Anthem

Medical Policy

Subject: Autologous and Allogeneic Pancreatic Islet Cell Transplantation
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Description/Scope

This document addresses autologous and allogeneic pancreatic islet cell transplantation. Islet cell transplantation involves the collection and infusion of isolated pancreatic islet cells into the portal vein of the liver. The goals of islet cell transplantation are to preserve endocrine functionc, glycemic control and to improve quality of life.

Note: For information on whole pancreas organ transplantation, please see:

- TRANS.00011 Pancreas Transplantation and Pancreas Kidney Transplantation

Position Statement

Medically Necessary:

Autologous pancreatic islet cell transplantation is considered **medically necessary** as an adjunct to a total or near total pancreatectomy for individuals with chronic pancreatitis.

Investigational and Not Medically Necessary:

Autologous pancreatic islet cell transplantation is considered **investigational and not medically necessary** when the above criteria are not met and for all other indications.

Allogeneic pancreatic islet cell transplantation is considered **investigational and not medically necessary** for all indications.

Note: For multi-organ transplant requests, criteria must be met for each organ requested. In those situations, an individual may present with a concurrent medical condition which would be considered an exclusion or a comorbidity that would preclude a successful outcome, but would be treated with the other organ transplant. Such cases will be reviewed on an individual basis for coverage determination to assess the member's candidacy for transplantation.

Rationale

Chronic Pancreatitis

A total or near-total pancreatectomy can relieve pain from chronic pancreatitis, but also results in insulin dependent diabetes. Autologous islet cell transplantation as an adjunct to a total or near-total pancreatectomy is a technique used to salvage and transplant beta cells which may prevent complications of chronic diabetes.

Several systematic reviews of the literature on islet autotransplantation (IAT) after total pancreatectomy (TP) or partial pancreatectomy (PP) have been published (Bramis, 2012; Kempeneers, 2019; Wu, 2015; Zhang 2019). Among the more recent systematic reviews, in 2019 Kempeneers and colleagues identified 15 observational studies with a total of 1255 individuals who had chronic pancreatitis who underwent TP with islet autotransplant. The pooled 30-day mortality rate was 2% and the 1-year mortality rate was 4%. Four studies assessed the insulin-free rate at 1 year and the other 11 studies reported the insulin-free rate at last follow-up. In pooled analyses, the insulin-free rate at 1 year was 30% (95% confidence interval [CI], 20-43%) and at last follow-up the insulin-free event rate was 1.31 (95% CI, 0.74 to 2.31) per 10 person-years. In the 5 studies that reported this outcome, pain assessed by a 100-point visual analogue scale (VAS) decreased by a mean of 58 points (from a preoperative mean of 79 to a post-operative mean of 22). In 6 studies, the pooled 1-year opioid-free rate was 63% (95% CI, 46-77%). Zhang and colleagues (2019) identified 17 studies of IAT in conjunction with TP. The pooled 30-day mortality rate was 1.3% and the 1-year mortality rate was 2.5%. In 8 studies that reported the rate of insulin independence, the pooled rate of independence at 1-year was 33.3%.

Regarding TP, Wu and colleagues (2015) conducted a systematic review of outcomes of IAT after TP. A total of 12 studies involving 677 subjects were included. The insulin independent rate for IAT after TP at last follow-up was 3.72 per 100 person-years (95% CI, 1.00-6.44). The 30-day mortality was 2.1% (95% CI, 1.2-3.8%). The mortality at last follow-up was 1.09 per 100 person-years (95% CI, 0.21-1.97). Factors associated with incidence density of insulin independence in univariate meta-regression analyses included islet equivalents per kg body weight.

