

Corporate Medical Policy

Islet Cell Transplantation

File Name: islet_cell_transplantation
Origination: 10/2001
Last Review: 12/2023

Description of Procedure or Service

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 patient's liver. Once implanted, the beta cells in these islets begin to make and release insulin. 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. Up to 3 donor pancreas transplants may be required to achieve insulin independence.

Autologous islet transplantation, performed in conjunction with pancreatectomy, is proposed to reduce the likelihood of insulin-dependent diabetes. Moreover, allogeneic islet cell transplantation is being investigated as a treatment or cure for patients with type 1 diabetes.

Primary risk factors for chronic pancreatitis include toxic-metabolic, idiopathic, genetic, autoimmune, recurrent and severe acute pancreatitis, or obstructive (the TIGAR-O classification system). Patients with chronic pancreatitis may experience intractable pain that can only be relieved with a total or near total pancreatectomy. The pain relief must be balanced against the certainty that the patient will become an insulin dependent diabetic if a pancreatectomy is performed. Autologous islet cell transplantation has been investigated as a technique to prevent this serious morbidity.

Allogeneic islet transplantation has been used for type 1 diabetes to restore normoglycemia and, ultimately, reduce or eliminate the long-term complications of diabetes such as retinopathy, neuropathy, nephropathy, and cardiovascular disease. Islet transplantation offers an alternative to whole-organ pancreas transplantation. However, a limitation of islet transplantation is that 2 or more donor organs are usually required for successful transplantation, although experimentation with single-donor transplantation is occurring. A pancreas that is rejected for whole organ transplant is typically used for islet transplantation. Islet transplantation is recommended only for those with frequent and severe metabolic complications who have consistently failed to achieve control with insulin-based management.

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

The U.S. 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. Lantidra (donislecel-jujn) is the only allogeneic (donor) pancreatic islet cellular therapy made from deceased donor pancreatic cells for the treatment of type 1 diabetes. Lantidra is approved for the treatment of adults with type 1 diabetes who are unable to approach target glycated hemoglobin (average blood glucose levels) because of current repeated episodes of severe hypoglycemia (low blood sugar) despite intensive diabetes management and education.

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Related Policies:

Insulin Therapy, Chronic Intermittent Intravenous (CIIT)
Pancreas Transplant
Donislecel-jujn (Lantidra™)

*****Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.**

Policy

BCBSNC will provide coverage for Autologous Islet Cell Transplantation when it is determined to be medically necessary because the medical criteria and guidelines shown below are met.

BCBSNC will provide coverage for allogeneic islet transplantation for the treatment of type 1 diabetes with donislecel-jujn (Lantidra™) when it is determined to be medically necessary because the medical criteria and guidelines shown below are met.

Benefits Application

This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

When Islet Cell Transplantation is covered

Autologous pancreas islet cell transplantation may be considered medically necessary as an adjunct to a total or near total pancreatectomy in patients with chronic pancreatitis.

Allogeneic islet transplantation with donislecel-jujn (Lantidra™) may be considered medically necessary for the treatment of type 1 diabetes when specific criteria found in the following policy are met:

- Donislecel-jujn (Lantidra™), which can be located at [Prescription drugs | Providers | Blue Cross NC](https://www.bluecrossnc.com/providers/prior-authorization/prescription-drugs) (<https://www.bluecrossnc.com/providers/prior-authorization/prescription-drugs>)

When Islet Cell Transplantation is not covered

When the criteria listed above are not met.

Allogeneic islet transplantation is considered investigational when the criteria listed above are not met.

Islet transplantation is considered investigational in all other situations.

Policy Guidelines

For individuals with chronic pancreatitis undergoing total or near total pancreatectomy who receive autologous pancreas islet transplantation, the evidence includes case series and systematic reviews. 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 significantly decrease the incidence of diabetes after total or near total

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pancreatectomy in patients with chronic pancreatitis. Also, this procedure itself is not associated with serious complications and is performed in patients who are already undergoing a pancreatectomy procedure. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals with type 1 diabetes who receive allogeneic pancreas islet transplantation, the evidence includes a randomized controlled trial, case series, and systematic reviews. The relevant outcomes are overall survival, change in disease status, medication use, resource utilization, and treatment-related morbidity. Results of a 2018 randomized trial have suggested some reduction in the number of severe hypoglycemic incidence annually, but limited follow-up and other trial limitations reduce the certainty in conclusions drawn. A wide range of insulin independence has been reported in case series. There is conflicting evidence on whether allogeneic islet transplantation reduces long-term diabetic complications. Long-term comparative studies are required to determine the effects of allogeneic islet transplantation in type 1 diabetics. The evidence is insufficient to determine the effects of the technology on health outcomes.

