Medical Coverage Policy

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Pancreatic Islet Cell Transplantation

Table of Contents

Related Coverage Resources

Kidney Transplantation, Pancreas-Kidney Transplantation, and Pancreas Transplantation Alone

INSTRUCTIONS FOR USE

The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment where appropriate and have discretion in making individual coverage determinations. Where coverage for care or services does not depend on specific circumstances, reimbursement will only be provided if a requested service(s) is submitted in accordance with the relevant criteria outlined in the applicable Coverage Policy, including covered diagnosis and/or procedure code(s). Reimbursement is not allowed for services when billed for conditions or diagnoses that are not covered under this Coverage Policy (see "Coding Information" below). When billing, providers must use the most appropriate codes as of the effective date of the submission. Claims submitted for services that are not accompanied by covered code(s) under the applicable Coverage Policy will be denied as not covered. Coverage Policies relate exclusively to the administration of health

benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Overview

This Coverage Policy addresses pancreatic islet cell transplantation.

Coverage Policy

Pancreatic islet cell transplantation is considered a core medical service, not a service that falls under the transplant services benefit. As such, individuals receiving such services are NOT eligible for transplant travel benefits.

Autologous pancreatic islet cell transplantation is considered medically necessary for an individual undergoing total or near-total pancreatectomy for severe chronic pancreatitis.

Allogeneic (cadaver) pancreatic islet cell transplantation including the use of Lantidra™ for the treatment of any condition (e.g., Type 1 diabetes) is considered experimental, investigational or unproven.

A bioartificial pancreas device is considered experimental, investigational, or unproven.

Health Equity Considerations

Health equity is the highest level of health for all people; health inequity is the avoidable difference in health status or distribution of health resources due to the social conditions in which people are born, grow, live, work, and age.

Social determinants of health are the conditions in the environment that affect a wide range of health, functioning, and quality of life outcomes and risks. Examples include safe housing, transportation, and neighborhoods; racism, discrimination and violence; education, job opportunities and income; access to nutritious foods and physical activity opportunities; access to clean air and water; and language and literacy skills.

General Background

The islets of Langerhans containing alpha, beta, and delta cells are located throughout the glandular tissue of the pancreas. Beta cells, which secrete insulin are used in islet cell transplantation and make up only 1–2% of the cells. Transplantation of autologous (same individual) beta cells has been proposed for an individual who is undergoing total or near total pancreatectomy for severe, chronic pancreatitis that is refractory to standard therapy. Transplantation of allogeneic (cadaver) beta cells has been proposed for an individual with type I diabetes mellitus (DM) or for those with type I DM who are undergoing kidney transplantation.

The islet cell transplantation process involves the harvest of a single pancreas from the individual undergoing transplantation (i.e., autologous) or donor islet cells from a deceased donor or donors (i.e., allogeneic). Islet cells are separated from the pancreatic tissue by a series of enzymatic processes. The isolated islet cells are then infused into the liver by percutaneous catheter via the

portal vein, or another venous tributary. Studies are evaluating other potential infusion sites such as the kidney capsule.

AUTOLOGOUS (same individual)
Pancreatic islet autologous transplantation (also known as autotransplantation or islet autotransplantation [IAT]) may be performed following total pancreatectomy—the surgical removal of the whole pancreas—in patients with severe and chronic pancreatitis that cannot be managed by other treatments. Total pancreatectomy with islet autotransplantation (TPIAT, TP-IAT) is a treatment option for patients with chronic pancreatitis that can provide pain relief and improvements in quality of life. The balance between the benefits and short and long-term risks of this operation requires careful scrutiny. Best practice to select patients for surgical management with TPIAT is in evolution. Removal of the pancreas in individuals with chronic severe pancreatitis may eliminate the debilitating chronic pain; however, surgical removal of the pancreas results in a state of frank diabetes. The surgeon first removes the pancreas and then extracts and purifies islets from the pancreas. Within hours, the islets are infused through a catheter into the patient's liver. Pancreatic islets begin to release insulin soon after transplantation. However, full islet function and new blood vessel growth from the new islets take time. The goal of autologous islet cell transplantation is to promote insulin therapy independence and reduce potential complications of diabetes in patients who have undergone total or near-total pancreatectomy. This procedure is not considered experimental. Patients with type 1 diabetes cannot receive pancreatic islet auto-transplantation.

