07.03.01 Pancreatic Islet Cell Transplant

Wellmark Blue Cross and Blue Shield is an Independent Licensee of the Blue Cross and Blue Shield Association.

Original Effective Date: October 2014

Review Date: October 2025

Revised: October 2023

DISCLAIMER/INSTRUCTIONS FOR USE

This policy contains information which is clinical in nature. The policy is not medical advice. The information in this policy is used by Wellmark to make determinations whether medical treatment is covered under the terms of a Wellmark member's health benefit plan. Physicians and other health care providers are responsible for medical advice and treatment. If you have specific health care needs, you should consult an appropriate health care professional. If you would like to request an accessible version of this document, please contact customer service at 800-524-9242.

Benefit determinations are based on the applicable contract language in effect at the time the services were rendered. Exclusions, limitations, or exceptions may apply. Benefits may vary based on contract, and individual member benefits must be verified. Wellmark determines medical necessity only if the benefit exists and no contract exclusions are applicable. This medical policy may not apply to FEP. Benefits are determined by the Federal Employee Program.

This Medical Policy document describes the status of medical technology at the time the document was developed. Since that time, new technology may have emerged, or new medical literature may have been published. This Medical Policy will be reviewed regularly and updated as scientific and medical literature becomes available; therefore, policies are subject to change without notice.

Related Policies:

- 05.05.16 Lantidra (donislecel-jujn)
- 07.03.09 Pancreas Transplants (Including Simultaneous Pancreas-Kidney, Pancreas alone, and Pancreas after Kidney)

Summary

Description

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

Allogeneic islet cellular therapy products (i.e., donislecel-jujn) are not discussed in this evidence review.

Summary of Evidence

For individuals with chronic pancreatitis undergoing total or near-total pancreatectomy who receive autologous pancreas islet transplantation, the evidence includes nonrandomized studies and systematic

reviews. Relevant outcomes are OS, 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 from chronic pancreatitis. The procedure appears to significantly decrease the incidence of diabetes after total or near-total pancreatectomy in patients with chronic pancreatitis. Also, the autologous islet cell transplant procedure is not associated with serious complications itself and is performed in individuals who are already undergoing a pancreatectomy procedure. The evidence is sufficient to determine autologous islet cell transplantation results in a meaningful improvement in net health outcomes.

For individuals with type I diabetes who receive allogeneic pancreas islet transplantation, the evidence includes a randomized controlled trial (RCT), single-arm prospective studies, registry studies, and systematic reviews. Results of the 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 dependence has been reported in single-arm prospective studies and case series. There is conflicting evidence 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 I diabetics. The evidence is insufficient to determine the effects of allogeneic pancreatic islet transplantation on net health outcomes.

Additional Information

None

OBJECTIVE

The objective of this evidence review is to determine whether autologous pancreas islet transplantation or allogeneic pancreas islet transplantation improves the net health outcome in individuals with chronic pancreatitis or type 1 diabetes.

PRIOR APPROVAL

Not applicable.

POLICY

Autologous Pancreas Islet Cell Transplantation

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

Autologous pancreas islet cell transplantation is considered **investigational** when the above criteria is not met and for all other indications because the evidence is insufficient to determine the technology results in an improvement in the net health outcomes.

Allogeneic Pancreas Islet Cell Transplantation

Allogeneic pancreas islet cell transplantation is considered **investigational** for all indications including the treatment of type 1 diabetes because the evidence is insufficient to determine the technology results in an improvement in the net health outcomes.

To review allogeneic islet cellular therapy products [i.e., Lantidra (donislecel-jujn)], please see the Lantidra (donislecel-jujn) policy.

POLICY GUIDELINES

Coding

See the Codes table for details.

BACKGROUND

The islet cells originate from the individual (autologous transplant) or from a cadaveric donor (allogeneic transplant). Islet cell transplantation may benefit an individual who is without a functioning pancreas.

Islet Transplantation

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

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

A modified immunosuppression regimen has increased the success of allogeneic islet transplantation, this regimen is known as the “Edmonton protocol” (sirolimus, tacrolimus and monoclonal antibody daclizumab).

Chronic Pancreatitis

Chronic pancreatitis is inflammation of the pancreas that does not heal or improve, it gets worse over time and leads to permanent damage. Chronic pancreatitis eventually impairs an individual’s ability to digest food and make pancreatic hormones. Individuals with chronic pancreatitis can experience intractable pain that can only be relieved with a total or near total pancreatectomy. However, the pain relief must be balanced against the certainty that the individual will be rendered an insulin-dependent diabetic.

Regulatory Status

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.

RATIONALE

This evidence review was created in October 2014 and has been updated regularly with searches of the PubMed database. The most recent literature update was performed through September 2025.

Evidence reviews assess the clinical evidence to determine whether the use of technology improves the net health outcome. Broadly defined, health outcomes are the length of life, quality of life, and ability to function-including benefits and harms. Every clinical condition has specific outcomes that are important to patients and managing the course of that condition. Validated outcome measures are necessary to

ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of technology, 2 domains are examined: the relevance, and quality and credibility. To be relevant, studies must represent 1 or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. Randomized controlled trials are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

Chronic Pancreatitis

Clinical Context and Therapy Purpose

The purpose of autologous pancreas islet transplantation for individuals with chronic pancreatitis who are undergoing total or near total pancreatectomy is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals who have chronic pancreatitis who are undergoing total or near-total pancreatectomy. Primary risk factors for chronic pancreatitis may be categorized as the following: toxic-metabolic, idiopathic, genetic, autoimmune, recurrent, and severe acute, or obstructive (TIGAR-O classification system). Individuals with chronic pancreatitis may experience intractable pain that can only be relieved with a total or near-total pancreatectomy. However, the pain relief must be balanced against the certainty that the individual will be rendered an insulin-dependent diabetic.

Interventions

The therapy being considered is autologous pancreas islet transplantation.

Comparators

The following practice is currently being used to make decisions about managing chronic pancreatitis: medical management, which may include medications or endoscopy.

Outcomes

The general outcomes of interest are overall survival (OS), insulin independence, change in disease status, medication use, resource utilization, and treatment-related morbidity.

Short-term follow-up (30 days) is required to monitor for transplant-related complications; long-term follow-up—1 to 3, 5, or even 10 years—is required to establish the durability of glucose control.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;

- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

Review of Evidence

Systematic Reviews

There are several systematic reviews of the literature on chronic pancreatitis individuals.

