Medical Benefit Drug Policy

Lantidra (donislecel-jujn) Suspension

Policy Number: MC/PC 024
Effective Date: October 1, 2024

Instructions for Use

Table of Contents **Page**

Coverage Rationale 1
Applicable Codes 2
Background 2
Clinical Evidence 2
U.S. Food and Drug Administration 4
References 4
Policy History/Revision Information 5
Instructions for Use 5

Related Policies

- n/a

Coverage Rationale

Treatment of adults with Type 1 diabetes

For initial coverage of **Lantidra (donislecel-jujn)** 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 following will be required:

- Diagnosis of Type 1 diabetes **and**
- Patient has been insulin dependent for 5 years **and**
- Patient is unable to approach target HbA1c because of repeated episodes of severe hypoglycemia despite adherence to intensive diabetes management and education **and**
- Patient has reduced awareness of hypoglycemia, as defined by the absence of adequate autonomic symptoms at glucose levels of less than 54 mg/dL **and**
- Patient has had at least one episode of severe hypoglycemia in the past 3 years with both of the following:
    - Patient required assistance of another person **and**
    - One of the following:
        - Symptoms were associated with a blood glucose level less than 54 mg/dL **or**
        - Prompt recovery after oral carbohydrate, intravenous glucose, or glucagon administration **and**
- Patient will be on concomitant immunosuppression (e.g., daclizumab, sirolimus, tacrolimus, etanercept, mycophenolate mofetil, etc. **and**
- Prescribed by or in consultation with an endocrinologist

For reauthorization coverage of Lantidra (donislecel-jujn), the following will be required:

- Patient has not achieved independence from exogenous insulin within one year of infusion or within one year after losing independence from exogenous insulin after previous infusion **and**

- Patient has not had more than three infusions of Lantidra in their lifetime

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

HCPCS Code	Description
J3590	Unclassified biologics

ICD-10 Code	Description
E10	Type 1 diabetes mellitus
E10.8	Type 1 diabetes mellitus with unspecified complications
E10.9	Type 1 diabetes mellitus without complications

Background

The classification of diabetes includes four clinical classes: 1) Type 1 diabetes (T1DM) which results from beta-cell (β -cell) destruction, usually leading to absolute insulin deficiency; 2) Type 2 diabetes (T2DM) which results from a progressive insulin secretory defect on the background of insulin resistance; 3) Specific types of diabetes due to other causes, e.g., genetic defects in β -cell function, genetic defects in insulin action, diseases of the exocrine pancreas (such as cystic fibrosis), and drug- or chemical-induced (such as with glucocorticoid use, in the treatment of HIV/AIDS or after organ transplantation); and 4) Gestational diabetes mellitus (diabetes diagnosed during pregnancy that is not clearly overt diabetes) (ADA 2024).

Type 1 diabetes is caused by an immune-mediated destruction and dysfunction of insulin-producing pancreatic β -cells. This leads to the development of insulin insufficiency which requires exogenous insulin therapy. Patients have historically been diagnosed at the onset of clinical signs and symptoms of hyperglycemia and diabetic ketoacidosis (DKA). Currently, through screening for diabetes-related autoantibodies and metabolic monitoring, patients can be identified before the development of these clinical symptoms. (Greenbaum CJ, et al. 2024)

Clinical Evidence

Lantidra (donislecel-jujn) Allogeneic Pancreatic Islet Cellular Suspension for hepatic portal vein infusion
The effectiveness of Lantidra in subjects with type 1 diabetes and hypoglycemic unawareness was demonstrated in 2 clinical trials (Study 1, Study 2) involving a combined 30 subjects, all of whom received at least one islet infusion and a maximum of 3 infusions. Both trials were prospective, open-label, single-arm studies. Subject demographics: median age 46.5 (range: 21 – 67) years, 80% female, 100% white, 97% non-Hispanic.

Subjects received a median islet number of 399,178 EIN (range 253,924 EIN to 858,856 EIN) per infusion. Subjects received a median islet dose of 6,570 EIN/kg (range 4,186 EIN/kg to 13,633 EIN/kg) per infusion. Thirty subjects participated in the combined Study 1 and Study 2, with 11 subjects receiving one infusion, 12 subjects receiving two infusions, and 7 subjects receiving three infusions. Of the 19 subjects who received a second infusion, 6 were insulin-independent at the time of their second infusion. Of the 11 subjects who did not receive a second infusion, 4 were

insulin-independent, 3 did not have a donor, and 4 were intolerant to immunosuppression or withdrew from the study within 6 months. All 7 subjects who received a third infusion were insulin-dependent. One subject was not able to get a third infusion because of infection. No subject was unable to receive a third infusion because of lack of a donor or intolerance to immunosuppression.