Professional Societies/Organizations - Autologous Islet Cell Transplantation

American College of Gastroenterology (ACG): The ACG 2020 Clinical Guideline on Chronic Pancreatitis states:

Key Concept #8: Total pancreatectomy with islet autotransplant (TPIAT) should be reserved for highly selected patients with refractory chronic pain in which all other symptom control measures have failed.

- TPIAT is increasingly being used as a means of treating pain in patients with refractory painful CP. Offered at only selected centers, TPIAT is a procedure whose outcomes or effectiveness have not been subjected to RCTs, systematic reviews, or meta-analyses. Data consist exclusively of case series and cohort studies (Chinnakotla, et al., 2015). As such, statements of its efficacy are limited, and it is critical that comparative effectiveness studies on important clinical outcomes be conducted in the future.
- It is recommended that patients considering TPIAT be evaluated at an expert center in which multidisciplinary evaluation is available. Patients undergoing TPIAT for treatment of painful CP need to be thoroughly vetted and appraised of the subsequent risks of type 3c DM and potential lifelong intestinal dysmotility disorders.
- Practical clinical approach. TPIAT should only be considered in patients in whom all medical treatment options have been exhausted. Resection procedures to treat painful CP should include discussion of islet cell replacement therapy (Gardner/ACG, et al., 2020).

Literature Review - Autologous Islet Cell Transplantation
In individuals who undergo islet cell autotransplantation after near total or total pancreatectomy, data supports the effectiveness of islet cells in preventing or reducing the impact of surgical diabetes by promoting a mechanism for internal insulin production. Autologous islet cell transplantation is considered a reasonable treatment option for these individuals (Sutherland, et al., 2012; Morgan, et al., 2018; Bellin, et al., 2019; Kempeneers, et al., 2019).

A systematic review included five observational studies in which 296 patients with chronic pancreatitis underwent total pancreatectomy followed by islet cell autotransplant. In the two studies that reported postoperative morphine requirements, there was a significant reduction in the frequency and severity of pain following surgery (Bramis, et al., 2012; Freedman, et al., 2021). In a meta-analysis including 12 studies and 677 patients, Wu et al. (2015) reported the insulin independence rate at 1 year follow-up was 28.4% of 362 patients in five studies. The insulin independence rate at 2 year follow-up was 19.7% of 297 patients reported by three studies.

ALLOGENEIC (cadaver)

Allogeneic transplantation is a procedure in which islets from the pancreas of a deceased organ donor(s) are purified, processed, and transferred into another person. It is proposed in the treatment of Type 1 diabetes mellitus. The goal is to give the body enough healthy islets to make insulin. Pancreatic islet allogeneic transplantation is currently considered an experimental procedure until the transplantation technology is considered successful enough to be labeled therapeutic.

U.S. Food and Drug Administration (FDA) – Allogeneic Islet Cell Transplantation

In much of the world, allogeneic islet transplantation is regulated as an organ transplant. However, in the U.S., allogeneic islet transplantation is regulated as a cell therapy. Each islet isolation facility is considered by the FDA as a unique drug manufacturing entity requiring its own biologic licensure.

The Islets For US Collaborative published a Position Statement with Arguments against the Requirement of a Biological License Application for Human Pancreatic Islets (Witkowski, et al., 2021). They concluded "Approval of the Biological License Application will result in adverse, potentially irreversible, downstream consequences for patient safety and limit access to the effective islet transplantation procedure. We call the FDA, HRSA, and the Secretary of the HHS to reconsider appropriate adjustments in the regulation for the benefit of enhancing the health and well-being of Americans with Type 1 diabetes mellitus and progress in the field of islet transplantation."

At this time, only one facility has received FDA Biologics License Application (BLA) approval for its deceased donor islet product (labeled donislecel for donor islet cell therapy). Lantidra™ (donislecel) (CellTrans Inc., Chicago, IL) received FDA BLA approval on June 28, 2023.

According to the packaging insert, 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. The recommended minimum dose is 5,000 equivalent islet number (EIN) per kg patient body weight for initial infusion (transplant) and 4,500 EIN/kg for subsequent infusions (same recipient). Administer cells through the hepatic portal vein. The estimated tissue volume should not exceed 10 cc per transplant infusion. LANTIDRA is contraindicated in patients for whom immunosuppression is contraindicated. ADVERSE REACTIONS: Ninety percent (90%) of subjects had at least one serious adverse reaction.

