Pharmacy Management Drug Policy

SUBJECT: Lantidra - (donislecel-jujn)
POLICY NUMBER: PHARMACY-115
EFFECTIVE DATE: 05/2024
LAST REVIEW DATE: 11/19/2025

If the member's subscriber contract excludes coverage for a specific service or prescription drug, it is not covered under that contract. In such cases, medical or drug policy criteria are not applied. This drug policy applies to the following line/s of business:

Policy Application

Category:	☒ Commercial Group (e.g., EPO, HMO, POS, PPO)	☒ Medicare Advantage
	☒ On Exchange Qualified Health Plans (QHP)	☐ Medicare Part D
	☒ Off Exchange Direct Pay	☒ Essential Plan (EP)
	☒ Medicaid & Health and Recovery Plans (MMC/HARP)	☒ Child Health Plus (CHP)
	☐ Federal Employee Program (FEP)	☐ Ancillary Services
	☒ Dual Eligible Special Needs Plan (D-SNP)	

DESCRIPTION:

In the United States, approximately 2 million Americans are diagnosed with type 1 diabetes, including roughly 304,000 children and adolescents. This accounts for 5-10% of diabetes cases.[1,2] Type 1 diabetes is primarily caused by autoimmune destruction of insulin producing pancreatic β-cells. Children typically present with polyuria, polydipsia, and diabetic ketoacidosis (DKA)—which can be life-threatening. Adults tend to have more variable symptoms, but certain features may differentiate a diagnosis of type 1 diabetes such as: younger age (<35 years), lower body mass index BMI of < 25 kg/m^2, ketoacidosis, plasma glucose >360 mg/dL, and unintentional weight loss. Genetic and environmental factors (e.g., diet, viruses) also play a role in precipitating autoimmune β-cell damage in type 1 diabetes.[2] A defining feature of the disease is the presence of autoantibodies, specifically those that target glutamic acid decarboxylase, insulin, tyrosine phosphatases islet antigen 2 (IA-2), IA-2β, and zinc transporter 8 (ZnT8). [2]

The absence of β-cell function requires intensive insulin replacement consisting of multiple daily injections or continuous subcutaneous insulin administered through a pump. According to the American Diabetes Association (ADA), continuous glucose monitoring (CGM) is recommended for adults with type 1 diabetes and automated insulin delivery systems should be considered.[3] The overarching goal of insulin therapy in type 1 diabetes is a customized treatment approach to prevent DKA, minimize hypoglycemia, and achieve an individual's glycemic targets. For some individuals, hypoglycemia and hypoglycemia unawareness can be especially challenging when managing type 1 diabetes.[3]

Beyond insulin, surgical treatments for type 1 diabetes include pancreas and islet transplantation to replace β-cells. According to the 2021 ADA/European Association for the Study of Diabetes (EASD) consensus report, β-cell replacement may serve as a therapeutic option for individuals who experience severe metabolic complications including severe hypoglycemia and hypoglycemia unawareness.[4] Whole pancreas transplant and pancreatic islet transplantation both require lifelong immunosuppression. The ADA/EASD suggests carefully considering the risks versus benefit of β-cell replacement because of the need for chronic immunosuppression. The consensus report does note that these approaches have not been compared to newer closed-loop technology, which could avoid immunosuppression altogether.[4]

On June 28, 2023, the Food and Drug Administration (FDA) approved Lantidra (donislecel-jujn), an allogenic pancreatic islet therapy, indicated 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.[5] Lifelong immunosuppression is required to maintain islet cell viability. Lantidra is manufactured from the deceased donor pancreatic cells and is administered via the hepatic portal vein as single infusion. A total of three infusion may be performed based on the patient's response.