Guidelines and Recommendations

National Institute for Health and 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 risk of adverse events.⁵⁵, 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 patients require insulin therapy in the long term... complications result mainly from the major surgery involved in pancreatectomy (rather than from the islet cell transplantation)."

American Diabetes Association

In 2022, the American Diabetes Association standards of medical care recommended autologous islet cell transplantation be considered in patients undergoing total pancreatectomy for chronic pancreatitis to prevent postsurgical diabetes. The standards of care note that islet cell transplantation may have a role in type 1 diabetes; however, it is considered experimental and improved blood glucose monitoring technology may be a better alternative. Because of the need for immunosuppressive agents post transplantation, the guideline notes that transplantation in type 1 diabetes should be reserved for patients also undergoing renal transplantation or experiencing recurrent ketoacidosis with severe hypoglycemia despite intensive management.

Billing/Coding/Physician Documentation Information

This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at www.bcbsnc.com. They are listed in the Category Search on the Medical Policy search page.

Applicable service codes: 0584T, 0585T, 0586T, 48160, 48999, C9399, G0341, G0342, G0343, , J3490, J3590, S2102

Note: Donislecel-jujn (Lantidra™) allogeneic pancreatic islet transplantation is limited to one transplant infusion per authorization and a total maximum of 3 transplant infusions per lifetime.

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

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Scientific Background and Reference Sources

BCBSA Medical Policy Reference Manual 7.03.12, 8/15/2001

Specialty Matched Consultant Advisory Panel - 7/2002

BCBSA Medical Policy Reference Manual [Electronic Version]. 7.03.12, 4/29/2003.
Specialty Matched Consultant Advisory Panel - 6/2004

BCBSA Medical Policy Reference Manual [Electronic Version]. 7.03.12, 12/14/2005.

Collaborative Islet Transplant Registry (CITR). 2005 Annual report. Sponsored by the National Institute of Diabetes & Digestive & Kidney Diseases, NIH. Retrieved 3/24/06 from <http://spitfire.emmes.com/study/isl/reports/CITR%202nd%20Annual%20Data%20Report%201%20July%202005.pdf>

Specialty Matched Consultant Advisory Panel - 5/2006

BCBSA Medical Policy Reference Manual [Electronic Version]. 7.03.12, 12/14/08

Specialty Matched Consultant Advisory Panel - 5/2008

BCBSA Medical Policy Reference Manual [Electronic Version]. 7.03.12, 6/10/10

Alejandro R, Barron FB, Hering BJ and Wease S. 2008 Update from the Collaborative Islet Transplant Registry Transplantation. 2008 Dec 27;86(12):1783-8.

Collaborative Islet Transplant Registry (CITR). Sixth annual report. (Nov. 2009). Retrieved on July 26, 2010 from <http://citregistry.org/>

Aguayo-Mazzucato C, Bonner-Weir S. Stem cell therapy for type 1 diabetes mellitus. Nat Rev Endocrinol 2010; 6(3):139-48.

de Vos P, Spasojevic M, Faas MM. Treatment of diabetes with encapsulated islets. Adv Exp Med Biol 2010; 670:38-53.

Specialty Matched Consultant Advisory Panel 8/2010

National Institute for Health and Clinical Excellence (NICE). Autologous pancreatic islet cell transplantation for improved glycaemic control after pancreatectomy. September 2008. Accessed June 2011 at <http://www.nice.org.uk/Guidance/IPG274>

BCBSA Medical Policy Reference Manual [Electronic Version]. 7.03.12, 6/9/2011

BCBSA Medical Policy Reference Manual [Electronic Version]. 7.03.12, 6/14/2012

Specialty Matched Consultant Advisory Panel – 7/2012

BCBSA Medical Policy Reference Manual [Electronic Version]. 7.03.12, 6/13/2013

Specialty Matched Consultant Advisory Panel – 7/2013

BCBSA Medical Policy Reference Manual [Electronic Version]. 7.03.12, 5/22/2014

Specialty Matched Consultant Advisory Panel – 7/2014

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BCBSA Medical Policy Reference Manual [Electronic Version]. 7.03.12, 5/21/2015