The review of this product was associated with the following National Clinical Trial (NCT) numbers: 00566813, 00679042, and 03791567. According to a June 28, 2023 FDA news release:

The primary mechanism of action of Lantidra is believed to be the secretion of insulin by the infused allogeneic islet beta cells. In some patients with type 1 diabetes, these infused cells can produce enough insulin, so the patient no longer needs to take insulin (by injections or pump) to

control their blood sugar levels. Lantidra is administered as a single infusion into the hepatic (liver) portal vein. An additional infusion of Lantidra may be performed depending on the patient's response to the initial dose.

The safety and effectiveness of Lantidra was evaluated in two non-randomized, single-arm studies in which a total of 30 participants with type 1 diabetes and hypoglycemic unawareness received at least one infusion and a maximum of three infusions. Overall, 21 participants did not need to take insulin for a year or more, with 11 participants not needing insulin for one to five years and 10 participants not needing insulin for more than five years. Five participants did not achieve any days of insulin independence.

Adverse reactions associated with Lantidra varied with each participant depending on the number of infusions they received and the length of time they were followed and may not reflect the rates observed in practice. The most common adverse reactions included nausea, fatigue, anemia, diarrhea and abdominal pain. A majority of participants experienced at least one serious adverse reaction related to the procedure for infusing Lantidra into the hepatic portal vein and the use of immunosuppressive medications needed to maintain the islet cell viability. Some serious adverse reactions required discontinuation of immunosuppressive medications, which resulted in the loss of islet cell function and insulin independence. These adverse events should be considered when assessing the benefits and risks of Lantidra for each patient. Lantidra is approved with patient-directed labeling to inform patients with type 1 diabetes about benefits and risks of Lantidra.

<u>Allogeneic islet cell products NOT FDA-approved:</u>

- Vertex Pharmaceuticals, Inc. is developing products VX-880 and VX-264. VX-880 is an investigational allogeneic stem cell–derived, fully differentiated pancreatic islet cell replacement therapy. VX-264 encapsulates the same VX-880 cells in a device designed to eliminate the need for immunosuppression.

- Sana Biotechnology, Inc., is investigating an engineered allogeneic, hypoimmune (HIP)-modified pancreatic islet cells product. These modified islet cells, which cluster into effective endocrine organoids, are termed "pseudo islet grafts" (p-islets).

Professional Societies/Organizations - Allogeneic Islet Cell Transplantation

Organ Procurement and Transplant Network (OPTN): The OPTN defines 'Islet infusion' as "An infusion of islets from a single deceased donor. If a recipient receives islets from multiple donors simultaneously, then each donor's islets must be counted as a separate infusion" (OPTN, 4.02.2024).

The OPTN Policy on Allocation of Pancreas, Kidney-Pancreas, and Islets (Policy 11.2.C, effective 4.02.2024) addresses Islet Registration Status as follows:

> A transplant hospital may register an islet candidate on the waiting list with an active status if the candidate meets *either* of the following requirements:
>
> 1. Is insulin dependent
> 2. Has a hemoglobin A1c (HbA1c) value greater than 6.5%

American Diabetes Association (ADA): The ADA Standards of Medical Care in Diabetes (2024) states the following:

- For patients with type 1 diabetes with level 3 hypoglycemia and hypoglycemia unawareness that persists despite medical treatment, human islet transplantation may be an option, but the approach remains experimental.
  (6. Glycemic Targets: Standards of Medical Care in Diabetes – 2024).

- Successful pancreas and islet transplantation can normalize glucose levels and mitigate microvascular complications of type 1 diabetes. However, people receiving these treatments require lifelong immunosuppression to prevent graft rejection and/or recurrence of autoimmune islet destruction. Given the potential adverse effects of immunosuppressive therapy, pancreas transplantation should be reserved for people with type 1 diabetes undergoing simultaneous renal transplantation, following renal kidney transplantation, or for those with recurrent ketoacidosis or severe hypoglycemia despite intensive glycemic management.

  In much of the world, allogeneic islet transplantation is regulated as an organ transplant. However, in the U.S., allogeneic 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.

  The 2021 ADA/EASD Consensus report (Holt, et al., 2021/2022) on the management of type 1 diabetes in adults offers a simplified overview of indications for b-cell replacement therapy in people with type 1 diabetes (9. Pharmacologic Approaches to Glycemic Treatment: Standards of Care in Diabetes—2024).

