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MEDICAL POLICY – 7.03.12

Islet Transplantation for Chronic Pancreatitis and Donislecel-jujn for Type 1 Diabetes

BCBSA Ref. Policy:	7.03.12	
Effective Date:	Jan. 1, 2025	RELATED MEDICAL POLICIES:
Last Revised:	Dec. 9, 2024	7.03.02 Allogeneic Pancreas Transplant
Replaces:	N/A	

Select a hyperlink below to be directed to that section.

POLICY CRITERIA | DOCUMENTATION REQUIREMENTS | CODING
RELATED INFORMATION | EVIDENCE REVIEW | REFERENCES | HISTORY

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Introduction

The pancreas is an organ that stretches lengthwise across the abdominal area below the stomach. Within the pancreas are cell clusters commonly called "the islets." Included in the islets are beta cells which make, store, and release insulin. Treating chronic inflammation of the pancreas may mean removing the pancreas. Removing the pancreas also removes the islets and the beta cells, which then leads to type 1 diabetes. To prevent the development of type 1 diabetes in people who have their pancreas removed, their own islet cells can be harvested and injected into a specific vein in the liver. Published medical studies show that islet cell transplantation appears to significantly decrease the development of diabetes after the pancreas is removed. In this situation, islet cell transplantation may be considered medically necessary. Islet cell transplantation using donor cells is being studied as a technique to treat existing type 1 diabetes. There is not enough medical evidence to show how well this works to treat type 1 diabetes. Larger and longer studies are needed. For these reasons, islet cell transplantation to treat existing type 1 diabetes is investigational (unproven).

Note: The Introduction section is for your general knowledge and is not to be taken as policy coverage criteria. The rest of the policy uses specific words and concepts familiar to medical professionals. It is intended for providers. A provider can be a person, such as a doctor, nurse, psychologist, or dentist. A provider also can be a place where medical care is given, like a hospital, clinic, or lab. This policy informs them about when a

service may be covered.

Policy Coverage Criteria

Procedure	Medical Necessity
Autologous pancreas islet transplantation	**Autologous pancreas islet transplantation may be considered medically necessary as an adjunct to a total or near total pancreatectomy in individuals with chronic pancreatitis.**

Procedure	Investigational
Allogeneic islet transplantation	**Allogeneic islet transplantation using an FDA approved cellular therapy product (donislecel-juin [i.e., Lantidra]) is considered investigational for the treatment of type 1 diabetes.**
Islet transplantation, all other situations	**Islet transplantation with donislecel-juin (Lantidra) is considered investigational in all other situations.**

Documentation Requirements
The individual's medical records submitted for review for all conditions should document that medical necessity criteria are met. The record should include the following: • Office visit notes that contain the relevant history and physical: ○ Individual had pancreas removed because of chronic pancreatitis

Coding

Code	Description
CPT	
48160	Pancreatectomy, total or subtotal, with autologous transplantation of pancreas or pancreatic islet cells
0584T	Islet cell transplant, includes portal vein catheterization and infusion, including all imaging, including guidance, and radiological supervision and interpretation, when performed; percutaneous

Code	Description
0585T	Islet cell transplant, includes portal vein catheterization and infusion, including all imaging, including guidance, and radiological supervision and interpretation, when performed; laparoscopic
0586T	Islet cell transplant, includes portal vein catheterization and infusion, including all imaging, including guidance, and radiological supervision and interpretation, when performed; open
HCPCS	
G0341	Percutaneous islet cell transplant, includes portal vein catheterization and infusion
G0342	Laparoscopy for islet cell transplant, includes portal vein catheterization and infusion
G0343	Laparotomy for islet cell transplant, includes portal vein catheterization and infusion
S2102	Islet cell tissue transplant from pancreas; allogeneic
ICD-10 PCS	
XW033DA	Introduction of Donislecel-jujn Allogeneic Pancreatic Islet Cellular Suspension into Peripheral Vein, Percutaneous Approach, New Technology Group 10 (used to report Lantidra) (new code effective 10/1/24)

Related Information

Only adult subjects were enrolled in donislecel-jujn (Lantidra) clinical studies, although clinical studies did not include sufficient numbers of patients aged 65 and over to determine whether they respond differently than younger patients. Risks of donislecel-jujn infusion in pregnancy have not been assessed.

There are risks associated with the infusion procedure and long-term immunosuppression. There is no evidence of donislecel-jujn benefit for individuals whose diabetes is well-controlled with insulin therapy or for those 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 donislecel-jujn (Lantidra) for individuals with liver disease, renal failure, or who have received a renal transplant.