Specialty Matched Consultant Advisory Panel – 7/2015

BCBSA Medical Policy Reference Manual [Electronic Version]. 7.03.12, 8/10/17

Lablanche S, Vantyghem MC, Kessler L, et al. Islet transplantation versus insulin therapy in patients with type 1 diabetes with severe hypoglycaemia or poorly controlled glycaemia after kidney transplantation (TRIMECO): a multicentre, randomised controlled trial. *Lancet Diabetes Endocrinol.* May 15 2018 6(7):527-537. PMID 29776895.

Kempeneers MA, Scholten L, Verkade CR, et al. Efficacy of total pancreatectomy with islet autotransplantation on opioid and insulin requirement in painful chronic pancreatitis: A systematic review and meta-analysis. *Surgery.* 2019; 166(3):263-270.

Specialty Matched Consultant Advisory Panel – 6/2020

BCBSA Medical Policy Reference Manual [Electronic Version]. 7.03.12, 8/8/19

BCBSA Medical Policy Reference Manual [Electronic Version]. 7.03.12, 8/13/2020

Specialty Matched Consultant Advisory Panel – 6/2021

Medical Director review 6/2021

National Institute for Health and Care Excellence (NICE). Autologous pancreatic islet cell transplantation for improved glycaemic control after pancreatectomy [IPG274]. 2008; <https://www.nice.org.uk/Guidance/IPG274>

American Diabetes Association. 4. Comprehensive Medical Evaluation and Assessment of Comorbidities: Standards of Medical Care in Diabetes-2021. *Diabetes Care.* Jan 2021; 44(Suppl 1): S40-S52. PMID 33298415

American Diabetes Association. 9. Pharmacologic Approaches to Glycemic Treatment: Standards of Medical Care in Diabetes-2021. *Diabetes Care.* Jan 2021; 44(Suppl 1): S111-S124. PMID 33298420

Centers for Medicare & Medicaid. National Coverage Determination (NCD) for ISLET CELL Transplantation in the Context of a Clinical Trial (260.3.1). 2004; [https://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?NCDId=286&ncdver=1&CoverageSelection=Both&ArticleType=All&PolicyType=Final&s=All&KeyW](https://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?NCDId=286&ncdver=1&CoverageSelection=Both&ArticleType=All&PolicyType=Final&s=All&Keyword=islet+cell&KeywordLookUp=Title&KeywordSearchType=And&bc=gAAAABAAAA&)

Specialty Matched Consultant Advisory Panel – 6/2022

Medical Director review 6/2022

Food and Drug Administration Center for Biologics Evaluation and Research. Cellular, Tissue and Gene Therapies Advisory Committee meeting minutes. April 15, 2021. <https://www.fda.gov/media/148461/download>.

Witkowski P, Philipson LH, Kaufman DB, et al. The demise of islet allotransplantation in the United States: A call for an urgent regulatory update. *Am J Transplant.* Apr 2021; 21(4): 1365-1375. PMID 33251712

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National Institute for Health and Care Excellence (NICE). Autologous pancreatic islet cell transplantation for improved glycaemic control after pancreatectomy [IPG274]. 2008; <https://www.nice.org.uk/Guidance/IPG274>.

Draznin B, Aroda VR, Bakris G, et al. 4. Comprehensive Medical Evaluation and Assessment of Comorbidities: Standards of Medical Care in Diabetes-2022. Diabetes Care. Jan 01 2022; 45(Suppl 1): S46-S59. PMID 34964869

Draznin B, Aroda VR, Bakris G, et al. 9. Pharmacologic Approaches to Glycemic Treatment: Standards of Medical Care in Diabetes-2022. Diabetes Care. Jan 01 2022; 45(Suppl 1): S125-S143. PMID 34964831

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Prescribing Label LANTIDRA (donislecel-jujn) Allogeneic Pancreatic Islet Cellular Suspension for hepatic portal vein infusion <https://www.fda.gov/media/169920/download>

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Policy Implementation/Update Information