American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD): A Consensus report on the Management of Type 1 Diabetes in Adults (Holt, et al., 2021/2022) noted the following:

- In the USA, islet transplantation is not yet approved for clinical use and reimbursement.
- Chronic systemic immunosuppression is needed in both whole organ pancreas and pancreatic islet transplantation to prevent allogeneic rejection therefore the indication must thoroughly balance risk and benefit.
- Islet transplantation is indicated in people with excessive glycemic lability and frequent Level 3 hypoglycaemia despite optimal medical therapy, and allows for inclusion of older people and those with coronary artery disease who would not be eligible for a whole-pancreas transplant
- Careful patient selection and protocol optimization have led to substantial clinical improvements. Insulin independence can be maintained for 5 years in 50% of recipients.
- Several multicenter clinical trials of islet transplants in people with type 1 diabetes and problematic hypoglycemia have adopted a combination of near-normal glycemic levels (HbA1c <7.0% [<53 mmol/mol]) together with the elimination of Level 3 hypoglycemia as the primary endpoint and the clinically relevant dual goal of intervention. These outcomes can translate into improved patient-reported outcomes, but research in this area is limited.

The Endocrine Society, the American Association of Endocrine Surgeons, American Association of Clinical Endocrinology, American College of Gastroenterology (ACG), and the American Gastroenterological Association (AGA) do not address allogeneic islet cell transplantation in their guidelines.

Literature Review - Allogeneic Islet Cell Transplantation: Although pancreas transplantation requires major surgery and life-long immunosuppression, it remains the gold standard for a

specific population of patients who suffer from type 1 diabetes and who do not respond to conventional therapy. Allogeneic islet transplantation is a proposed alternative to pancreas transplantation; however, patient outcomes remain less than optimal and significant progress is required in order for this procedure to be considered a reliable therapy. Although short-term improvement in metabolic control and hypoglycemic unawareness has been noted, sustainable insulin independence has not been achieved in a majority of study participants. Contributing factors may include autoimmune destruction of the transplanted cells, alloimmune rejection of the donor tissue, and toxicity of varying immunosuppressive drug regimens.

There remain unresolved concerns including the duration of islet cell function, limited islet supply, and effect of islet cell transplantation on the incidence and progression of diabetic complications in recipients, and the risk of transmission of adventitious disease if multiple donors are used. Additionally, long-term effects of immunosuppressant therapy, variance in study protocols, including participant eligibility criteria and differing immunosuppressive regimens, and inconsistency in islet isolation and infusion techniques are issues that require resolution. At this time the role of allogeneic islet cell transplantation has not been established for any indication, including the treatment of type I diabetes mellitus.

Lantidra™ (donislecel): At this time, there are no published studies in the peer-reviewed scientific literature specific to donislecel. See the results from the FDA-reviewed clinical trials under the 'U.S. Food and Drug Administration (FDA)' section above.

Purified human pancreatic islets (PHPI): The Clinical Islet Transplantation Consortium Protocol 07 (CIT-07) trial was a multicenter prospective clinical trial of transplantation of a standardized, well-defined allogeneic islet product (purified human pancreatic islets, PHPI) in subjects with type 1 diabetes (T1D), impaired awareness of hypoglycemia, and intractable severe hypoglycemic events (SHEs). Pancreata from deceased donors 15–65 years of age were processed within 12 hours of procurement at the transplant site (eight centers in North America). Donor exclusion criteria included history of diabetes. The authors stated the study was performed in accordance with U.S. FDA regulations and Good Clinical Practice Guidelines under a U.S. Investigational New Drug application for PHPI. The primary end point was the composite of achieving an HbA1c level of <7.0% (53 mmol/mol) at day 365 after the initial islet transplantation and freedom from SHEs from day 28 to day 365 after the initial islet transplantation. Results demonstrated the primary end point was met by 42 of the 48 subjects; 87.5% of the subjects achieved the primary end point of freedom from SHE along with glycemic control (HbA1C <7%) at 1 year post-initial islet transplantation. The same subjects reported consistent, statistically significant, and clinically meaningful improvements in condition-specific health-related quality of life as well as self-assessments of overall health. Safety events occurred related to the infusion procedure and immunosuppression, including bleeding and decreased renal function. The authors stated that transplantation of human islets is an effective treatment for T1D complicated by IAH and SHEs, resulting in the restoration of hypoglycemia awareness, elimination of SHEs, and normal or near-normal glycemic control in 87.5% of participants. The authors concluded that islet transplantation should be considered for patients with T1D and IAH in whom other, less invasive current treatments have been ineffective in preventing SHEs (Hering, et al., 2016; Foster, et al., 2018).