Zhang et al (2020) published a systematic review and meta-analysis of 17 studies that reported clinical outcomes following total pancreatectomy with islet transplant in patients with chronic pancreatitis. Most studies were single-center, small case series from the United States. The median age was 53 years. Insulin independence was 33.29% (95% CI, 27.77% to 39.05%; I2=32.3%) at 1 year (8 studies). Mortality at 30 days was 1.32% (95% CI, 0.68% to 2.16%; I2=0.0%) and mortality at 1 year was 2.54% (95% CI, 1.32% to 4.16%; I2=17.6%).

Kempeneers et al (2019) published a systematic review of studies examining pain, endocrine function, or quality of life (QOL) outcomes in patients with chronic pancreatitis undergoing total pancreatectomy with islet transplantation. The review included 15 observational studies evaluating 1,255 patients, of whom 28% had had endoscopic and 23% operative therapy. One year after total pancreatectomy with islet cell auto-transplantation, the opioid-free rate had improved from between 0% and 15% to 63% (95% CI 46-77), and the insulin-free rate had decreased from between 89.5% and 100% to 30% (95% CI 20-43). An alcoholic etiology was associated with a lesser insulin-free rate after total pancreatectomy with islet cell auto-transplantation. Quality of life improved statistically after total pancreatectomy with islet cell auto-transplantation. Publication bias was present for both opioid and insulin outcomes. The authors concluded in selected patients with painful, treatment refractory, chronic pancreatitis, evidence shows that total pancreatectomy with islet cell auto-transplantation is effective for pain control in almost two-thirds of patients, whereas the insulin-free rate is relatively low.

Wu et al (2015) published a systematic review and meta-analysis of studies on islet transplantation after total pancreatectomy (TP) for chronic pancreatitis (CP). Twelve studies reporting the outcomes of 677 patients were included in this review. The insulin independent rate for islet autologous transplant (IAT) after total pancreatectomy (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 (IEQ/kgBW) (P=0.026). Our systematic review suggests that IAT is a safe modality for patients with CP need to undergo TP. A significant number of patients will achieve insulin independence for a long time after receiving enough IEQ/kgBW.

Dong et al (2011) published a systematic review that included studies irrespective of design or sample size. After reviewing 84 studies, 15 observational studies met eligibility criteria. Eleven studies assessed total pancreatectomy, 2 studies evaluated partial pancreatectomy, and 2 studies included both types of surgery. Sample sizes in individual studies ranged from 3 to 173 patients. Thirteen studies included patients with chronic pancreatitis and 2 included patients with benign pancreatic tumors. The pooled 30-day mortality rate was 5% (95% CI, 2% to 10%), and the cumulative mortality at 1 year (reported by 10 studies) was 4.9% (95% CI, 2.6% to 7.3%). In a pooled analysis of data from 14 studies, the rate of insulin dependence at last follow-up was 4.6 per 100 person-years (95% CI, 1.53 to 7.62). The pooled

rate of insulin independence was 27% (95% CI, 21% to 33%) at 1 year (5 studies) and 21% (95% CI, 16% to 27%) at 2 years (3 studies).

Table 1. Comparison of Studies Included in Systematic Reviews Assessing Autologous Pancreas Islet Transplants

Study	Zhang et al (2020)	Kempeneers et al (2019)	Wu et al (2015)	Dong et al (2011)
Cameron et al (1981)	●		●	●
Hinshaw et al (1981)	●		●	●
Toledo-Pereyra et al (1983)				●
Fontana et al (1994)				●
Rastellini et al (1997)	●		●	●
Jindal et al (1998)				●
Rabkin et al (1999)				●
Oberholzer et al (2000)	●		●	●
Berney et al (2004)				●
Ahmad et al (2005)			●	●
Argo et al (2008)	●	●	●	●
Dixon et al (2008)	●	●	●	●
Sutherland et al (2008)				●
Webb et al (2008				●
Jung et al (2009)				●
Takita et al (2010)		●	●	
Sutherland et al (2012)	●		●	
Walsh et al (2012)	●	●	●	
Dorlon et al (2013)			●	
Garcea et al (2013)	●	●	●	
Gruessner et al (2014)	●	●		
Wilson et al (2014)		●		
Chinnakotla et al (2015)		●		

Study	Zhang et al (2020)	Kempeneers et al (2019)	Wu et al (2015)	Dong et al (2011)
Georgiev et al (2015)		●		
Takita et al (2015)		●		
Tai et al (2015)	●			
Wilson et al (2015)	●			
Mokadem et al (2016)	●	●		
Shahbazov et al (2016)		●		
Fan et al (2017)		●		
Quartuccio et al (2017)	●			
Shahbazov et al (2017)	●			
Solomina et al (2017)	●	●		
Morgan et al (2018)	●	●		

Table 2. Characteristics of Systematic Reviews Assessing Autologous Pancreas Islet Transplants

Study	Dates	Trials	Participants	N (Range)	Design	Duration, mo
Zhang et al (2020)	1977-2018	17	Individuals with chronic pancreatitis	1024 (5-409)	Observational	1-210
Kempeneers et al (2019)	1977-2017	15	Individuals with chronic pancreatitis	1255 (7-490)	Observational	6-138
Wu et al (2015)	1977-2014	12	Individuals with chronic pancreatitis	677 (5-409)	Case series	1-210
Dong et al (2011)	1977-2007	15	Individuals with chronic pancreatitis or benign pancreatic disease	384 (3-173)	Case series	3-100

Table 3. Results of Systematic Reviews Assessing Autologous Pancreas Islet Transplants

Study	Insulin-Independence Rate	Mortality Rate
Zhang et al (2020)		
n	NR	NR
30-day follow-up (95% CI)	NR	1.32 (0.68 to 2.16)

Study	Insulin-Independence Rate	Mortality Rate
I^2, %	NR	0.0
n	603	NR
1-year follow-up (95% CI)	33.29 (27.77 to 39.05)	2.54 (1.32 to 4.16)
I^2, %	32.3	17.6
Kempeneers et al (2019)		
n	NR	1036
30-day follow-up (95% CI)	NR	2 (1 to 4)
I^2, %	NR	35
n	653	669
1-year follow-up (95% CI)	30 (20 to 43)	4 (2 to 6)
I^2, %	82	0
n	NR	NR
2-year follow-up (95% CI)	NR	NR
I^2, %	NR	NR
Wu et al (2015)		
n	NR	672
30-day follow-up (95% CI)	NR	2.1 (1.2 to 3.8)
I^2, %	NR	0
n	362	NR
1-year follow-up (95% CI)	28.4 (15.7 to 46.0)	NR
I^2, %	69	NR
n	297	NR
2-year follow-up (95% CI)	19.7 (5.1 to 52.6)	NR
I^2, %	87	NR
Dong et al (2011)		
n	NR	176
30-day follow-up (95% CI)	NR	5 (2 to 10)
I^2, %	NR	0
n	221	NR
1-year follow-up (95% CI)	27 (21 to 33)	NR
I^2, %	NR	NR
n	201	NR
2-year follow-up (95% CI)	21 (16 to 27)	NR