Concomitant study medications were provided as described in Table 1:

Medication	**Study 1 (N=10)**	**Study 2 (N=20)**
Anakinra; n (%)	1 (10%)	0 (0%)
Daclizumab; n (%)	10 (100%)	5 (24%)
Basiliximab; n (%)	5 (10%)	19 (95%)
Mycophenolate mofetil; n (%)	6 (60%)	5 (24%)
Etanercept; n (%)	6 (60%)	20 (100%)
Everolimus; n (%)	1 (10%)	2 (10%)
Sirolimus; n (%)	10 (100%)	20 (100%)
Tacrolimus; n (%)	10 (100%)	20 (100%)
Cyclosporine; n (%)	1 (10%)	3 (15%)
Anti-thymocyte immunoglobulin; n (%)	1 (10%)	4 (20%)

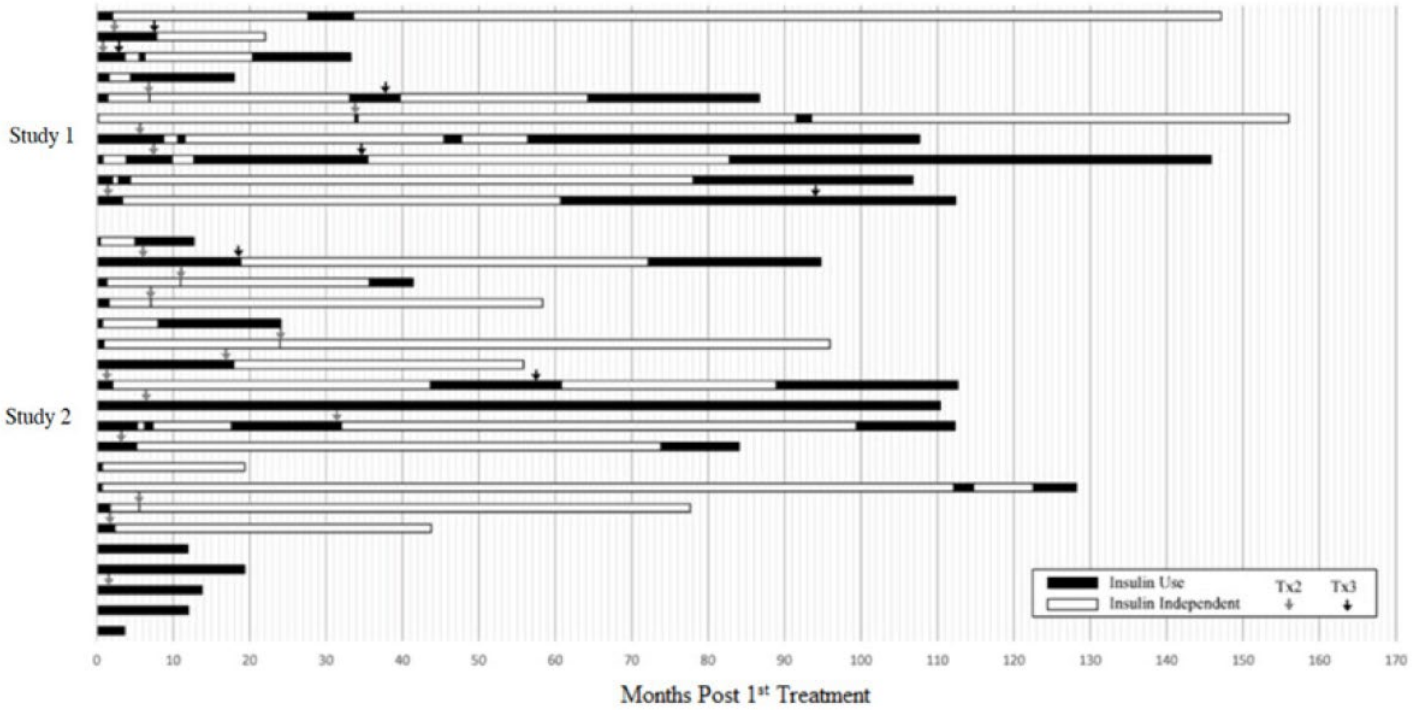
A glucagon-like peptide-1 (GLP-1) agonist (e.g., exenatide 5 mcg subcutaneously within 60 minutes before infusion), was administered and was supposed to be continued (5 mcg BID), for up to 6 months after transplant. Exenatide was not given to the first 4 subjects in Study 1, and 11 of the remaining 26 subjects used exenatide less than the per protocol 6-months post-transplant because of adverse reactions. Because of the variability of exenatide use in the clinical studies, there are insufficient data to support exenatide use in patients receiving Lantidra. Insulin independence, defined as not requiring exogenous insulin to achieve adequate glycemic control, was also determined. Results are summarized in Table 2.