In a parallel trial of allogeneic islet product (purified human pancreatic islets, PHPI) transplant conducted by the CIT Consortium in patients with Type 1 diabetes (T1D) after kidney transplant (Protocol CIT06), Markmann et al. (2020) prospectively reported on 24 subjects with T1D who had previously received a kidney transplant. PHPI were manufactured at 10 manufacturing facilities, each associated with that clinical site (10 centers in North America). The primary endpoint of achieving an HbA1c ≤ 6.5% or a reduction in HbA1c of ≥1 point in the absence of experiencing severe hypoglycemic event (SHE) at day 365 was achieved by 15 subjects (62.5%; $p < .001$). Fourteen (58.3%; $p = .0012$) and 11 (45.8%; $p = .0369$) subjects also achieved the primary

endpoint criteria evaluated at day 730 and day 1095, respectively. No patients experienced renal allograft rejection. The 24 subject recipients in CIT06 experienced 22 serious adverse events (SAE) from induction immunosuppression initiation through day 365 post-transplant and 24 additional SAEs through day 1095 after final transplant. The authors noted that the results of CIT06, like those of CIT07, find PHPI to be safe and effective at achieving on-target glycemic control in the absence of SHEs and better disease-specific QOL scores.

TRIMECO was a randomized controlled trial involving 15 university hospitals in France and three islet preparation units (two in France and one in Switzerland) (Lablanche, et al., 2018). Patients (total participants = 50) were aged 18–65 years with type 1 diabetes diagnosed at least 5 years previously. To be eligible for allogeneic islet transplantation, patients had to have severe glycemic lability, associated with at least two severe hypoglycemic events per year, severe impairment of quality of life related to hypoglycemia, or hypoglycemia unawareness. Patients with type 1 diabetes who had received a kidney graft were eligible for islet transplantation if they had a functional kidney graft and poor glycemic control or substantial deterioration in quality of life related to diabetes. Patients were randomly assigned to immediate islet transplantation (n=26) or to insulin therapy for 6 months followed by islet transplantation (insulin group, n=24). Median follow-up was 184-185 days. At 6 months, 16 (64%) of 25 patients in the immediate islet transplantation group had a modified β-score of 6 or higher versus none (0%) of the 22 patients in the insulin group ($p<0{\cdot}0001$). At 12 months after first islet infusion, 29 (63%) of the 46 transplantation recipients in the overall study cohort had a modified β-score of 6 or higher. Insulin independence was achieved in 27 (59%) of these patients. The authors noted immunosuppression can affect kidney function, necessitating careful selection of patients. They concluded that although studies with longer-term follow-up are needed, their findings suggest that islet transplantation is a valid option for patients with severe, unstable type 1 diabetes who are not responding to intensive medical treatments.

The Clinical Islet Transplantation Consortium Protocol 07 (CIT-08) (Rickels, et al., 2022) trial is a prospective observational cohort study of islet-alone (n = 48) and islet-after-kidney (n = 24) transplant recipients followed for up to 8 years after intraportal infusion of one or more purified human pancreatic islet (PHPI) products under standardized immunosuppression. All subjects had documented histories of impaired awareness of hypoglycemia and had experienced severe hypoglycemia episodes before PHPI transplantation. The primary outcome was the duration of sustained islet graft function. Individuals who remained insulin dependent after 75 (islet-alone) or 30 (islet-after-kidney) days from receiving an initial PHPI product could receive one or two additional PHPI products. Of the 48 islet-alone and 24 islet-after-kidney transplantation recipients, 26 and 8 completed long-term follow-up with islet graft function, 15 and 7 withdrew from follow-up with islet graft function, and 7 and 9 experienced islet graft failure, respectively. Actuarial islet graft survival at median and final follow-up was 84% and 56% for islet-alone and 69% and 49% for islet-after-kidney (P = 0.007). Insulin independence was achieved by 74% of islet-alone and islet-after-kidney transplantation recipients, with more than one-half maintaining insulin independence during long-term follow-up. There were 104 serious adverse events (islet-alone, 71; islet-after-kidney, 33). A limitation of this study is the loss to follow-up (Rickels, et al., 2022).