Study	Insulin-Independence Rate	Mortality Rate
I^2, %	NR	NR

CI: confidence interval; NR: not reported

Nonrandomized Studies

Wilson et al (2014) reported on 166 patients with chronic pancreatitis who underwent total pancreatectomy and islet transplantation at a single center. Actuarial survival rate at 5 years was 94.6%. Five or more years of data were available for 112 (67%) patients. At 1 year, 38% of patients were insulin-independent and that declined to 27% at the 5-year follow-up. Daily insulin requirement, however, remained stable over the 5 years. Fifty-five percent of patients were independent of opioid analgesics at 1 year and this improved to 73% at 5 years.

Chinnakotla et al (2014) included 484 patients with chronic pancreatitis who underwent total pancreatectomy and immediate islet auto transplantation. The 10-year survival rate was 84%. Patient survival at 5 years was 90.3% in the 80 patients with hereditary/genetic pancreatitis and 89.7% in the 404 patients with nonhereditary pancreatitis; the difference between groups was not statistically significant. Pancreatitis pain decreased significantly after the procedures, and there was no statistically significant difference in the rate of pancreatitis pain between the groups.

Sutherland et al (2012) reported on 409 patients with chronic pancreatitis who underwent total pancreatectomy and islet transplantation at a single center. Fifty-three (13%) of the 409 patients were children between the ages of 5 and 18 years. Actuarial survival post surgery was 96% in adults and 98% in children after 1 year and 89% in adults and 98% in children after 5 years. A total of 15.9% of patients experienced surgical complications requiring reoperation during the initial admission. The most common reason for reoperation was bleeding, occurring in 9.5% of patients. At 3 years, 30% of patients were insulin-independent (25% of adults, 55% of children). A survey of quality-of-life outcomes was initiated in 2008; responses were available for 102 patients. At baseline, all 102 patients reported using opioid analgesia for pain control. At 12 months, the proportion of patients on narcotics decreased to 56% (n=32), and at 24 months, 41% of respondents (n=21) reported using narcotics.

Tables 4 and 5 provide the characteristics and results of the nonrandomized studies assessed.

Table 4. Summary of Key Nonrandomized Study Characteristics

Study	Study Type	Country	Dates	Participants	Treatment	FU, y
Wilson et al (2014)	Cohort	U.S.	2000-2013	Individuals with chronic pancreatitis	Total pancreatectomy and islet auto-transplantation (N=166)	≥ 5
Chinnakotla et al (2014)	Cohort	U.S.	1977-2012	Individuals with chronic pancreatitis	Total pancreatectomy and islet auto-transplantation (N=484)	NR
Sutherland et al (2012	Cohort	U.S.	1977-2011	Individuals with chronic pancreatitis	Total pancreatectomy and islet auto-transplantation (N=409)	NR

FU: follow-up; NR: not reported.

Table 5. Summary of Key Nonrandomized Study Results

Study	Survival Rate, %		Insulin-Independence Rate, %		
	1-Year	5-Year	1-Year	3-Year	5-Year
Wilson et al (2014)	98.2	94.6	38	NR	27
Chinnakotla et al (2014)					
Hereditary/genetic pancreatitis		90.27	20.0	NR	NR
Nonhereditary pancreatitis		89.72	32.9	NR	NR
p-value		.166	.022		
Sutherland et al (2012)	97	90	26	30	NR

NR: not reported.

Section Summary: Chronic Pancreatitis

Autologous islet transplantation is frequently performed as an adjunct to total or near total pancreatectomies for chronic pancreatitis. Evidence from nonrandomized studies and systematic reviews has demonstrated that autologous islet transplantation decreases the incidence of diabetes in the setting of pancreatectomies for the treatment of chronic pancreatitis.

Type I Diabetes

Clinical Context and Therapy Purpose

The purpose of allogeneic pancreas islet transplantation for individuals who have type I diabetes is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals with type 1 diabetes.

Glucose control is a challenge for individuals with type 1 diabetes. Failure to prevent disease progression can lead to long-term complications such as retinopathy, neuropathy, nephropathy, and cardiovascular disease.

Interventions

The therapy being considered is allogeneic pancreas islet transplantation. Islet transplantation is provided in a hospital setting with specialized staff who are equipped to perform the cell isolation and re-infusion procedures and manage post-transplant care.

Comparators

The following practice is currently being used to make decisions about managing type 1 diabetes: medical management, which generally includes daily insulin injections as well as diet and lifestyle changes.

Outcomes

General outcomes of interest are overall survival (OS), insulin independence, change in disease status, medication use, resource utilization, and treatment-related morbidity.

According to U.S. Food and Drug Administration (FDA, 2009) industry guidance on evaluating allogeneic pancreatic islet cell products, single-arm trials with historical controls may be acceptable alternatives to randomized controlled trials (RCTs) for evaluating the safety and efficacy of islet cell products in individuals with metabolically unstable or "brittle" type I diabetes. Attainment of a normal hemoglobin A1C (HbA1C) range (i.e., $\leq$ 6.5%) and elimination of hypoglycemia are acceptable primary end points. To assess the durability of the islet cell procedure, primary end points should be measured at 12 months after the final infusion. Other key clinical outcomes include insulin independence, measures of glucose metabolic control such as fasting plasma glucose levels and loss of hypoglycemia unawareness.