One of the largest series was published in 2012 by Sutherland and colleagues. The authors reported data from a single center series of 409 individuals with chronic pancreatitis who were treated between 1977 and 2011 with TP and IAT to relieve pain and preserve β-cell mass. Fifty-three of the 409 participants (13%) were children between the ages of 5 and 18 years. Post TP and IAT actuarial survival at 1 year was 96% in adults and 98% in children, and 5-year survival was 89% in adults and 98% in children. Overall, at 15 years post-surgery, two-thirds (66%) of the individuals were reported alive. Insulin independence at 3 years was noted in 30% of individuals (25% of adults and 55% of children), while partial function was reported in 33%. Surgical complications requiring reoperation during the initial admission occurred in a total of 15.9% of the individuals, with bleeding as the most common reason for reoperation experienced in 9.5%. There were a total of 5 (1.2%) in-hospital deaths, and 53 deaths following initial discharge with 3 of those deaths related to chronic pancreatitis disease processes. Insulin independence at 6 months was observed in 25% of individuals, 33% had partial islet function and less than one-fifth were dependent on insulin. Narcotic use for pain control declined after TP and IAT. The proportion of individuals requiring narcotics were, 91%, 61%, 54% and 51% at 3, 6, 12 and 24 months, respectively. A survey of integrated quality-of-life outcomes, initiated in October 2008, had 219 participants eligible to participate and 193 completed the survey. At 1 year, 85% of the participants reported improvement compared to the prior year. The authors concluded TP alleviates pain caused by chronic pancreatitis and IAT can help to preserve glycemic control in most individuals.

As part of their 2021 Standards of Medical Care in Diabetes, the American Diabetes Association recommended that autologous islet transplantation be considered for individuals undergoing TP for refractory chronic pancreatitis to prevent postsurgical diabetes.

According to the available studies, autologous pancreatic islet cell transplantation appears to significantly decrease the incidence of

diabetes and pain after total or near-total pancreatectomy for chronic pancreatitis. Additionally, this procedure is not associated with serious complications and is performed as an adjunct to the pancreatectomy procedure.

Type 1 Diabetes

Type I diabetes mellitus is a result of cell-mediated autoimmune destruction of insulin producing pancreatic beta cells. Allogeneic pancreatic islet cell transplantation is proposed to restore normal glycemic levels in labile type 1 diabetes.

In 2018, the first randomized controlled trial (RCT) evaluating islet transplantation in individuals with type 1 diabetes was published by Lablanche and colleagues. The study included 50 individuals with severe glycemic lability, defined as at least 2 severe hypoglycemic events per year, severely impaired quality of life related to hypoglycemia or hypoglycemia unawareness. All individuals had failed previous attempts to reach optimal glycemic control and 9 had previously received a kidney graft. Study participants were randomly assigned to immediate islet transplantation or a wait list control group that was offered islet transplantation 6 months later. Islet cells were obtained from the pancreases of brain-dead organ donors. The primary study outcome was the proportion of participants with a modified *B*-score of 6 or higher after 6 months. This score can range from 0 to 8, with a score of 6 or higher indicating graft success. Two points are given for each of the following: normal fasting glucose, normal HbA1c, stimulated or basal C-peptide and absence of insulin or oral hypoglycemic drug use. One point is given for intermediate (near-normal) values. In the "classic" *B*-score, the overall score is 0 when the C-peptide is negative, and this element was removed for the current study. Individual outcomes in the *B*-score were evaluated as secondary outcomes. Data from 3 individuals were missing for the primary outcome assessment.

At 6 months, 16 (64%) of 25 participants in the immediate transplantation group had a modified *B*-score of 6 or higher compared with 0 of the 22 individuals in the delayed treatment group, $p<0.0001$. Each of the individual components of the modified *B*-score favored the immediate transplantation group, with the exception of fasting glucose which was similar in the 2 groups. For example, mean HbA1c was significantly lower in the immediate transplantation group (5.6%) than in the control group (8.2%), $p<0.001$. Moreover, the proportion of individuals with HbA1c of less than 7% without severe hypoglycemia was significantly higher in the immediate transplantation group (84%) than in the delayed treatment group (0%), $p<0.0001$. The median number of severe hypoglycemic events per year was 0 in the immediate transplantation group and 2 in the delayed treatment group, $p<0.001$. (It is important to note that outcomes were assessed at 6 months, so the annual number of severe hypoglycemic events was not available).

After 6 months, all but 1 of the individuals in the delayed treatment group underwent islet transplantation. That participant had died of cardiac arrest related to prolonged nocturnal hypoglycemia while on the waiting list. Data on 46 individuals were available at 12 months. At the 12-month follow-up, 29 of 46 participants (63%) had a modified *B*-score of 6 or higher and the median modified *B*-score was 7. The median number of severe hypoglycemic events at 12 months was 0 for the 46 participants. A total of 135 severe adverse events (SAEs) were reported through 12 months in the entire study population. About two-thirds of SAEs were related to immunosuppression, and bleeding events were associated with over 6% of islet transplantations. The study has several limitations that preclude drawing conclusions on the efficacy and safety of islet cell transplantation in individuals with type 1 diabetes. There were only 6 months of comparative data and 12 months overall follow-up. Longer-term data are needed, especially given concerns about adverse events, especially related to immunosuppression. Moreover, the authors noted that standards of diabetes care have changed since the study was conducted and more individuals might now achieve adequate glycemic control without islet transplantation. At the time the study was conducted, only 7 of the study participants (15%) had used continuous glucose monitoring for glycemic control.