Approval of Lantidra was based on two non-randomized single-arm, open-label studies involving a combined 30 participants (UIH-001 and UIH-002), all of whom received at least one islet infusion and a maximum of 3 infusions.[5] A total of 11 participants received 1 infusion, 12 participants received 2 infusions, and 7 participants received 3 infusions. The primary efficacy analysis used a composite endpoint of an HbA1c ≤ 6.5% and absence of severe hypoglycemic events (SHE) through one year after the subject's last transplant. This data was deemed uninterpretable according to the FDA based on substantial missing data and the enrolled population having met or nearly met the primary endpoint at baseline.[6] Insulin independence was a primary endpoint in the UIH-001 trial and a pre-specified secondary endpoint in the UIH-002 trial. In all, 25 (83.3%) of 30 participants were able to achieve insulin independence for any duration 4 days to 12.9 years. For the 25 individuals who achieved insulin independence, 4 participants (13.3%) were insulin independent for less than 1 year, 12 participants (36.7%) for 1 to 5 years, and 9 participants (33.3%) for greater than 5 years.[5,6]

From a safety perspective, 90% of individuals experienced a serious adverse reaction, with two deaths reported: one due to multi-organ failure with sepsis (1.6 years after first infusion) and the other from progressive confusion, global atrophy and micro-ischemic disease (9.7 years after first infusion).[5] Immunosuppression related adverse reactions were common and included infections in 26 patients (87%) and malignancy in 11 patients (37%).[5] Types of malignancies included skin cancer, breast cancer, thyroid cancer, and post-transplant lymphoproliferative disease. Anemia occurred in 24 participants, with 9 severe reactions (Hgb < 6.5 gm/dL) and 27 moderately severe reactions (<10-8 gm/dL).[5] Procedural complications included one liver laceration, one intraabdominal hemorrhage and two perihepatic hematomata. Other common side effects included nausea, fatigue, diarrhea, abdominal pain, asthenia, and headache.[5]

Despite the FDA advisory committee vote in favor of approval (12 to 4, with 1 abstention), concerns were raised regarding the study design including patient selection, lack of control group comparing current standard of care therapies, and serious side effects reported.[6] Additionally, the FDA Biologics License Application Clinical Review Memorandum cites "numerous protocol deviations across the studies that could impair the interpretation of both efficacy and safety data."[6]

POLICY:

Commercial/Essential/Medicaid criteria:

Based upon our criteria and assessment of the peer-reviewed evidence, the use of Lantidra (donislecel-jujn) has not been medically proven to be effective and, therefore, is considered **investigational** 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. The justification for Lantidra (donislecel-jujn) to be considered investigational is as follows:

A. Based on our assessment of the peer-reviewed literature, there is inconclusive evidence that the drug has a definite positive effect on health outcomes.

B. Based upon our assessment of the peer-reviewed medical literature, there is inconclusive evidence that the drug, over time, leads to improvement in health outcomes (e.g., the beneficial effects of the service outweigh any harmful effects).
C. Based upon our assessment of peer-reviewed medical literature, there is inconclusive evidence that the drug is at least as effective in improving health outcomes as established services or technologies
D. Based upon our assessment of peer-reviewed medical literature, there is inconclusive evidence that the drug provides improvement in health outcomes in standard conditions of medical practice, outside the clinical investigatory settings.

Refer to Corporate Medical Policy #11.01.03 Experimental or Investigational Services

Medicare criteria:

Medicare reviews are to follow the current National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) issued by CMS. The NCD for Islet Cell Transplantation in the Context of a Clinical Trial can be found at: NCD - Islet Cell Transplantation in the Context of a Clinical Trial (260.3.1) (cms.gov).