Short-term (30 days) follow-up is required to monitor for transplant related complications; the long-term follow-up to assess the durability of glucose control and monitor immunosuppression is lifelong.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

Review of Evidence

Systematic Reviews

A systematic review by Health Quality Ontario (2015) reported on allogeneic islet transplantation for patients with type I diabetes. The search yielded 1,354 citations. One health technology assessment, 11 additional observational studies to update the health technology assessment, one registry report, and four guidelines were included; the observational studies examined islet transplantation alone, islet-after-kidney transplantation, and simultaneous islet-kidney transplantation. In general, low to very low quality of evidence exists for islet transplantation in patients with type 1 diabetes with difficult-to-control blood glucose levels, with or without kidney disease, for these outcomes: health-related quality of life, secondary complications of diabetes, glycemic control, and adverse events. However, high quality of evidence exists for the specific glycemic control outcome of insulin independence compared with intensive insulin therapy. For patients without kidney disease, islet transplantation improves glycemic control and diabetic complications for patients with type 1 diabetes when compared with intensive insulin therapy. However, results for health-related quality of life outcomes were mixed, and adverse events were increased compared with intensive insulin therapy. For patients with type 1 diabetes with kidney disease, islet-after-kidney transplantation or simultaneous islet-kidney transplantation also improved glycemic control and secondary diabetic complications, although the evidence was more limited for this patient group. Compared with intensive insulin therapy, adverse events for islet-after-kidney transplantation or simultaneous islet-kidney transplantation were increased but were in general less severe than with whole pancreas transplantation. The authors concluded, for patients with type 1 diabetes with difficult-to-control blood glucose levels, islet transplantation may be a beneficial β-cell replacement therapy to improve glycemic control and secondary complications of diabetes. However, there is uncertainty in the estimates of effectiveness because of the generally low to very low quality of evidence for all outcomes of interest.

Additional long-term comparative studies are required for better understanding of continuing effects of transplanted islets and the immunosuppression protocols used.

(2004) A TEC Assessment evaluated the evidence on islet cell transplantation in type 1 diabetes. The Assessment found that published data on clinical outcomes of islet-alone transplantation were limited by small sample sizes (i.e., ≤ 35 enrolled patients), few transplant centers, short duration of follow-up, and lack of standardized methods of reporting clinical outcomes. Also, rare, serious adverse events have occurred in patients given islet transplants, although recent procedure modifications reportedly minimized risks of these adverse events. No procedure-related deaths, cytomegalovirus infection, or post transplantation lymphoproliferative disease have been reported for islet-alone transplantation.

Randomized Controlled Trials

Leblanche et al (2018) published a multicenter, open label, randomized controlled trial (TRIMECO trial) evaluating patients with type I diabetes with severe hypoglycemia or poorly controlled glycaemia after kidney transplantation. Patients with type I diabetes were randomly assigned (1:1) at 15 university hospital to receive immediate allogeneic islet transplantation or intensive insulin therapy (followed by delayed islet transplantation). Eligible patients were aged 18-65 years and had severe hypoglycemia or hypoglycemia unawareness, or kidney grafts with poor glycemic control. We used computer-generated randomization, stratified by center and type of patient. Islet recipients were scheduled to receive 11,000 islet equivalents per kg bodyweight in one to three infusions. The primary outcome was proportion of patients with a modified β-score (in which an overall score of 0 was not allocated when stimulated C-peptide was negative) of 6 or higher at 6 months after first islet infusion in the immediate transplantation group or 6 months after randomization in the insulin group. The primary analysis included all patients who received the allocated intervention; safety was assessed in all patients who received islet infusions. This trial is registered with ClinicalTrials.gov, number NCT01148680, and is completed. Between July 8, 2010, and July 29, 2013, 50 patients were randomly assigned to immediate islet transplantation (n=26) or insulin treatment (n=24), of whom three (one in the immediate islet transplantation group and two in the insulin therapy group) did not receive the allocated intervention. Median follow-up was 184 days (IQR 181-186) in the immediate transplantation group and 185 days (172-201) in the insulin therapy group. At 6 months, 16 (64% [95% CI 43-82]) of 25 patients in the immediate islet transplantation group had a modified β-score of 6 or higher versus none (0% [0-15]) of the 22 patients in the insulin group (p<0·0001). At 12 months after first infusion, bleeding complications had occurred in four (7% [2-18]) of 55 infusions, and a decrease in median glomerular filtration rate from 90·5 mL/min (IQR 76·6-94·0) to 71·8 mL/min (59·0-89·0) was observed in islet recipients who had not previously received a kidney graft and from 63·0 mL/min (55·0-71·0) to 57·0 mL/min (45·5-65·1) in islet recipients who had previously received a kidney graft. Trial limitations include possible bias from open-label design as well as an inadequate follow-up period to demonstrate transplant durability. The authors concluded for the indications assessed in this study, islet transplantation effectively improves metabolic outcomes. Although studies with longer-term follow-up are needed, islet transplantation seems to be a valid option for patients with severe, unstable type 1 diabetes who are not responding to intensive medical treatments. However, immunosuppression can affect kidney function, necessitating careful selection of patients.

Registry Studies

LaBlanche et al (2021) reported 10-year outcomes from the Swiss-French GRAIL Network of 44 patients who received islet transplant for type 1 diabetes between 2003 and 2010. Thirty-one patients were still being followed at 10 years; 6 patients died between years 1 and 10 posttransplant. Median HbA1c levels were 7.2% (range, 6.2% to 8.0%) after 10 years compared to 8.0% pretransplant (p<.001). One patient was insulin independent at 10 years and 73.9% were free of severe hypoglycemia. Insulin requirements were significantly lower posttransplant (0.3 units/kg/day vs. 0.5 units/kg/day; p<.001). Islet graft survival was 51.9% at 10 years.

In a report from the Collaborative Islet Transplant Registry, which collects and monitors data on allogeneic islet transplantation in North America, Europe, and Australia, Alejandro et al (2008) assessed data on 325 adult recipients. Three years after the first cell infusions, 23% of islet-alone recipients were insulin-independent (defined as insulin-independent ≥ 2 weeks), 29% were insulin-dependent with detectable C-peptide, 26% had lost function, and 22% had missing data. Seventy percent achieved insulin independence at least once, 71% of whom were still insulin-independent 1 year later and 52% at 2 years. Factors that favored primary outcomes were a higher number of islet infusions, a greater number of total islet equivalents infused, lower pretransplant HbA1c levels, processing centers related to the transplant center, and larger islet size.