Chetboun et al. (2023) reported on a retrospective, multicentre cohort study to test the hypothesis that primary graft function (PGF) is an independent predictor of 5-year clinical islet transplantation outcomes. The cohort included 1210 patients from the Collaborative Islet Transplant (CIT) Registry (CITR) who received one or more intraportal infusions of allogeneic pancreatic islets; either islet transplantation alone (ITA recipients) or islet-after kidney transplantation (IAK recipients) between Jan 19, 1999, and July 17, 2020, with a calculable PGF measured 28 days after last islet infusion with a validated composite index. Of 1210 patients, 452 (37.4%) received a single islet infusion and 758 (62.6%) received multiple islet infusions. Mean PGF was 14.3. The 5-year cumulative incidence of unsuccessful islet transplantation was 70.7%.

The authors stated that the association between early graft potency and 5-year islet transplantation outcomes has important clinical implications for β-cell replacement. Study limitations include its retrospective design and the absence of analysis of complications.

Marfil-Garza, et al. (2022) retrospectively reported the outcomes from the University of Alberta (Edmonton, AB, Canada) on a cohort of 255 type 1 diabetes patients undergoing allogeneic islet transplantation between March 11, 1999, and Oct 1, 2019. Candidates were older than 18 years, with type 1 diabetes duration of longer than 5 years, and a negative stimulated C-peptide, measured following mixed-meal tolerance tests where possible or post-prandial if hyperglycemic. Patients who underwent islet-after-kidney transplantation and islet transplantation alone were included. Patients having extrahepatic infusions, with less than 1 year of follow-up, or undergoing whole-pancreas transplantation before islet transplantation were excluded. Patients undergoing islet transplantation before whole-pancreas transplantation were included; however, follow-up was censored at the time of whole-pancreas transplantation. Over a median follow-up of 7·4 years, 230 (90%) patients survived. Median graft survival was 5·9 years, and graft failure occurred in 91 (36%) patients. 178 (70%) recipients had sustained graft survival, and 77 (30%) had non-sustained graft survival.

Bioartificial Pancreas
Various bioartificial pancreas devices are under development with the goals of achieving glycemic control in type 1 diabetes, while resolving the issues of organ (or cell/tissue) shortage and need for lifelong immunosuppression. The term 'bioartificial pancreas' or 'bioartificial pancreas device' is used to describe the technical solution of encapsulating native islets of Langerhans in a semipermeable, immunoprotective and biocompatible membrane.

Berney et al. (2022) proposes that constructing a bioartificial pancreas will require four main issues to be addressed: 1) what types of cells of tissues will be utilized as a source of insulin, 2) what encapsulation strategy will be utilized, 3) what types of (bio)materials or accessory cells will be utilized to provide the adequate microenvironment, and 4) what will be the optimal site to implant the construct? The author notes that current research is looking at encapsulation strategies, porcine xenotransplantation and regenerative medicine.

Photiadis et al. (2021) states that numerous models are in development and take different approaches to cell source, encapsulation method, and device implantation location.

In a review article, de Jongh et al. (2023) stated that "The field of regenerative medicine offers potential therapies for Type 1 Diabetes, whereby metabolically active cellular components are combined with synthetic medical devices. These therapies are sometimes referred to as 'bioartificial pancreases'. For these emerging and rapidly developing therapies to be clinically translated to patients, researchers must overcome not just scientific hurdles, but also navigate complex legal, ethical and psychosocial issues."

Medicare Coverage Determinations

	Contractor	Determination Name/Number	Revision Effective Date
NCD	National	Islet Cell Transplantation in the Context of a Clinical Trial (260.3.1)	10/1/2004
LCD		No Determination found.	

Note: Please review the current Medicare Policy for the most up-to-date information.
(NCD = National Coverage Determination; LCD = Local Coverage Determination)

Coding Information

Notes:

1. This list of codes may not be all-inclusive since the American Medical Association (AMA) and Centers for Medicare & Medicaid Services (CMS) code updates may occur more frequently than policy updates.
2. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

CPT®* Codes	Description
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
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 Codes	Description
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

Considered Experimental/Investigational/Unproven:

HCPCS Codes	Description
J3590†	Unclassified biologics
L8699††	Prosthetic implant, not otherwise specified
S2102	Islet cell tissue transplant from pancreas; allogeneic

†Note: Considered Experimental/Investigational/Unproven when used to report Lantidra™.
††Note: Considered Experimental/Investigational/Unproven when used to report bioartificial pancreas device.

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Revision Details

Type of Revision	Summary of Changes	Date
Annual Review	• No clinical policy statement changes.	6/15/2024
Focused Review	• Updated to new template and formatting standards. • Updated allogeneic policy statement with clarifying language.	9/15/2023