POLICY GUIDELINES:

1. Unless otherwise stated above within the criteria, approval time-period will be for 1 year.
   - Continued approval at time of recertification will require documentation that the drug is providing ongoing benefit to the patient in terms of improvement or stability in disease state or condition.
2. Clinical documentation must be submitted for each request (initial and recertification) unless otherwise specified (e.g., provider attestation required). Supporting documentation includes, but is not limited to, progress notes documenting previous treatments/treatment history, diagnostic testing, laboratory test results, genetic testing/biomarker results, imaging and other objective or subjective measures of benefit which support continued use of the requested product is medically necessary. Also, ongoing use of the requested product must continue to reflect the current policy's preferred formulary. Recertification reviews may result in the requirement to try more cost-effective treatment alternatives as they become available (i.e., generics, biosimilars, or other guideline supported treatment options). Requested dosing must continue to be consistent with FDA-approved or off-label/guideline-supported dosing recommendations.
3. Prior authorization is contract dependent
4. Not all contracts cover all Medical Infusible drugs. Refer to specific contract/benefit plan language for exclusions of Injectable Medications.
5. Lantidra is administered through hepatic portal vein and will be considered for coverage under the medical benefit
6. See related policy: *Corporate Medical Policy # 7.02.01 Pancreas Transplant: (Pancreas Transplant Alone, Pancreas Transplant after Kidney Transplant, Simultaneous Pancreas Kidney Transplant): Islet Cell Transplant*
7. This policy does not apply to Medicare Part D and D-SNP pharmacy benefits. The drugs in this policy may apply to all other lines of business including Medicare Advantage.
8. For members with Medicare Advantage, medications with a National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) will be covered pursuant to the criteria outlined by the NCD and/or LCD. NCDs/LCDs for applicable medications can be found on the CMS website at https://www.cms.gov/medicare-coverage-database/search.aspx. Indications that have not been addressed by the applicable medication's LCD/NCD will be covered in accordance with criteria determined by the Health Plan (which may include review per the Health Plan's Off-Label Use of

FDA Approved Drugs policy). Step therapy requirements may be imposed in addition to LCD/NCD requirements.

9. All requests will be reviewed to ensure they are being used for an appropriate indication and may be subject to an off-label review in accordance with our Off-Label Use of FDA Approved Drugs Policy (Pharmacy-32).
10. All utilization management requirements outlined in this policy are compliant with applicable New York State insurance laws and regulations. Policies will be reviewed and updated as necessary to ensure ongoing compliance with all state and federally mandated coverage requirements.
11. Manufacturers may either discontinue participation in, or may not participate in, the Medicaid Drug Rebate Program (MDRP). Under New York State Medicaid requirements, physician-administered drugs must be produced by manufacturers that participate in the MDRP. Products made by manufacturers that do not participate in the MDRP will not be covered under Medicaid Managed Care/HARP lines of business. Drug coverage will not be available for any product from a non-participating manufacturer. For a complete list of New/Reinstated & Terminated Labelers please visit: https://www.medicaid.gov/medicaid/prescriptiondrugs/medicaid-drug-rebate-program/newreinstated-terminated-labeler-information/index.html

CODES:

Eligibility for reimbursement is based upon the benefits set forth in the member's subscriber contract. CODES MAY NOT BE COVERED UNDER ALL CIRCUMSTANCES. PLEASE READ THE POLICY AND GUIDELINES STATEMENTS CAREFULLY.

Codes may not be all inclusive as the AMA and CMS code updates may occur more frequently than policy updates.

Code Key:
Experimental/Investigational = (E/I),
Not medically necessary/ appropriate = (NMN).

UPDATES:

Date	Revision
11/19/2025	Revised
03/06/2025	Revised
02/06/2025	P&T Committee Review & Approval
12/15/2024	Revised
09/13/2024	Revised
06/20/2024	Revised
05/08/2024	Created and Implemented
02/08/2024	P&T Committee Approval

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3. American Diabetes Association Professional Practice Committee. 6. Glycemic Goals and Hypoglycemia: Standards of Care in Diabetes-2024. *Diabetes Care*. 2024;47(Suppl 1):S111-S125. doi:10.2337/dc24-S006
4. 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). *Diabetes Care*. 2021;44(11):2589-2625. doi:10.2337/dci21-0043
5. Lantidra [package insert]. Chicago, IL: CellTrans Inc.; 2023
6. Lantidra. U.S. Food and Drug Administration. August 7, 2023. https://www.fda.gov/vaccines-blood-biologics/lantidra. Accessed February 1, 2024.