Islet transplantation does not supplant future whole pancreatic transplantation (see **Related Policy**).

A specific target of hemoglobin A1c (HbA1c) cannot be provided for all patients, as the target can be different based on age, duration of diabetes, and diabetic complications.

"Current repeated episodes" indicates risk within 1 year of the intended transplantation and is not related to events more than 1 year prior to the intended transplantation.

Evidence Review

Description

Performed in conjunction with pancreatectomy for chronic pancreatitis, autologous islet transplantation is proposed to reduce the likelihood of insulin-dependent diabetes. Allogeneic islet cell transplantation with donislecel-juin (Lantidra) is also being investigated as a treatment or cure for individuals with type 1 diabetes.

Background

Islet Transplantation

In autologous islet transplantation during the pancreatectomy procedure, islet cells are isolated from the resected pancreas using enzymes, and a suspension of the cells is injected into the portal vein of the individual's liver.[1] Once implanted, the beta cells in these islets begin to make and release insulin.

Allogeneic islet transplantation potentially offers an alternative to whole-organ pancreas transplantation in patients with type 1 diabetes.[2] In the case of allogeneic islet cell transplantation, cells are harvested from a deceased donor's pancreas, processed, and injected into the recipient's portal vein. Islet transplantation has generally been reserved for individuals with frequent and severe metabolic complications who have consistently failed to achieve

control with insulin-based management. Allogeneic transplantation may be performed in the radiology department.

In 2000, a modified immunosuppression regimen increased the success of allogeneic islet transplantation. This regimen is known as the "Edmonton protocol."

Summary of Evidence

For individuals with chronic pancreatitis undergoing total or near total pancreatectomy who receive autologous pancreas islet transplantation, the evidence includes nonrandomized studies and systematic reviews. The relevant outcomes are overall survival, change in disease status, medication use, resource utilization, and treatment-related morbidity. Autologous islet transplants are performed in the context of total or near total pancreatectomies to treat intractable pain for chronic pancreatitis. The procedure appears to decrease significantly the incidence of diabetes after total or near total pancreatectomy in individuals with chronic pancreatitis. Also, this islet procedure is not associated with serious complications and is performed in individuals who are already undergoing a pancreatectomy procedure. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with type 1 diabetes who receive allogeneic pancreas islet transplantation with donislecel-jujn (Lantidra), the evidence includes single-arm prospective trials conducted at a single study site without strict protocols demonstrating insulin independence for over one year in a majority of participants, with mean insulin independence of approximately five years, resulting in US Food and Drug Administration (FDA) approval of donislecel-juin (Lantidra) for adults who are unable to approach target hemoglobin A1c (HbA1c) because of current repeated episodes of severe hypoglycemia despite intensive diabetes management and education and for use in conjunction with concomitant immunosuppression. Additional well-designed studies are required to determine the effects of allogeneic islet transplantation in patients with type 1 diabetes. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Ongoing and Unpublished Clinical Trials

Some currently ongoing trials that might influence this review are listed in **Table 1**.

Table 1. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT05287737	Clinical Outcome After Total Pancreatectomy With Islet Autotransplantation	100	Mar 2047
NCT04711226	An Open-Label Study to Evaluate the Safety, Tolerability and Efficacy of Immunomodulation With AT-1501 in Adults With Type 1 Diabetes Undergoing Islet Cell Transplant	6	June 2026
NCT00706420	Islet Transplantation Alone (ITA) in Patients With Difficult to Control Type I Diabetes Mellitus Using a Glucocorticoid-free Immunosuppressive Regimen	17	Nov 2024
NCT00306098	Islet Cell Transplantation Alone in Patients With Type 1 Diabetes Mellitus: Steroid-Free Immunosuppression	40	May 2026
NCT01897688	A Phase 3 Single Center Study of Islet Transplantation in Non-uremic Diabetic Patients	40	Mar 2027
NCT00679042[a]	Islet Transplantation in Type 1 Diabetic Patients Using the University of Illinois at Chicago (UIC) Protocol, Phase 3	21	Jun 2026
NCT05662267	Targeted Trial Emulation of Kidney Alone Versus Islet-After-Kidney in Type 1 Diabetic Transplant Recipients: a French Nationwide Cohort Study	500	Mar 2023
NCT01630850	Islet Transplantation in Patients With "Brittle" Type I Diabetes	20	Jun 2030
Ongoing			
NCT03698396	A Phase I/II, Open-Arm Study Evaluating the Safety of Islet Transplant in Patients With Type I Diabetes	10	Dec 2023 (unknown status)

NCT: national clinical trial. [a] Denotes industry-sponsored or cosponsored trial.