Prior to the RCT, only uncontrolled studies had been published on the safety and efficacy of islet transplantation for individuals with type 1 diabetes. These studies were summarized in a systematic review published by Health Quality Ontario in 2015. A total of 17 studies published through November 27, 2014 were identified. One of these was a technology assessment that included 13 case series. An additional 11 observational studies were identified as well as 4 guidelines and 1 registry report. Four observational studies compared islet transplantation alone to intensive insulin therapy in individuals without kidney disease. Three of the 4 studies found significantly greater changes in HbA1c after islet transplantation. In addition, 12 case series reported on glycemic control and found insulin independence rates ranging from 30% to 70% at 1 year post-transplantation. The review authors concluded:

> From these studies, we determined that islet transplantation can improve blood sugar control and may reduce diabetic complications for patients with type 1 diabetes, with or without kidney disease. Improvements in health-related quality of life can occur; however, the results were inconsistent. Compared with insulin therapy, there were more adverse (undesired) events with islet transplantation, but these were less severe than with pancreas transplantation. The body of evidence was generally considered to be of low to very low quality.

Registry data were available from the Collaborative Islet Transplant Registry (CITR), which has collected and monitored data on allogeneic islet transplantation in North America, Europe, and Australia since 1999. A 2008 report from CITR (Close, 2007), stated that the registry was comprised of 325 adult recipients and 649 islet infusions from 712 donors. Recipients of allogeneic islet transplants all had type 1 diabetes for more than 5 years, were between 18 and 65 years of age, and had poor diabetes control. At 3 years post first infusion only 23% of islet-alone recipients were insulin independent (defined as insulin independent 2 or more weeks), 29% were insulin dependent with detectable C-peptide, 26% had lost function, and 22% had missing data. A total of 70% achieved insulin independence at least once, of which 71% were still insulin independent 1 year later and 52% at 2 years. There have been seven reported deaths among allograft recipients with causes ranging from unknown reasons to viral meningitis possibly related to immunosuppressant therapy, drug toxicity and stroke.

A 2012 CITR report (Barton, 2012) focused on changes in outcomes over time. The number of individuals receiving islet transplants was 214 during 1999-2002, 255 between mid-2003 and 2006, and 208 from 2007 to 2010. A total of 575 of the 677 (85%) islet transplant recipients received islets only and the remainder underwent simultaneous kidney and islet transplants. In the 1999-2002 group, rates of insulin independence were 51% after 1 year, 36% after 2 years, and 27% after 3 years. Rates for the 2007-2010 group were 66%, 55% and 44%, respectively. The incidence of clinically reportable adverse events in the first year after infusion decreased from 50% to 53% in 1999-2006 to 38% in 2007-2010. The rates of peritoneal hemorrhage or gallbladder infusion were 5.4% in 1999-2003 and 3.1% in 2007-2010. Findings were not reported separately for the subset of individuals who underwent islet only transplantation. Limitations to the database updates were increasing levels of missing data from medical records and pending entry of data into the registry.

Several uncontrolled studies have reported 5-year outcomes after islet transplantation in individuals with type 1 diabetes. Qi and colleagues (2014) reported a small single center 5-year follow-up of type 1 diabetics transplanted with allogeneic islets. A total of 10 individuals were enrolled in an open-label prospective trial. The first 4 subjects underwent islet transplantation with the Edmonton immunosuppressive regimen and the remaining 6 subjects received the Edmonton regimen plus etanercept and exenatide. All 10 individuals achieved insulin independence after 1-3 transplants. At 5 years of follow-up, 6 of the initial 10 subjects were free of exogenous insulin.

