7.03.12	Islet Transplantation for Chronic Pancreatitis and Donislecel-jujn for Type 1 Diabetes		
Original Policy Date:	October 1, 2017	**Effective Date:**	November 1, 2023
Section:	7.0 Surgery	**Page:**	Page 1 of 17

Policy Statement

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

II. Allogeneic islet transplantation using an FDA-approved cellular therapy product (donislecel-jujn [i.e., Lantidra]) is considered **investigational** for the treatment of type 1 diabetes.

III. Islet transplantation with donislecel-jujn is considered **investigational** in all other situations.

NOTE: Refer to Appendix A to see the policy statement changes (if any) from the previous version.

Policy Guidelines

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

There are risks associated with the infusion procedure and long-term immunosuppression. There is no evidence of donislecel-jujn benefit for individuals whose diabetes is well-controlled with insulin therapy or for those with hypoglycemic unawareness who are able to prevent current repeated severe hypoglycemic events (neuroglycopenia requiring active intervention from a third party) using intensive diabetes management (including insulin, devices, and education).

Repeated intraportal islet infusions are not recommended in patients who have experienced prior portal thrombosis, unless the thrombosis was limited to second- or third-order portal vein branches. There is no evidence to support donislecel-jujn for individuals with liver disease, renal failure, or who have received a renal transplant.

Islet transplantation does not supplant future whole pancreatic transplantation (see Blue Shield of California Medical Policy: Allogeneic Pancreas Transplant).

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

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

Coding

CPT code 48160 explicitly describes autologous pancreas islet cell transplantation at the time of pancreatectomy. CPT instructs the use of code 48999 (unlisted procedure, pancreas) for transplantation of islet cells as a stand-alone procedure.

Three HCPCS codes are specific to these procedures:

- **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

Description

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

Related Policies

- Allogeneic Pancreas Transplant
- Chronic Intermittent Intravenous Insulin Therapy

Benefit Application

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control. 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.

Some state or federal mandates (e.g., Federal Employee Program [FEP]) prohibits plans from denying Food and Drug Administration (FDA)-approved technologies as investigational. In these instances, plans may have to consider the coverage eligibility of FDA-approved technologies on the basis of medical necessity alone.

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. Donislecel-jujn (Lantidra™), a first-in-class deceased donor-derived allogeneic pancreatic islet cellular therapy product, was approved by the FDA in June 2023 for the treatment of type 1 diabetes in adults who are unable to approach target hemoglobin A1c due to repeated episodes of severe hypoglycemia despite intensive diabetes management and education.[3,]

Rationale

Background

Islet Transplantation

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

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

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

Literature Review

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.

Promotion of greater diversity and inclusion in clinical research of historically marginalized groups (e.g., People of Color [African-American, Asian, Black, Latino and Native American]; LGBTQIA (Lesbian, Gay, Bisexual, Transgender, Queer, Intersex, Asexual); Women; and People with Disabilities [Physical and Invisible]) allows policy populations to be more reflective of and findings more applicable to our diverse members. While we also strive to use inclusive language related to these groups in our policies, use of gender-specific nouns (e.g., women, men, sisters, etc.) will continue when reflective of language used in publications describing study populations.

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). Patients 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 patient 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.[4,]

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 patients. 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.[5,] 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%; I^2=32.3%) at 1 year (8 studies). Mortality at 30 days was 1.32% (95% CI, 0.68% to 2.16%; I^2=0.0%) and mortality at 1 year was 2.54% (95% CI, 1.32% to 4.16%; I^2=17.6%).

Kempeneers et al (2019) published a systematic review of studies examining pain, endocrine function, or quality of life outcomes in patients with chronic pancreatitis undergoing total pancreatectomy with islet transplantation.[6,] A total of 15 studies met the inclusion criteria. All included studies were retrospective and observational. The median age was 41 years. Pooled insulin free rate was 30% (95% CI, 20% to 43%) at 1 year (4 studies). The pooled mortality rate was 2% (95% CI, 1% to 4%) at 30 days (11 studies) and 4% at 1 year (6 studies). At 1 year, 63% (95% CI, 46% to 77%, I^2=89%) of patients were opioid free (6 studies, 657 patients). An analysis revealed a high risk for publication bias among the included studies, which could have led to an overestimation of the true effect.