10/01	Original policy issued.
8/02	Specialty Matched Consultant Advisory Panel review 7/1/2002. No criteria changes. Format changes.
6/24/04	Specialty Matched Consultant Advisory Panel review. No changes to criteria. Benefit Application and Billing/Coding section updated for consistency. Added CPT code 48160 which is specific to this policy and removed 48146. References added.
10/14/04	Codes G0341, G0342 and G0343 added to the Billing/Coding section.
6/19/06	Specialty Matched Consultant Advisory Panel review 5/18/2006. Name changed from "Islet Cell Transplantation, Autologous" to "Islet Transplantation". Information added to "Description of Procedure or Service" section related to allogeneic use and FDA regulation. Additional policy statement added to indicate "Allogeneic islet transplantation is considered investigational for the treatment of type 1 diabetes. Statement added to "When Not Covered" section also. Rationale added to "Policy Guidelines" section. CPT codes 0141T, 0142T, 0143T and HCPCS code S2102 added to "Billing/Coding" section. References added.
6/30/08	Specialty Matched Consultant Advisory Panel review 5/29/08. No change to policy statement. References added. (btw)
6/22/10	Policy Number(s) removed (amw)
9/28/10	Specialty Matched Consultant Advisory Panel review 8/2010. Updated references. Updated Policy Guidelines. (mco)

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- 8/30/11 Description section and Policy Guidelines section updated. No change in medical coverage criteria. Specialty Matched Consultant Advisory Panel review 7/27/11. Policy accepted as written. (adn)
- 1/1/12 Coding update. CPT Codes 0141T, 0142T, 0143T deleted. (adn)
- 8/7/12 Added Related Policy. Policy Guidelines Section revised. Specialty Matched Consultant Advisory Panel Review 7/18/12. No change to policy statement. (sk)
- 7/30/13 Medical Director review. CPT code 48999 added to Policy Guidelines. References updated. Specialty Matched Consultant Advisory Panel Review 7/17/12. No changes to policy statement. (sk)
- 8/26/14 Related policy “Pancreas Transplant” added. The statement “islet transplantation is considered investigational in all other situations” added to the When Not Covered section. Reference added. Specialty Matched Consultant Advisory Panel Review 7/29/14. (sk)
- 7/1/15 Reference added. (sk)
- 9/1/15 Specialty Matched Consultant Advisory Panel Review 7/29/15. (sk)
- 8/30/16 Specialty Matched Consultant Advisory Panel review meeting 7/27/2016. No change to policy. (an)
- 8/11/17 Description section updated. Specialty Matched Consultant Advisory Panel review meeting 7/26/2017. No change to policy statement. (an)
- 7/27/18 Description section updated. Policy Guidelines section updated. Reference added. Specialty Matched Consultant Advisory Panel review 6/27/2018. No change to policy statement. (an)
- 7/16/19 Specialty Matched Consultant Advisory Panel 6/19/19. (eel)
- 12/31/19 Coding section updated with new codes : 0584T, 0585T, and 0586T. (eel)
- 7/14/20 Specialty Matched Consultant Advisory Panel review 6/17/20. References added. Policy Guidelines updated. No change to policy statement. (eel)
- 7/1/21 **Guidelines and Recommendations** added to Policy Guidelines. Reference added. Specialty Matched Consultant Advisory Panel review 6/2021. No change to policy statement. (bb)
- 7/12/22 References added. Policy Guidelines updated. Specialty Matched Consultant Advisory Panel review 6/2022. Medical Director review 6/2022. No changes to policy statement or intent. (tt)
- 6/30/23 References added. Description and Policy Guidelines updated. Specialty Matched Consultant Advisory Panel review 6/2023. Medical Director review 6/2023. No changes to policy statement or intent. (tt)
- 12/29/23 Added coverage criteria for donislecel-jujn (Lantidra™) to align with Corporate Pharmacy policy. Description, policy statement, and references updated. Related policy added. Billing/coding section updated with allogeneic islet transplantation

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infusion limit and added HCPCS codes: C9399, J3490, J3590. Medical Director review 12/2023. (tt)

Medical policy is not an authorization, certification, explanation of benefits or a contract. Benefits and eligibility are determined before medical guidelines and payment guidelines are applied. Benefits are determined by the group contract and subscriber certificate that is in effect at the time services are rendered. This document is solely provided for informational purposes only and is based on research of current medical literature and review of common medical practices in the treatment and diagnosis of disease. Medical practices and knowledge are constantly changing and BCBSNC reserves the right to review and revise its medical policies periodically.