In 2015, LaBlanche and colleagues reported 5-year metabolic, functional and safety results of individuals with type 1 diabetes transplanted with allogeneic islet cells within a Swiss-French multicenter network between 2003 and 2010. A total of 44 subjects received islet cell transplantation of which 24 (54.5%) received islet transplantation alone (ITA) and 20 (45.5%) received islet after

kidney (IAK). Thirty-four subjects completed the 5-year follow-up and 10 subjects completed the 4-year follow-up. At 1, 4, and 5 years post islet transplantation, respectively, 83%, 67%, and 58% of the ITA recipients and 80%, 70%, and 60% of the IAK transplant recipients reached HbA1c under 7% and were free of severe hypoglycemia, while none of the ITA recipients and only 10% of the IAK transplant recipients met this criterion at the preinfusion stage. Thirty-three of 44 subjects (75%) experienced insulin independence during the follow-up period, with a median duration of insulin independence of 19.25 months. A total of 55 adverse events occurred in 29 of 44 recipients. Of the adverse events, 14% were deemed mild, 9% were moderate, 67% were serious and 9% were life-threatening. Two individuals died due to a cardiovascular event at 55 and 48 months post-transplant; however, no deaths related to islet transplantation were reported during the follow-up period.

The ADA Standards of Medical Care (2023) stated: “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”.

However, a 2021 consensus report by a working group of the ADA and the European Association for the Study of Diabetes (EASD) stated: “Islet transplantation, a less invasive procedure, is indicated in people with excessive glycaemic lability and frequent Level 3 hypoglycaemia despite optimal medical therapy”.

There are significant issues requiring further investigation before islet cell transplantation for treatment of diabetes could be considered outside of clinical trials. These issues include:

- Limited islet supply: Based on the number of pancreas donors each year, only a limited number of islet cells are suitable for transplant.
- Toxicity of immunosuppression: Transplant recipients receive potent immunosuppressive medications for the rest of their lives after a transplant. Therefore, these individuals also contend with a higher risk for infections resulting from a weakened immune system.
- Normal blood sugar levels not achieved: A low percentage of transplant recipients report normal blood sugar levels at three years post infusion.
- Long-term safety: There are insufficient data on long-term consequences.

In June, 2023, the Food and Drug Administration (FDA) approved donislecel-jujn (Lantidra™), an allogeneic pancreatic islet cellular therapy. The FDA-approved indication is “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 product is intended to be used in conjunction with immunosuppression.

According to the FDA label (2023), the safety and efficacy of Lantidra was evaluated in two uncontrolled observational studies. Findings of these studies have not been published in peer-reviewed journals. The studies included a total of 30 participants with type 1 diabetes and hypoglycemic unawareness, of which 11 individuals received 1 infusion, 12 participants received 2 infusions and 7 participants received 3 infusions. The interval between infusions was highly variable, between 1 month and 7.8 years. Duration of follow-up varied from 0.3 to 14.5 years (mean of 3 years) after the first infusion. Following Lantidra infusion, 25 (83%) of participants achieved some degree of insulin independence. Four participants (13%) were insulin independent for less than 1 year, 12 participants (37%) were insulin independent for 1 to 5 years and 9 participants (33%) were insulin dependent for more than 5 years.

Serious adverse events were reported in 27 (90%) of individuals. This included 2 deaths, 1 death from multiorgan failure with sepsis 1.6 years after the first infusion and 1 from “progressive confusion, global atrophy and micro-ischemic disease” 9.7 years after the first infusion. Both of these individuals were using immunosuppression at the time of death. In addition, 8 (27%) of study participants experienced at least one life-threatening adverse reaction and 26 (87%) experienced at least one severe reaction. There were 211 immunosuppressive-related infections reported in 26 participants, of which 1 was life-threatening and 22 were severe. Discontinuation of immunosuppression resulting in loss of islet cell function occurred in 8 (27%) of participants. Malignancy, which the FDA document noted is associated with immunosuppression, occurred in 8 participants and 3 of the malignancies were life-threatening. In addition, anemia were reported in 24 (80%) of participants.

Limitations of the data on Lantidra, as reported in the FDA document, include a lack of a comparison group receiving current standard of care glucose monitoring and insulin dosing, lack of clear inclusion/exclusion criteria, failure to report other efficacy outcomes of interest such as glycemic control, hypoglycemic episodes or diabetes-related sequelae, and lack of a clear and consistent treatment and follow-up protocol. The study found a high-rate of complications, including 2 deaths and other life-threatening adverse reactions. Many of the serious adverse events were likely related to immunosuppression, and concerns remain over the risk of long-term, immunosuppression-related complications.