Table 2: Achievement and Maintenance of Glycemic Control following LANTIDRA Infusion (Studies Study 1 & Study 2)

Total Duration Insulin Independent (years)	**N**	**Mean**	**Std Dev**	**Min**	**Max**
Study 1	10	5.1	4.2	0.2	12.8
Study 2	20	3.2	3.1	0	9.9

Five subjects had no days of insulin independence. For the 25 subjects who achieved insulin independence, 4 subjects (13.3%) were insulin independent for less than one year, 12 subjects (36.7%) for 1 to 5 years, and 9 subjects (33.3%) for greater than 5 years. Figure 1 shows the entire experience of the individual subjects.

Figure 1: Periods of Insulin Use and Insulin Independence following Initial Infusion, by Patient (Pooled Population)



This figure shows the total duration of follow-up for each subject. The period of insulin dependence (use) is denoted in black and the period of insulin independence in white. Time zero (0) is the time of the first infusion. The arrows denote the time of second and third infusions.

Place in Therapy

The American Diabetes Association has published a supplemental guideline stating that for Type 1 diabetes patients that are unable to achieve their target hemoglobin A1c (HbA1c) despite intensive diabetes management and education, Lantidra is a treatment option to restore glycemic control, eliminate hypoglycemia episodes, and reduce or eliminate exogenous insulin injections. (Rios et al. 2024)

U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

LANTIDRA is an allogeneic pancreatic islet cellular 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. Use in conjunction with concomitant immunosuppression.

References

1. American Diabetes Association (ADA). Standards of Medical Care in Diabetes−2024. Diabetes Care. 2023;47(Suppl 1):S1-S321. https://diabetesjournals.org/care/issue/47/Supplement_1. Accessed July 1, 2024.

2. Greenbaum CJ, Lord S, and Speake C. Type 1 diabetes mellitus: Disease prediction and screening. UpToDate. Updated April 27, 2024. www.uptodate.com. Accessed July 1, 2024.
3. LANTIDRA (donislecel-jujn) Allogeneic Pancreatic Islet Cellular Suspension for hepatic portalvein infusion [package insert], Chicago, IL: CellTrans.; June 2023.
4. Rios P, McGarrigle JJ, Lamonica G, Li Y, Cook J, et al.; 35-OR: Lantidra, First FDA-Approved Cellular Therapy to Treat Type 1 Diabetes. Diabetes 14 June 2024; 73 (Supplement_1): 35–OR. https://doi.org/10.2337/db24-35-OR

Policy History/Revision Information

Date	Summary of Changes
9/18/2024	Approved by OptumRx P&T Committee

Instructions for Use

This Medical Benefit Drug Policy provides assistance in interpreting standard benefit plans. When deciding coverage, the member specific benefit plan document must be referenced as the terms of the member specific benefit plan may differ from the standard plan. In the event of a conflict, the member specific benefit plan document governs. Before using this policy, please check the member specific benefit plan document and any applicable federal or state mandates. The insurance reserves the right to modify its Policies and Guidelines as necessary. This Medical Benefit Drug Policy is provided for informational purposes. It does not constitute medical advice.

OptumRx may also use tools developed by third parties to assist us in administering health benefits. OptumRx Medical Benefit Drug Policies are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.

Archived Policy Versions (Internal Only)

Effective Date	Policy Number	Policy Title
mm/dd/yyyy – mm/dd/yyyy	######	Title of Policy Hyperlinked to KL or Other Internal Location

Nondiscrimination & Language Access Policy

Discrimination is Against the Law. Aspirus Health Plan, Inc. complies with applicable Federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability, or sex, (including sex characteristics, including intersex traits; pregnancy or related conditions; sexual orientation, gender identity and sex stereotypes), consistent with the scope of sex discrimination described at 45 CFR § 92.101(a)(2). Aspirus Health Plan, Inc. does not exclude people or treat them less favorably because of race, color, national origin, age, disability, or sex.

Aspirus Health Plan, Inc.:
Provides people with disabilities reasonable modifications and free appropriate auxiliary aids and services to communicate effectively with us, such as:

- Qualified sign language interpreters.
- Written information in other formats (large print, audio, accessible electronic formats, other formats).

Provides free language assistance services to people whose primary language is not English, which may include:

- Qualified interpreters.
- Information written in other languages.

If *you* need reasonable modifications, appropriate auxiliary aids and services, or language assistance services, contact the Nondiscrimination Grievance Coordinator at the address, phone number, fax number, or email address below.