Wu et al (2015) published a systematic review of studies on islet transplantation after total pancreatectomy for chronic pancreatitis.[7,] Studies could use any design type but had to include at least 5 patients or have a median follow-up of at least 6 months. Twelve studies (N=677 patients) met reviewers' inclusion criteria. The mean age was 38 years and the mean duration of pancreatitis was 6.6 years. A meta-analysis of the insulin-independence rate at 1 year (5 studies, 362 patients) was 28.4% (95% CI, 15.7% to 46.0%). At 2 years, the pooled insulin-independence rate (3 studies, 297 patients) was 19.7% (95% CI, 5.1% to 52.6%). The pooled 30-day mortality rate (11 studies) was 2.1% (95% CI, 1.2% to 3.8%). Long-term mortality data were not pooled.

Dong et al (2011) published a systematic review that included studies irrespective of design or sample size.[8,] 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 provides a crosswalk of studies included in the systematic reviews discussed. Tables 2 and 3 provide the characteristics and results of these systematic reviews.

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

Study	Zhang et al (2020)[5]	Kempeneers et al (2019)[6]	Wu et al (2015)[7]	Dong et al (2011)[8]
Cameron et al (1981)[9]	●		●	●
Hinshaw et al (1981)[10]	●		●	●
Toledo-Pereyra et al (1983)[11]				●
Fontana et al (1994)[12]				●
Rastellini et al (1997)[13]	●		●	●
Jindal et al (1998)[14]				●
Rabkin et al (1999)[15]				●
Oberholzer et al (2000)[16]	●		●	●
Berney et al (2004)[17]				●
Ahmad et al (2005)[18]			●	●
Argo et al (2008)[19]	●	●	●	●
Dixon et al (2008)[20]	●	●	●	●
Sutherland et al (2008)[21]				●
Webb et al (2008)[22]				●
Jung et al (2009)[23]				●
Takita et al (2010)[24]		●	●	
Sutherland et al (2012)[25]	●		●	
Walsh et al (2012)[26]	●	●	●	
Dorlon et al (2013)[27]			●	
Garcea et al (2013)[28]	●	●	●	
Gruessner et al (2014)[29]	●	●		
Wilson et al (2014)[30]		●		
Chinnakotla et al (2015)[31]		●		
Georgiev et al (2015)[32]		●		
Takita et al (2015)[33]		●		
Tai et al (2015)[34]	●			
Wilson et al (2015)[35]	●			
Mokadem et al (2016)[36]	●	●		
Shahbazov et al (2016)[37]		●		
Fan et al (2017)[38]		●		
Quartuccio et al (2017)[39]	●			
Shahbazov et al (2017)[37]	●			
Solomina et al (2017)[40]	●	●		
Morgan et al (2018)[41]	●	●		

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

Study	Dates	Trials	Participants	N (Range)	Design	Duration, mo
Zhang et al (2020)[5]	1977-2018	17	Individuals with chronic pancreatitis	1024 (5-409)	Observational	1-210
Kempeneers et al (2019)[6]	1977-2017	15	Individuals with chronic pancreatitis	1255 (7-490)	Observational	6-138
Wu et al (2015)[7]	1977-2014	12	Individuals with chronic pancreatitis	677 (5-409)	Case series	1-210