Background/Overview

Islet cells are obtained from the resected pancreas by injecting a collagenase solution into the pancreas, which frees the cells from acinar tissue. The resultant dispersed pancreatic islet tissue is collected, washed and diluted in plasma. Most often the plasma is then injected slowly into the portal vein of the liver. In some cases, islet cells are transplanted elsewhere in the peritoneal cavity, for example, beneath the kidney capsule. A research group in Italy studied islet transplantation in the bone marrow, but they concluded this is not an acceptable alternative to the liver (Maffi, 2018).

Three types of islet transplants have been reported: allogeneic transplants isolated from human adult islet tissue (including the use of multiple donors for one recipient in order to obtain a sufficient number of islet cells); transplants isolated from fetal human or animal tissue; and autologous transplants. Islet cells for autologous transplants can be prepared within a hospital or prepared in an external facility. At least one commercial autologous islet cell product, Kyslecel™ (Koligo Therapeutics, Louisville, KY) is available. Kyslecel is made from islet cells extracted from a pancreas shipped to their facility after pancreatectomy. Kyslecel is shipped back to the hospital in an IV bag for intraportal infusion and has a 6-hour expiration time.

A variety of tissue sources, methods of islet isolation and preservation, sites of cell implantation and immunosuppressive regimens continue to be investigated to identify improved islet cell procurement techniques, optimal selection criteria, and long-term durability of outcomes.

Chronic Pancreatitis

Chronic pancreatitis is a progressive inflammatory disease of the pancreas that results in irreversible deterioration of pancreatic structure and function. Pathological features include atrophy and fibrosis. Individuals with chronic pancreatitis may experience intractable pain that can require a total or near-total pancreatectomy. Pain relief must be balanced against the outcome of insulin-dependent diabetes. Autologous islet cell transplantation has been investigated as a technique to prevent this morbidity. During the removal of the pancreas, a suspension of isolated islet cells is created from the pancreas specimen and then injected into the portal vein of the liver, where the cells function as a free graft.

Type 1 Diabetes

Type 1 diabetes is a chronic disease that occurs when the pancreas does not produce enough insulin to properly control blood glucose levels. Transplantation of pancreatic islet cells has been investigated as an alternative to insulin injections or pancreas transplantation. Islet cell transplantation is proposed as a treatment for type I diabetes, whether due to unknown causes or to partial or total pancreatectomy.

On June 28, 2023, the FDA approved Lantidra (donislecel-jujn) allogeneic pancreatic islet cellular therapy (CellTrans, Inc., Chicago, IL).

The FDA-approved indication is:

> 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 FDA label included the following warnings and precautions, and information on adverse reactions:

Warnings and Precautions:

- Risks from Concomitant Immunosuppression: Increased risk of severe infections including opportunistic infections, malignancy, and severe anemia. Monitor closely. Administer PCP and CMV prophylaxis. (5.1)
- Procedural Complications: Liver laceration and hemorrhage have occurred. Monitor for bleeding, portal hypertension, and portal vein thrombosis during and immediately following infusion. (5.2)
- Increased Risk of Graft Rejection: Patients with a positive T- and B-cell crossmatch between recipient serum and donor lymphocytes may be at increased risk for graft rejection. (5.3)
- Transmission of Donor-Derived Infections: Monitor for signs of infection following infusion and treat accordingly. (5.4)
- Panel Reactive Antibodies (PRA): Product administration may elevate PRA and negatively impact candidacy for renal transplant. (5.5)

Adverse Reactions:

Ninety percent (90%) of subjects had at least one serious adverse reaction. (6.1)
The major causes are attributed to:

- Infusion procedure
  - liver laceration/hematoma, hemorrhage, and intra-abdominal bleeding (13%)
  - elevation of portal pressure (7%)
- Immunosuppression
  - Infection (87%)
  - Malignancy (37%)

Definitions

Acinar: Any secreting cell lining a gland, especially as applied to the cells of the pancreas that furnish pancreatic juice and enzymes to distinguish them from the islets of Langerhans, which secrete hormones.

Allogeneic: Derived from individual(s) other than the recipient.

Autologous: Derived from the individual's own body.