If *you* believe that Aspirus Health Plan, Inc. has failed to provide these services or discriminated in another way on the basis of race, color, national origin, age, disability, or sex, *you* can file a *grievance* with:

Nondiscrimination Grievance Coordinator
Aspirus Health Plan, Inc.
PO Box 1890
Southampton, PA 18966-9998
Phone: 1-866-631-5404 (TTY: 711)
Fax: 763-847-4010
Email: customerservice@aspirushealthplan.com

You can file a *grievance* in person or by mail, fax, or email. If *you* need help filing a *grievance*, the Nondiscrimination Grievance Coordinator is available to help *you*.

You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights, electronically through the Office for Civil Rights Complaint Portal, available at https://ocrportal.hhs.gov/ocr/portal/lobby.jsf, or by mail or phone at:

U.S. Department of Health and Human Services
200 Independence Avenue, SW
Room 509F, HHH Building
Washington, D.C. 20201
1.800.368.1019, 800.537.7697 (TDD)

Complaint forms are available at http://www.hhs.gov/ocr/office/file/index.html. This notice is available at Aspirus Health Plan, Inc.'s website: https://aspirushealthplan.com/webdocs/70021-AHP-NonDiscrim_Lang-Assist-Notice.pdf.

Language Assistance Services

Albanian: KUJDES: Nëse flitni shqip, për ju ka në dispozicion shërbime të asistencës gjuhësore, pa pagesë.Telefononi në 1-800-332-6501 (TTY: 711).

Arabic تنبيه: إذا كنت تتحدث اللغة العربية، فإن خدمات المساعدة اللغوية متاحة لك مجاناً. اتصل بن اعلى رقم الهاتف1-800-332-6501(رقم هاتف الصم والبك : 711)

French: ATTENTION: Si vous parlez français, des services d'aide linguistique vous sont proposés gratuitement. Appelez le 1-800-332-6501 (ATS: 711).

German: ACHTUNG: Wenn Sie Deutsch sprechen, stehen Ihnen kostenlos sprachliche Hilfsdienstleistungen zurVerfügung. Rufnummer: 1-800-332-6501 (TTY: 711).

Hindi: _यान द_: य_द आप ि हंदी बोलते ह_ तो आपके ि लए मु_त म_ भाषा सहायता सेवाएं उपल_ध ह_।1-800-332-6501 (TTY: 711) पर कॉल कर_।

Hmong: LUS CEEV: Yog tias koj hais lus Hmoob, cov kev pab txog lus, muaj kev pab dawb rau koj. Hu rau 1-800-332-6501 (TTY: 711).

Korean: 주의: 한국어를 사용하시는 경우, 언어 지원 서비스를 무료로 이용하실 수 있습니다.1-800-332-6501 (TTY: 711)번으로 전화해 주십시오.

Polish: UWAGA: Jeżeli mówisz po polsku, możesz skorzystać z bezpłatnej pomocy językowej. Zadzwoń pod numer1-800-332-6501 (TTY: 711).

Russian: ВНИМАНИЕ: Если вы говорите на русском языке, то вам доступны бесплатные услуги перевода.Звоните 1-800-332-6501 (телетайп: 711).

Spanish: ATENCIÓN: si habla español, tiene a su disposición servicios gratuitos de asistencia lingüística. Llame al1-800-332-6501 (TTY: 711).

Tagalog: PAUNAWA: Kung nagsasalita ka ng Tagalog, maaari kang gumamit ng mga serbisyo ng tulong sa wika nangwalang bayad. Tumawag sa 1-800-332-6501 (TTY: 711).

Traditional Chinese: 注意：如果您使用繁體中文， 您可以免費獲得語言援助服務。請 致電 1-800-332-6501 (TTY: 711)

Vietnamese: CHÚ Ý: Nếu bạn nói Tiếng Việt, có các dịch vụ hỗ trợ ngôn ngữ miễn phí dành cho bạn. Gọi số 1-800-332-6501 (TTY: 711).

Pennsylvania Dutch: Wann du Deitsch (Pennsylvania German / Dutch) schwetzscht, kannscht du mitaus Koschte ebbergricke, ass dihr helft mit die englisch Schprooch. Ruf selli Nummer uff: Call 1-800-332-6501 (TTY: 711).

Lao: ໂປດຊາບ: ຖ້າວ່າ ທ່ານເວົ້າພາສາ ລາວ, ການບໍລິການຊ່ວຍເຫຼືອດ້ານພາສາ,ໂດຍບໍ່ເສັງຄ່າ, ແມ່ນມີພ້ອມໃຫ້ທ່ານ. ໂທຣ 1-800-332-6501 (TTY: 711).

70021 07-24 ©2024 Aspirus Health Plan, Inc. All rights reserved.