Study	Dates	Trials	Participants	N (Range)	Design	Duration, mo
Dong et al (2011)[8,]	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)[5,]		
n	NR	NR
30-day follow-up (95% CI)	NR	1.32 (0.68 to 2.16)
P, %	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)
P, %	32.3	17.6
Kempeneers et al (2019)[6,]		
n	NR	1036
30-day follow-up (95% CI)	NR	2 (1 to 4)
P, %	NR	35
n	653	669
1-year follow-up (95% CI)	30 (20 to 43)	4 (2 to 6)
P, %	82	0
n	NR	NR
2-year follow-up (95% CI)	NR	NR
P, %	NR	NR
Wu et al (2015)[7,]		
n	NR	672
30-day follow-up (95% CI)	NR	2.1 (1.2 to 3.8)
P, %	NR	0
n	362	NR
1-year follow-up (95% CI)	28.4 (15.7 to 46.0)	NR
P, %	69	NR
n	297	NR
2-year follow-up (95% CI)	19.7 (5.1 to 52.6)	NR
P, %	87	NR
Dong et al (2011)[8,]		
n	NR	176
30-day follow-up (95% CI)	NR	5 (2 to 10)
P, %	NR	0
n	221	NR
1-year follow-up (95% CI)	27 (21 to 33)	NR
P, %	NR	NR
n	201	NR
2-year follow-up (95% CI)	21 (16 to 27)	NR
P, %	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.[30,] Actutimes 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 autotransplantation.[4,] 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.[25,] Fifty-three (13%) of the 409 patients were children between the ages of 5 and 18 years. Actutimes survival postsurgery 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)[30,]	Cohort	U.S.	2000-2013	Individuals with chronic pancreatitis	Total pancreatectomy and islet auto-transplantation (N=166)	≥5
Chinnakotla et al (2014)[4,]	Cohort	U.S.	1977-2012	Individuals with chronic pancreatitis	Total pancreatectomy and islet auto-transplantation (N=484)	NR
Sutherland et al (2012)[25,]	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)[30,]	98.2	94.6	38	NR	27
Chinnakotla et al (2014)[4,]					
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)[25,]	97	90	26	30	NR

NR: not reported.

Section Summary: Chronic Pancreatitis

Autologous islet transplantation is frequently performed as an adjunct to a total or near-total pancreatectomy 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.

Donislecel-jujn for Pancreatic Islet Cell Transplantation in Type 1 Diabetes

Clinical Context and Therapy Purpose

The purpose of donislecel-jujn in allogeneic pancreas islet transplantation for individuals who have type 1 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.[42,]

Interventions

The therapy being considered is donislecel-jujn for allogeneic pancreas islet transplantation.

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; and, whole pancreatic transplant.

Outcomes

The 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 RCTs for evaluating the safety and efficacy of islet cell products in patients with metabolically unstable, or "brittle," type 1 diabetes.[43,] Attainment of a normal hemoglobin A_{1c} (HbA_{1c}) range (i.e., ≤6.5%) and elimination of hypoglycemia are acceptable primary endpoints. To assess the durability of the islet cell procedure, primary endpoints should be measured at least 12 months after the final infusion. Other key clinical outcomes include insulin independence, measures of glucose metabolic control such as fasting plasma glucose level, 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

In June 2023, the FDA approved donislecel-jujn for the treatment of adults with type 1 diabetes who are unable to approach target HbA_{1c} because of repeated episodes of severe hypoglycemia despite intensive diabetes management and education.[3,] The approval was based on a phase 1/2 trial in patients with brittle type 1 diabetes complicated by hypoglycemic unawareness, metabolic lability with documented severe hypoglycemia, or ketoacidosis despite intensive insulin therapy (N=10);[44,45,] a single-arm, open-label phase 3 trial with similar eligibility criteria (N=20);[46,] and an expanded access protocol with similar eligibility criteria.[47,48,] In the FDA analysis of these trials (as described in the product labeling), median participant age was 46.5 years (range, 21 to 67 years); 80% of participants were female, 100% were White, and 97% were of non-Hispanic ethnicity.[49,] Patients received up to 3 islet cell infusions; among 30 participants in the approval trials, 11 received 1 islet cell infusion, 12 received 2 infusions, and 7 received 3 infusions. Twenty-five participants (83%) achieved exogenous