Hypoglycemia:

- Level 1 (mild): Blood glucose level less than less than 70 mg/dL
- Level 2 (moderate): Blood glucose level less than 54 mg/dL
- Level 3: Also known as severe hypoglycemia, blood glucose level less than approximately 40 mg/dL. Level 3 hypoglycemia refers to glucose levels that are so low that the individual has impaired mental or physical functioning and requires assistance.

Islet of Langerhans: Groups of cells found within the pancreas; A-cells and B-cells which secrete insulin and glucagon.

Pancreas: A glandular organ lying below and behind the stomach that secretes insulin and glucagon (both regulate blood sugar), as well as digestive enzymes.

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

When services are Medically Necessary:

CPT	
48160	Pancreatectomy, total or subtotal, with autologous transplantation of pancreas or pancreatic islet cells
ICD-10 Procedure	
3E030U0-3E033U0	Introduction of autologous pancreatic islet cells into peripheral vein [by approach; includes codes 3E030U0, 3E033U0]
3E0J3U0-3E0J8U0	Introduction of autologous pancreatic islet cells into biliary and pancreatic tract [by approach; includes codes 3E0J3U0, 3E0J7U0, 3E0J8U0]
ICD-10 Diagnosis	
K86.0-K86.1	Chronic pancreatitis

When services are Investigational and Not Medically Necessary:
For the procedure codes listed above for all other diagnoses not listed; or when the code describes a procedure indicated in the

Position Statement section as investigational and not medically necessary.

When services are also Investigational and Not Medically Necessary for allogeneic transplantation:

CPT	
48999	Unlisted procedure, pancreas [when specified as pancreatic islet cell transplantation]
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	
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 Procedure	
3E030U1-3E033U1	Introduction of nonautologous pancreatic islet cells into peripheral vein [by approach; includes codes 3E030U1, 3E033U1]
3E0J3U1-3E0J8U1	Introduction of nonautologous pancreatic islet cells into biliary and pancreatic tract [by approach; includes codes 3E0J3U1, 3E0J7U1, 3E0J8U1]
ICD-10 Diagnosis	
	All diagnoses

References

Peer Reviewed Publications:

1. Barton FB, Rickels MR, Alejandro R, et al. Improvement in outcomes of clinical islet transplantation: 1999-2010. Diabetes Care. 2012; 35(7):1436-1445.
2. Bramis K, Gordon-Weeks AN, Friend PJ, et al. Systematic review of total pancreatectomy and islet autotransplantation for chronic pancreatitis. Br J Surg. 2012; 99(6):761-766.
3. Close N, Alejandro R, Hering B, Appel M.; CITR Investigators. Second annual analysis of the collaborative islet transplant registry. Transplant Proc. 2007; 39(1):179-182.
4. Health Quality Ontario. Pancreas islet transplantation for patients with type 1 diabetes mellitus: A clinical evidence review. Ont Health Technol Assess Ser. 2015; 15(16):1-84.
5. 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.
6. 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. 2018; 6(7):527-537.
7. Lablanche S, Borot S, Wojtusciszyn A, et al. GRAGIL Network. Five-year metabolic, functional, and safety results of patients with type 1 diabetes transplanted with allogenic islets within the Swiss-French GRAGIL Network. Diabetes Care. 2015; 38(9):1714-1722.
8. Maffi P, Nano R, Monti P et al. Islet allotransplantation in the bone marrow of patients with type 1 diabetes: a pilot randomized trial. Transplantation. 2018; 103(4): 839-851.
9. Qi M, Kinzer K, Danielson KK, et al. Five-year follow-up of patients with type 1 diabetes transplanted with allogeneic islets: the UIC experience. Acta Diabetol. 2014; 51(5):833-843.
10. Sutherland DE, Radosevich DM, Bellin MD, et al. Total pancreatectomy and islet autotransplantation for chronic pancreatitis. J Am Coll Surg. 2012; 214(4):409-424.
11. Sutherland DE, Radosevich D, Gruessner R, et al. Pushing the envelope: living donor pancreas transplantation. Curr Opin Organ Transplant. 2012; 17(1):106-115.
12. Wu Q, Zhang M, Qin Y, et al. Systematic review and meta-analysis of islet autotransplantation after total pancreatectomy in chronic pancreatitis patients. Endocr J. 2015; 62(3):227-234.
13. Zhang YJ, Duan DD, Yuan H. Efficacy and safety of islet autotransplantation after total pancreatectomy in chronic pancreatitis: a systematic review and meta-analysis including 17 studies. Clin Res Hepatol Gastroenterol. 2020; 44(4):598-608.