Barton et al (2012) updated the Collaborative Islet Transplantation Registry (CITR) report, which focused on changes in outcomes over time. A total of 677 allogeneic islet transplant-alone or islet-after-kidney recipients with type I diabetes in the CITR were analyzed for five primary efficacy outcomes and overall safety to identify any differences by early (1999-2002), mid (2003-2006), or recent (2007-2010) transplant era based on annual follow-up to 5 years. Insulin independence at 3 years after transplant improved from 27% in the early era (1999-2002, n = 214) to 37% in the mid (2003-2006, n = 255) and to 44% in the most recent era (2007-2010, n = 208; P = 0.006 for years-by-era; P = 0.01 for era alone). C-peptide ≥0.3 ng/mL, indicative of islet graft function, was retained longer in the most recent era (P < 0.001). Reduction of HbA(1c) and resolution of severe hypoglycemia exhibited enduring long-term effects. Fasting blood glucose stabilization also showed improvements in the most recent era. There were also modest reductions in the occurrence of adverse events. The islet reinfusion rate was lower: 48% by 1 year in 2007-2010 vs. 60-65% in 1999-2006 (P < 0.01). Recipients that ever-achieved insulin-independence experienced longer duration of islet graft function (P < 0.001). The authors concluded the CITR shows improvement in primary efficacy and safety outcomes of islet transplantation in recipients who received transplants in 2007-2010 compared with those in 1999-2006, with fewer islet infusions and adverse events per recipient.

Other small case series have reported some success and also adverse events. For example, O'Connell et al. (2013) reported on 17 patients with type I diabetes with severe hypoglycemia who underwent allogeneic islet transplantation. The aim of this single-arm, multicenter study was to evaluate an immunosuppressive protocol of initial antithymocyte globulin (ATG), tacrolimus and mycophenolate mofetil (MMF) followed by switching to sirolimus and MMF. Islets were cultured for 24 h prior to transplantation. The primary endpoint was an HbA1c of < 7% and cessation of severe hypoglycemia. Seventeen recipients were followed for ≥ 12 months. Nine islet preparations were transported interstate for transplantation. Similar outcomes were achieved at all three centers. Fourteen of the 17 (82%) recipients achieved the primary endpoint. Nine (53%) recipients achieved insulin independence for a median of 26 months (range 7-39 months) and 6 (35%) remain insulin independent. All recipients were C-peptide positive for at least 3 months. All subjects with unstimulated C-peptide > 0.2 nmol/L had cessation of severe hypoglycemia. Nine of the 17 recipients tolerated switching from tacrolimus to sirolimus with similar graft outcomes. There was a small but significant reduction in renal function in the first 12 months. The combination of islet culture, ATG, tacrolimus and MMF is a viable alternative for islet transplantation. Most adverse events were related to immunosuppression. Seven (41%) of the 17 patients developed mild lymphopenia and 1 developed clostridium difficile colitis; all responded to treatment. Eight patient developed anemia shortly after transplant and one required a blood transfusion. Procedure-related complications included 1 portal vein thrombosis and 3 postoperative bleeds; 2 of the bleeds required transfusion.

Thompson et al (2011) published findings from a prospective, crossover, cohort study comparing allogeneic islet cell transplantation (ICT) with intensive medical therapy on the progression of diabetic neuropathy, retinopathy, and neuropathy. The study included 45 patients; at the time of data analysis, 32

had receive islet cell transplants. Median follow-up was 47 months pretransplant and 66 months post-transplant. The overall HbA1C level was 7.8% pretransplant and 6.7% post-transplant (p<0.001). In the 16 patients for whom sufficient pre- and post-transplant data were available on renal outcomes, the median decline in glomerular filtration rate was -6.7 mL/min/1.73 m2/y pretransplant and -1.3 mL/min/1.73 m2/y posttransplant (p=0.01). Retinopathy was assessed using a scale that categorized nonproliferative diabetic retinopathy as mild, moderate, or severe. Retinopathy progressed in 10 (12%) of 82 eyes pretransplant versus 0 of 51 post-transplant (p<0.01). The authors concluded, the rate of decline in glomerular filtration rate is slower after ICT than on medical therapy. There was significantly more progression of retinopathy in medically treated patients than post ICT. There was a nonsignificant trend for improved nerve condition velocity post ICT. Islet cell transplantation is associated with less progression of microvascular complications than intensive medical therapy which might have been due in part to the choice of maintenance immunosuppression. The study used a combination of tacrolimus and mycophenolate mofetil. Multicenter randomized trials are needed to further study the role of ICT in slowing the progression of diabetic complications.

Prospective Trials

Two prospective, Phase 3, single-arm, open-label, multicenter trials of purified human pancreatic islet cell transplant have been conducted in North America under the guidance of the National Institutes of Health-sponsored Clinical Islet Transplantation (CIT) Consortium. Hering et al (2016) studied 48 patients with type 1 diabetes, hypoglycemic unawareness, and a history of experiencing severe hypoglycemic events (Protocol CIT07). The primary outcome (HbA1c level ≤ 7% and freedom from severe hypoglycemia after 1 year) was achieved in 87.5% and 71% of patients at 1 and 2 years. Median HbA1c level decreased from 7.2% at baseline to 5.6% at 1 and 2 years (both p<.001). Only 2 patients experienced severe hypoglycemia in the first year posttransplant. Insulin independence was achieved in 52.1% of patients at 1 year, and median insulin use decreased from 0.49 units/kg/day at baseline to 0 units/kg/day at 1 year (p<.0003). Glomerular filtration rate decreased posttransplant (p<.0008 vs. baseline) due to adverse effects of immunosuppression. Twenty-two serious adverse events during the first year were attributed to the procedure or subsequent immunosuppression.

Markmann et al (2021) conducted a similar trial in 24 patients with type 1 diabetes and hypoglycemic unawareness who had previously received a kidney transplant (Protocol CIT06). The primary outcome (HbA1c level ≤6.5% or a reduction in HbA1c level of at least 1% and freedom from severe hypoglycemia after 1 year) was achieved by 62.5% of patients. At 2 and 3 years, 58.3% and 45.8% had achieved these glycemic targets. Severe hypoglycemia was eliminated in 79.2% of patients at 1 year, 75% at 2 years, and 62.5% at 3 years. Median insulin requirements decreased from 0.5 units/kg/day at baseline to 0 units/kg/day at 1, 2, and 3 years (p<.001, p<.001, and p=.002, respectively). Kidney function remained stable throughout follow-up. Thirteen serious adverse events were considered related or possibly related to islet transplant or immunosuppression.