Practice Guidelines and Position Statements

The purpose of the following information is to provide reference material. Inclusion does not imply endorsement or alignment with the policy conclusions.

Guidelines or position statements will be considered for inclusion if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are

informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

National Institute for Care Excellence

In 2008, NICE published guidance indicating the evidence on allogeneic pancreatic islet cell transplantation for type 1 diabetes has shown that serious procedure-related complications may occur, and the long-term immunosuppression required is associated with the risk of adverse events.[51] A related 2008 guidance addressed autologous islet cell transplantation for improved glycemic control after pancreatectomy and stated that studies have shown "some short-term efficacy, although most individuals require insulin therapy in the long term...complications result mainly from the major surgery involved in the pancreatectomy (rather than from the islet cell transplantation)."[52]

American Diabetes Association

In 2024, the American Diabetes Association (ADA) standards of medical care recommended autologous islet cell transplantation be considered in individuals undergoing total pancreatectomy for chronic pancreatitis to prevent postsurgical diabetes.[53] The standards of care note that islet cell transplantation may have a role in type 1 diabetes. Because of the need for immunosuppressive agents posttransplantation, the guideline notes that transplantation in type 1 diabetes should be reserved for individuals also undergoing renal transplantation or experiencing recurrent ketoacidosis with severe hypoglycemia despite intensive management. The ADA also states that 'In much of the world, allogenic islet transplantation is regulated as an organ transplant. However, in the US, allogenic islet transplantation is regulated as a cell therapy, and the first such allogeneic islet cell therapy, donislecel-jujn, was approved in 2023. Donislecel is indicated for the treatment of adults with type 1 diabetes who are unable to approach their A1C goal because of current repeated episodes of severe hypoglycemia despite intensive diabetes management and education.' However, no recommendation was provided for the use of allogenic islet transplantation.

International Consensus Guidelines for Chronic Pancreatitis

In 2020, the International Consensus Guidelines for Chronic Pancreatitis panel released a statement on the role of total pancreatectomy and islet transplantation in individuals with

chronic pancreatitis.[54] The panel stated that islet transplantation should be considered for individuals undergoing total pancreatectomy due to the potential for insulin independence and better long-term glycemic outcomes compared to pancreatectomy alone (weak recommendation based on low quality evidence). However, there is not enough information to definitively conclude when transplantation should be performed relative to other interventions. Major indications for pancreatectomy with islet transplantation include debilitating pain or recurrent pancreatitis episodes that diminish quality of life (strong recommendation based on low quality evidence). Contraindications to pancreatectomy with islet transplantation include active alcoholism, pancreatic cancer, end-stage systemic illness, or psychiatric illness or socioeconomic status that would hinder either the procedure itself or posttransplant care (strong recommendation based on low quality evidence). Pancreatectomy with islet transplantation improves quality of life, opioid use, and pancreatic pain in this population, but evidence about the effect on healthcare utilization is limited.

Medicare National Coverage

Medicare covers pancreatic islet transplantation in individuals with type 1 diabetes participating in a clinical trial sponsored by the National Institutes of Health.[55] Partial pancreatic tissue transplantation or islet transplantation performed outside a clinical trial are not covered.

Regulatory Status

The US Food and Drug Administration (FDA) regulates human cells and tissues intended for implantation, transplantation, or infusion through the Center for Biologics Evaluation and Research, under Code of Federal Regulation title 21, parts 1270 and 1271. Allogeneic islet cells are included in these regulations. Donislecel-jujn (Lantidra), a first-in-class deceased donor-derived allogeneic pancreatic islet cellular therapy product, was approved by the FDA in June 2023 for the treatment of type 1 diabetes in adults who are unable to approach target hemoglobin A1c due to repeated episodes of severe hypoglycemia despite intensive diabetes management and education.[3]