Government Agency, Medical Society, and Other Authoritative Publications:

1. ElSayed NA, Aleppo G, Aroda VR et al. 6. Glycemic targets: Standards of care in diabetes-2023. Diabetes Care. 2023;46(Suppl 1):S97-S110.
2. Holt RIG, DeVries JH, Hess-Fischl A et al. The management of type 1 diabetes in adults. A consensus report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). Diabetologia. 2021 Sep 30:1-44.
3. U.S. Food & Drug Administration. Guidance for Industry: considerations for allogeneic pancreatic islet cell products. September 2009. Available at: http://www.fda.gov/downloads/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/CellularandGeneTherapy/UCM182441.pdf Accessed on June 30, 2023.
4. U.S. Food and Drug Administration. Lantidra. Updated 6/2023. Available at:https://www.fda.gov/vaccines-blood-biologics/lantidra. Accessed on June 30, 2023.

Websites for Additional Information

1. Collaborative Islet Transplant Registry (CITR). Available at:http://citregistry.org/. Last accessed on June 30, 2023.
2. National Institute of Diabetes and Digestive and Kidney Diseases. Pancreatic Islet Transplantation. Available at: https://www.niddk.nih.gov/health-information/diabetes/overview/insulin-medicines-treatments/pancreatic-islet-transplantation. Last accessed on June 30, 2023.

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Document History

Status	Date	Action
Reviewed	08/10/2023	Medical Policy & Technology Assessment Committee (MPTAC) review. Updated Rationale, Background/Overview, References and Index sections.
Reviewed	11/10/2022	MPTAC review. References sections updated.
Reviewed	11/11/2021	MPTAC review. Rationale, Definitions and References sections updated.
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Reviewed	01/24/2019	MPTAC review. Rationale, Background/Overview and References sections updated.
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Reviewed	02/13/2014	MPTAC review. Updated Rationale, References and Web Sites sections.
Reviewed	02/14/2013	MPTAC review. Updated Rationale, References and Web Sites sections.
Revised	02/16/2012	MPTAC review. Clarified investigational and not medically necessary Position Statements. Updated Rationale, and References sections. Added Web Sites section.
	01/01/2012	Updated Coding section with 01/01/2012 CPT changes; removed codes 0141T, 0142T, 0143T deleted 12/31/2011.
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Reviewed	02/25/2010	MPTAC review. Rationale and references updated.
Reviewed	02/26/2009	MPTAC review. Rationale, background and references updated.
Reviewed	02/21/2008	MPTAC review. Rationale, background and references updated. Clarified note for multi-organ requests. The phrase “investigational/not medically necessary” was clarified to read “investigational and not medically necessary.” This change was approved at the November 29, 2007 MPTAC meeting.
Reviewed	03/08/2007	MPTAC review. References and coding updated.
Reviewed	03/23/2006	MPTAC review. References and codes updated.
	01/01/2006	Updated Coding section with 01/01/2006 CPT/HCPCS changes
	11/18/2005	Added reference for Centers for Medicare and Medicaid Services (CMS) National Coverage Determination (NCD).
Revised	04/28/2005	MPTAC review. Revision based on Pre-merger Anthem and Pre-merger WellPoint Harmonization.

Pre-Merger Organizations	Last Review Date	Document Number	Title
Anthem, Inc.	04/27/2004	TRANS.00010	Autologous and Allogeneic Islet Cell Transplant
WellPoint Health Networks, Inc.	12/02/2004	7.06.05	Transplantation-Autologous and Allogeneic Islet Cell

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Applicable to Commercial HMO members in California: When a medical policy states a procedure or treatment is investigational, PMGs should not approve or deny the request. Instead, please fax the request to Anthem Blue Cross Grievance and Appeals at fax # 818-234-2767 or 818-234-3824. For questions, call G&A at 1-800-365-0609 and ask to speak with the Investigational Review Nurse.

Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage. The member’s contract benefits in effect on the date that services are rendered must be used. Medical Policy, which addresses medical efficacy, should be considered before utilizing medical opinion in adjudication. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.