4. Gangemi A, Salehi P, Hatipoglu B, et al. Islet Transplantation for Brittle Type 1 Diabetes: The UIC Protocol. American Journal of Transplantation 2008; 8: 1250–1261.
5. American Diabetes Association. 9. Pharmacologic Approaches to Glycemic Treatment: Standards of Medical Care in Diabetes-2021. Diabetes Care 2021;44(Suppl. 1):S111–S124.

6. ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2021 July 27. Identifier NCT03791567, Islet Transplantation in Type I Diabetic Patients Using the University of Illinois at Chicago (UIC) Protocol. Available at: https://clinicaltrials.gov/ct2/show/NCT03791567. Accessed December 13, 2021.

Coding Implications [Pending]
Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
Pending	Pending

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created pre-emptively	11.30.21	02.22
Template changes applied to other diagnoses/indications and continued therapy section.	10.06.22	

Important Reminder
This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or

regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.