Thompson et al (2011) in Canada published findings from a prospective crossover study of intensive medical therapy (pretransplant) versus islet cell transplantation in patients with type 1 diabetes The article reported on 45 patients; at the time of data analysis, 32 had received islet cell transplants. Median follow-up was 47 months pretransplant and 66 months posttransplant. The overall mean HbA1c level was 7.8% pretransplant and 6.7% posttransplant (p<.001). In the 16 patients for whom sufficient pre- and posttransplant data were available on renal outcomes, the median decline in glomerular filtration rate was -6.7 mL/min/1.73 m2/year pretransplant and -1.3 mL/min/1.73 m2/year posttransplant (p=.01). Retinopathy was assessed using a scale that categorized nonproliferative diabetic retinopathy as mild, moderate, or severe. Retinopathy progressed in 10 (12%) of 82 eyes pretransplant versus 0 of 51 posttransplant (p<.01). (The numbers of patients in the retinopathy analyses were not reported.) The authors noted that their finding of reduced microvascular complications after islet transplantation might

have been due, in part, to their choice of maintenance immunosuppression. The study used a combination of tacrolimus and mycophenolate mofetil.

Case Series

Other small case series have reported some success and also adverse events. Lemos et al (2021) reported 20-year results for a retrospective series of 49 patients with type 1 diabetes, hypoglycemic unawareness, and severe hypoglycemia who underwent islet transplant. Median follow-up time after transplant was 13.8 years. Median duration of graft function while on immunosuppression was 4.4 years (interquartile range, 1.3 to 12.2 years). Kaplan-Meier survival analysis showed cumulative survival of >80% at 20 years; 2 patients died during follow-up, 1 from myocardial infarction and 1 from suspected hypoglycemia.

In another case series, O'Connell et al (2013) reported on 17 patients with type 1 diabetes and severe hypoglycemia who underwent islet transplantation in Australia. Fourteen (82%) patients attained the primary endpoint, which was an HbA1c level of less than 7% and no severe hypoglycemic events 2 months after the initial transplant. Nine (53%) patients attained insulin independence for a median of 26 months. Most adverse events were related to immunosuppression. Seven (41%) of the 17 patients developed mild lymphopenia and 1 developed Clostridium difficile colitis; all responded to treatment. Eight patients developed anemia shortly after transplant and 1 required a blood transfusion. Procedure-related complications included 1 partial portal vein thrombosis and 3 postoperative bleeds; 2 of the bleeds required transfusion.

Section Summary: Type I Diabetes

Allogeneic islet transplantation has been investigated in the treatment of type I diabetes. One randomized controlled trial (RCT) found the quality of life (QOL) was significantly improved after islet transplantation; however, the short length of follow-up limits these conclusions. Evidence from registry studies and systematic reviews has demonstrated varying ranges of insulin independence post-transplantation. There is conflicting evidence that allogeneic islet transplantation reduces long-term diabetic complications. Long term comparative studies are needed to determine the effects of allogeneic islet transplantation in type 1 diabetic and post-transplant immunosuppression.

SUPPLEMENTAL INFORMATION

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

Practice Guidelines and Position Statements

Guidelines or position statements will be considered for inclusion in ‘Supplemental Information' if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

American Diabetes Association (ADA)

In 2025 the American Diabetes Association (ADA) 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; 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.

International Consensus Guidelines for Chronic Pancreatitis

In 2020, the International Consensus Guidelines for Chronic Pancreatitis panel released a statement on the role of total pancreatectomy and islet transplant in patients with chronic pancreatitis. The panel stated that islet transplant should be considered for patients undergoing total pancreatectomy due to the potential for insulin independence and better long-term glycemic outcomes compared to pancreatectomy alone (weak recommendation based on low quality evidence). However, there is not enough information to definitively conclude when transplant should be performed relative to other interventions. Major indications for pancreatectomy with islet transplant include debilitating pain or recurrent pancreatitis episodes that diminish quality of life (strong recommendation based on low quality evidence). Contraindications to pancreatectomy with islet transplant include active alcoholism, pancreatic cancer, end-stage systemic illness, or psychiatric illness or socioeconomic status that would hinder either the procedure itself or posttransplant care (strong recommendation based on low quality evidence). Pancreatectomy with islet transplant improves quality of life, opioid use, and pancreatic pain in this population, but evidence about the effect on healthcare utilization is limited.

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. 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).

Organ Procurement and Transplantation Network (OPTN)

Islet Registration Status

(2022) The following is the allocation policy of the Organ Procurement and Transplantation Network (OPTN) for the allocation of islet cells.

Islet Registration Status

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:

- Is insulin dependent
- Has a hemoglobin A1c (HcA1c) value greater than 6.5%

An islet candidate that does not meet either of these requirements above must have an inactive status on the waiting list. If the transplant hospital changes a candidate’s status from inactive to active, the transplant hospital must document that the candidate met one of the above requirements.

If a candidate’s clinical condition changes and the candidate becomes inactive, the transplant hospital must report this to the OPTN Contractor within 72 hours of the transplant hospital’s knowledge of this change. The transplant hospital must document in the candidate’s medical record when the transplant hospital learned of this change.

If the candidate is active and is insulin independent, then the transplant hospital must document in the candidate’s medical record the candidate’s insulin status and HbA1c value. The transplant hospital must use the most recent HbA1c test performed within the last six months when determining whether the candidate meets the criteria for active status.

Ongoing and Unpublished Clinical Trials

Some currently ongoing and unpublished trials that might influence this review can be located at clinicaltrials.gov.