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History

Date	Comments
11/13/01	Add to Surgery Section - New Policy
03/08/05	Replace Policy - Policy reviewed; added information on islet transplantation for type I diabetes and statement that this indication is considered investigational; added Medicare coverage policy information on islet transplantation for type 1 diabetes; removed "autologous" from the policy title; HCPCS codes updated.
12/13/05	Replace Policy - Policy reviewed with literature search; reference added. Policy statement and title updated with removal of "cell" when describing islet transplantation rather than "islet cell transplantation."
05/26/06	Scope and Disclaimer Updates - No other changes.
09/12/06	Replace Policy - Policy updated with literature search; no change to policy statement; reference added.
03/11/08	Replace Policy - Policy updated with literature search; no change to policy statement; reference added.
07/14/09	Replace Policy - Policy updated with literature search; no change to policy statement. Benefit Application section updated. References added.
09/14/10	Replace Policy - Policy updated with literature review; rationale section extensively edited. References numbers 16 – 18 have been added; the policy statements remain unchanged.
08/09/11	Replace Policy – Policy updated with literature review. Reference numbers 13 and 17 added; other references renumbered or removed; policy statements unchanged. ICD-10 codes added to policy.
08/20/12	Replace Policy. Rationale section revised based on literature review through April 2012. References 1-3 and 14 added, other references renumbered or removed. Policy statements unchanged.
09/28/12	Update Coding Section – ICD-10 codes are now effective 10/01/2014.
01/10/13	Coding update. CPT codes 0141T – 0143T removed from policy; they were deleted as of 1/1/12.
08/16/13	Replace policy. Policy guidelines reformatted for readability. Rationale updated with literature review through April 18, 2013. Ongoing clinical trial added. Reference numbers 7,9,11 and 16 added; others renumbered or removed. Policy statements unchanged.
03/11/14	Coding Update. Codes 52.85 and 52.86 were removed per ICD-10 mapping project; these codes are not utilized for adjudication of policy.
07/31/14	Annual Review. Policy updated with literature review through March 26, 2014. Reference numbers 4, 10, 11 and 20 added. Statement added that islet transplantation is considered investigational in all other situations.

Date	Comments
07/14/15	Annual Review. Policy updated with literature review through April 8, 2015; references 1, 3, 6, and 11 added. Policy statements unchanged. ICD-9 and ICD-10 procedure codes removed; these were listed for informational purposes only.
12/01/16	Annual Review, approved November 8, 2016. Policy updated with literature review through October 10, 2016; reference 17 added. Policy statements unchanged.
10/01/17	Annual Review, approved September 21, 2017. Policy updated with literature review through June 22, 2017; clinical trials section added; reference 14 added; reference 17 updated. Removed CPT code 48999. Policy statements unchanged.
10/01/18	Annual Review, approved September 20, 2018. Policy updated with literature review through June 2018; references 1 and 10 added. Policy statements unchanged.
10/10/18	Minor update, added Documentation Requirements section.
11/01/19	Annual Review, approved October 4, 2019. Policy updated with literature review through June 2019; no references added. Policy statements unchanged.
01/01/20	Coding update, added CPT codes 0584T, 0585T, and 0586T (new codes effective 1/1/20).
08/01/20	Coding update. Removed CPT codes 0584T, 0585T and 0586T.
11/01/20	Annual Review, approved October 22, 2020. Policy updated with literature review through June, 2020; references added. Policy statements unchanged. Added CPT codes 0584T, 0585T, 0586T.
11/01/21	Annual Review, approved October 5, 2021. Policy updated with literature review through June 22, 2021; references added. Policy statements unchanged.
11/01/22	Annual Review, approved October 24, 2022. Policy updated with literature review through June 17, 2022; references added. Minor editorial refinements to policy statement; intent unchanged. Changed the wording from "patient" to "individual" throughout the policy for standardization.
06/01/24	Annual Review, approved May 14, 2024. Policy updated with literature review through June 30, 2023; references added. Policy title updated from “Islet Transplantation” to “Islet Transplantation for Chronic Pancreatitis and Donislecel-jujn for Type 1 Diabetes.” Investigational statement added for use of donislecel-jujn in type 1 diabetes. Added HCPCS codes J3590 and C9399 for Lantidra. Removed HCPCS codes J3590 and C9399.
01/01/25	Interim Review, approved December 9, 2024. Policy updated with literature review through July 30, 2024; reference added. Policy statements unchanged. Added Code ICD-10 PCS XW033DA.

booklet or contact a member service representative to determine coverage for a specific medical service or supply. CPT codes, descriptions and materials are copyrighted by the American Medical Association (AMA).

Scope: Medical policies are systematically developed guidelines that serve as a resource for Company staff when determining coverage for specific medical procedures, drugs or devices. Coverage for medical services is subject to the limits and conditions of the member benefit plan. Members and their providers should consult the member benefit booklet or contact a customer service representative to determine whether there are any benefit limitations applicable to this service or supply. This medical policy does not apply to Medicare Advantage.