REFERENCES

1. Tillou JD, Tatum JA, Jolissaint JS, et al. Operative management of chronic pancreatitis: A review. Am J Surg. Aug 2017; 214(2): 347-357. PMID 28325588
2. Vantyghem MC, de Koning EJP, Pattou F, et al. Advances in β-cell replacement therapy for the treatment of type 1 diabetes. Lancet. Oct 05 2019; 394(10205): 1274-1285. PMID 31533905
3. U.S. Food & Drug Administration (FDA). FDA Approves First Cellular Therapy to Treat Patients with Type 1 Diabetes. June 28, 2023. https://www.fda.gov/news-events/press-announcements/fda-approves-first-cellular-therapy-treat-patients-type-1-diabetes. AccessedSeptember 22, 2025.
4. Chinnakotla S, Radosevich DM, Dunn TB, et al. Long-term outcomes of total pancreatectomy and islet auto transplantation for hereditary/genetic pancreatitis. J Am Coll Surg. Apr 2014; 218(4): 530-43. PMID 24655839
5. 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. Sep 2020; 44(4): 598-608. PMID 31523018
6. 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. Sep 2019; 166(3): 263-270. PMID 31085044
7. 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): 227-34. PMID 25735805
8. Dong M, Parsaik AK, Erwin PJ, et al. Systematic review and meta-analysis: islet autotransplantation after pancreatectomy for minimizing diabetes. Clin Endocrinol (Oxf). Dec 2011; 75(6): 771-9. PMID 21605156
9. Cameron JL, Mehigan DG, Broe PJ, et al. Distal pancreatectomy and islet autotransplantation for chronic pancreatitis. Ann Surg. Mar 1981; 193(3): 312-7. PMID 6782958
10. Hinshaw DB, Jolley WB, Hinshaw DB, et al. Islet autotransplantation after pancreatectomy for chronic pancreatitis with a new method of islet preparation. Am J Surg. Jul 1981; 142(1): 118-22. PMID 6266268
11. Toledo-Pereyra LH. Islet cell autotransplantation after subtotal pancreatectomy. Arch Surg. Jul 1983; 118(7): 851-8. PMID 6407457
12. Fontana I, Arcuri V, Tommasi GV, et al. Long-term follow-up of human islet autotransplantation. Transplant Proc. Apr 1994; 26(2): 581. PMID 8171565
13. Rastellini C, Shapiro R, Corry R, et al. Treatment of isolated pancreatic islets to reverse pancreatectomy-induced and insulin-dependent type I diabetes in humans: a 6-year experience. Transplant Proc. 1997; 29(1-2): 746-7. PMID 9123507

14. Jindal RM, Fineberg SE, Sherman S, et al. Clinical experience with autologous and allogeneic pancreatic islet transplantation. Transplantation. Dec 27 1998; 66(12): 1836-41. PMID 9884286

15. Rabkin JM, Olyaei AJ, Orloff SL, et al. Distant processing of pancreas islets for autotransplantation following total pancreatectomy. Am J Surg. May 1999; 177(5): 423-7. PMID 10365884

16. Oberholzer J, Triponez F, Mage R, et al. Human islet transplantation: lessons from 13 autologous and 13 allogeneic transplantations. Transplantation. Mar 27 2000; 69(6): 1115-23. PMID 10762216

17. Berney T, Mathe Z, Bucher P, et al. Islet autotransplantation for the prevention of surgical diabetes after extended pancreatectomy for the resection of benign tumors of the pancreas. Transplant Proc. May 2004; 36(4): 1123-4. PMID 15194391

18. Ahmad SA, Lowy AM, Wray CJ, et al. Factors associated with insulin and narcotic independence after islet autotransplantation in patients with severe chronic pancreatitis. J Am Coll Surg. Nov 2005; 201(5): 680-7. PMID 16256909

19. Argo JL, Contreras JL, Wesley MM, et al. Pancreatic resection with islet cell autotransplant for the treatment of severe chronic pancreatitis. Am Surg. Jun 2008; 74(6): 530-6; discussion 536-7. PMID 18556996

20. Dixon J, DeLegge M, Morgan KA, et al. Impact of total pancreatectomy with islet cell transplant on chronic pancreatitis management at a disease-based center. Am Surg. Aug 2008; 74(8): 735-8. PMID 18705576

21. Sutherland DE, Gruessner AC, Carlson AM, et al. Islet autotransplant outcomes after total pancreatectomy: a contrast to islet allograft outcomes. Transplantation. Dec 27 2008; 86(12): 1799-802. PMID 19104425

22. Webb MA, Illouz SC, Pollard CA, et al. Islet auto transplantation following total pancreatectomy: a long-term assessment of graft function. Pancreas. Oct 2008; 37(3): 282-7. PMID 18815550

23. Jung HS, Choi SH, Kim SJ, et al. Delayed improvement of insulin secretion after autologous islet transplantation in partially pancreatectomized patients. Metabolism. Nov 2009; 58(11): 1629-35. PMID 19604519

24. Takita M, Naziruddin B, Matsumoto S, et al. Variables associated with islet yield in autologous islet cell transplantation for chronic pancreatitis. Proc (Bayl Univ Med Cent). Apr 2010; 23(2): 115-20. PMID 20396418

25. Sutherland DE, Radosevich DM, Bellin MD, et al. Total pancreatectomy and islet autotransplantation for chronic pancreatitis. J Am Coll Surg. Apr 2012; 214(4): 409-24; discussion 424-6. PMID 22397977

26. Walsh RM, Saavedra JR, Lentz G, et al. Improved quality of life following total pancreatectomy and auto-islet transplantation for chronic pancreatitis. J Gastrointest Surg. Aug 2012; 16(8): 1469-77. PMID 22673773

27. Dorlon M, Owczarski S, Wang H, et al. Increase in postoperative insulin requirements does not lead to decreased quality of life after total pancreatectomy with islet cell autotransplantation for chronic pancreatitis. Am Surg. Jul 2013; 79(7): 676-80. PMID 23815999

28. Garcea G, Pollard CA, Illouz S, et al. Patient satisfaction and cost-effectiveness following total pancreatectomy with islet cell transplantation for chronic pancreatitis. Pancreas. Mar 2013; 42(2): 322-8. PMID 23407482

29. Gruessner RW, Cercone R, Galvani C, et al. Results of open and robot-assisted pancreatectomies with autologous islet transplantations: treating chronic pancreatitis and preventing surgically induced diabetes. Transplant Proc. 2014; 46(6): 1978-9. PMID 25131087

30. Wilson GC, Sutton JM, Abbott DE, et al. Long-term outcomes after total pancreatectomy and islet cell autotransplantation: is it a durable operation?. Ann Surg. Oct 2014; 260(4): 659-65; discussion 665-7. PMID 25203883

31. Chinnakotla S, Beilman GJ, Dunn TB, et al. Factors Predicting Outcomes After a Total Pancreatectomy and Islet Autotransplantation Lessons Learned From Over 500 Cases. Ann Surg. Oct 2015; 262(4): 610-22. PMID 26366540

32. Georgiev G, Beltran del Rio M, Gruessner A, et al. Patient quality of life and pain improve after autologous islet transplantation (AIT) for treatment of chronic pancreatitis: 53 patient series at the University of Arizona. Pancreatology. 2015; 15(1): 40-5. PMID 25455347

33. Takita M, Lara LF, Naziruddin B, et al. Effect of the Duration of Chronic Pancreatitis on Pancreas Islet Yield and Metabolic Outcome Following Islet Autotransplantation. J Gastrointest Surg. Jul 2015; 19(7): 1236-46. PMID 25933581

34. Tai DS, Shen N, Szot GL, et al. Autologous islet transplantation with remote islet isolation after pancreas resection for chronic pancreatitis. JAMA Surg. Feb 2015; 150(2): 118-24. PMID 25494212

35. Wilson GC, Sutton JM, Smith MT, et al. Completion pancreatectomy and islet cell autotransplantation as salvage therapy for patients failing previous operative interventions for chronic pancreatitis. Surgery. Oct 2015; 158(4): 872-8; discussion 879-80. PMID 26173686

36. Mokadem M, Noureddine L, Howard T, et al. Total pancreatectomy with islet cell transplantation vs intrathecal narcotic pump infusion for pain control in chronic pancreatitis. World J Gastroenterol. Apr 28 2016; 22(16): 4160-7. PMID 27122666

37. Shahbazov R, Yoshimatsu G, Haque WZ, et al. Clinical effectiveness of a pylorus-preserving procedure on total pancreatectomy with islet autotransplantation. Am J Surg. Jun 2017; 213(6): 1065-1071. PMID 27760705

38. Fan CJ, Hirose K, Walsh CM, et al. Laparoscopic Total Pancreatectomy With Islet Autotransplantation and Intraoperative Islet Separation as a Treatment for Patients With Chronic Pancreatitis. JAMA Surg. Jun 01 2017; 152(6): 550-556. PMID 28241234

39. Quartuccio M, Hall E, Singh V, et al. Glycemic Predictors of Insulin Independence After Total Pancreatectomy With Islet Autotransplantation. J Clin Endocrinol Metab. Mar 01 2017; 102(3): 801-809. PMID 27870552

40. Solomina J, Gołębiewska J, Kijek MR, et al. Pain Control, Glucose Control, and Quality of Life in Patients With Chronic Pancreatitis After Total Pancreatectomy With Islet Autotransplantation: A Preliminary Report. Transplant Proc. Dec 2017; 49(10): 2333-2339. PMID 29198673

41. Morgan KA, Lancaster WP, Owczarski SM, et al. Patient Selection for Total Pancreatectomy with Islet Autotransplantation in the Surgical Management of Chronic Pancreatitis. J Am Coll Surg. Apr 2018; 226(4): 446-451. PMID 29289751

42. Thompson DM, Meloche M, Ao Z, et al. Reduced progression of diabetic microvascular complications with islet cell transplantation compared with intensive medical therapy. Transplantation. Feb 15 2011; 91(3): 373-8. PMID 21258272

43. Food and Drug Administration (FDA). Guidance for Industry: Considerations for Allogeneic Pancreatic Islet Cell Products. 2009; https://www.fda.gov/regulatory-information/search-fda-guidance-documents/considerations-allogeneic-pancreatic-islet-cell-products. Accessed September 22, 2025.

44. National Institute for Health and Care Excellence (NICE). Allogenic pancreatic islet cell transplantation for type 1 diabetes mellitus [IPG257]. 2008; https://www.nice.org.uk/guidance/ipg257. Accessed September 22, 2025.

45. 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. Accessed September 22, 2025.

46. ElSayed NA, Aleppo G, Aroda VR, et al. 9. Pharmacologic Approaches to Glycemic Treatment: Standards of Care in Diabetes-2023. Diabetes Care. Jan 01 2023; 46(Suppl 1): S140-S157. PMID 36507650

47. Abu-El-Haija M, Anazawa T, Beilman GJ, et al. The role of total pancreatectomy with islet autotransplantation in the treatment of chronic pancreatitis: A report from the International Consensus Guidelines in chronic pancreatitis. Pancreatology. Jun 2020; 20(4): 762-771. PMID 32327370

48. 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/view/ncd.aspx?NCDId=286&ncdver=1. Accessed September 22, 2025.

49. Hayes, a symplyr company. Health Technology Assessment. Total Pancreatectomy with islet Autotransplantation for Chronic Pancreatitis. Hayes, Inc. December 22, 2015. Annual Review: January 17, 2020. Available at: www.hayesinc.com. Accessed September 22, 2025.

50. Hayes,a symplyr company. Health Technology Assessment. Islet Cell Transplantation for the Treatment of Type 1 Diabetes. Hayes, Inc. August 1, 2004. Annual Review: July 21, 2009. Available at: www.hayesinc.com. Accessed September 22, 2025.

51. ElSayed NA, McCoy RG, Aleppo G, et al. 9. Pharmacologic Approaches to Glycemic Treatment: Standards of Care in Diabetes-2025. Diabetes Care. Jan 01 2025; 48(1 Suppl 1): S181-S206. PMID 39651989

52. Gangemi A, Salehi P, Hatipoglu B, et al. Islet transplantation for brittle type 1 diabetes: the UIC protocol. Am J Transplant. Jun 2008; 8(6): 1250-61. PMID 18444920

53. LANTRIDA. U.S. Food and Drug Administration. August 7, 2023. https://www.fda.gov/vaccines-blood-biologics/lantidra. Accessed July 5, 2025.

CODES

To report provider services, use appropriate CPT codes, HCPCS codes, Revenue codes, and/or ICD diagnosis codes.

Codes	Number	Description
CPT		
	48160	Pancreatectomy, total or subtotal, with autologous transplantation of pancreas or pancreatic islet cells.
	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	Transplant, islet cell tissue, allogeneic
Type of Service	Surgery	
Place of Service	Inpatient	

POLICY HISTORY

Date	Reason	Action
October 2025	Annual Review	Policy Renewed

Date	Reason	Action
October 2024	Annual Review	Policy Renewed
October 2023	Annual Review	Policy Revised
October 2022	Annual Review	Policy Renewed
October 2021	Annual Review	Policy Renewed
October 2020	Annual Review	Policy Renewed
October 2019	Annual Review	Policy Renewed
October 2018	Annual Review	Policy Revised
October 2017	Annual Review	Policy Renewed
October 2016	Annual Review	Policy Renewed
November 2015	Annual Review	Policy Renewed
December 2014	Annual Review	Policy Revised
February 2014	Annual Review	Policy Revised
March 2013	Annual Review	Policy Renewed
July 2012	Annual Review	Policy Renewed
August 2011	Annual Review	Policy Renewed

New information or technology that would be relevant for Wellmark to consider when this policy is next reviewed may be submitted to:

Wellmark Blue Cross and Blue Shield
Medical Policy Analyst
PO Box 9232
Des Moines, IA 50306-9232

*CPT® is a registered trademark of the American Medical Association.