insulin independence (defined as not requiring exogenous insulin to achieve adequate glycemic control) of any duration, including 4 patients (13.3%) with independence for less than 1 year, 12 patients (36.7%) with independence for 1 to 5 years, and 9 patients (33.3%) with independence for more than 5 years. Mean duration of exogenous insulin dependence in the phase 1/2 and phase 3 studies were 5.1 years (standard deviation [SD] 4.2, range 0.2 to 12.8) and 3.2 years (SD 3.1, range 0 to 9.9), respectively. Serious adverse reactions were reported in 90%, including 2 deaths (7%) from multiorgan failure with sepsis (1.6 years after first infusion) and progressive confusion, global atrophy, and micro-ischemic disease (9.7 years after first infusion); most serious adverse reactions were attributed to immunosuppression. Infections were reported in 26 patients (87%), totaling 211 episodes, 1 of which was classified as life-threatening and 22 as severe. Malignancy was reported in 11 subjects (37%), including 12 skin cancers and 1 each of posttransplant lymphoproliferative disease, breast cancer, and thyroid cancer. Common adverse events included, but were not limited to nausea, fatigue, anemia, diarrhea, abdominal pain, asthenia, headache, and hyponatremia. Most adverse reactions were low-grade by Common Terminology Criteria for Adverse Events, version 5; the most common grade ≥3 adverse events included low density lipoprotein elevations (37%), anemia (27%), and pneumonia (17%).

The FDA also reviewed the Clinical Islet Transplantation (CIT) consortium's phase 3, open-label, single-arm, multicenter trial (CIT-07) data.[50,] The trial enrolled patients with hypoglycemia unawareness and a history of severe hypoglycemic episodes. Although 8 centers participated in the trial, only the 4 patients from the single site who were treated with the particular donislecel-jujn product were included in the review. All patients received 1 or 2 islet transplants. The primary endpoint was the proportion of subjects who achieved a HbA_{1c} less than 7% at 1 year with no hypoglycemic events from Day 28 to Day 365 after transplantation. Analysis of the primary endpoint was limited because 2 subjects had HbA_{1c} levels less than 7% at baseline and another had near target HbA_{1c} (7.3%). Severe hypoglycemic events were not reported. The 3 subjects who completed Day 730 follow up, were insulin independent at that time.

The FDA Biologics License Application Clinical Review Memorandum states numerous protocol deviations across the above studies that could impair the interpretation of both efficacy and safety data, as well as provides examples of missing and incongruent data and insufficient data monitoring during the study.[50,] Multiple information requests were generated by the FDA in order to achieve adequate data for a substantive, complete review. Given that the studies were conducted at a single site raises concern; and, other factors that might affect occurrence or duration of insulin independence were not able to be elucidated from the existing studies, including cell product factors (number of cells, viability, purity, and potency) and delivery device (e.g., type of catheter).

Section Summary: Donislecel-jujn for Pancreatic Islet Cell Transplantation in Type 1 Diabetes

Allogeneic islet transplantation with donislecel-jujn has been investigated in the treatment of type 1 diabetes. A single-arm prospective trial of the allogeneic islet cellular therapy product donislecel-jujn demonstrated insulin independence for over 1 year in a majority of participants, with mean insulin independence of approximately 5 years, resulting in donislecel-jujn's FDA approval for certain adults with type 1 diabetes. A single-arm, open-label study reviewed by the FDA (CIT-07) included data from 4 patients who received donislecel-jujn. However, the primary outcome was intended to evaluate the proportion of patients with a HbA_{1c} less than 7% and low baseline HbA_{1c} levels precluded analysis.

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.

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.[51,] A related 2008 guidance addressed autologous islet cell transplantation for improved glycemic control after pancreatectomy and stated that studies have shown "some short-term efficacy, although most 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)."[52,]

American Diabetes Association

In 2023 , the American Diabetes Association standards of medical care recommended autologous islet cell transplantation be considered in patients undergoing total pancreatectomy for chronic pancreatitis to prevent postsurgical diabetes.[53,]The standards of care note that islet cell transplantation may have a role in type 1 diabetes. Because of the need for immunosuppressive agents posttransplantation, the guidelines note 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.[54,] 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.

U.S. Preventive Services Task Force Recommendations

Not applicable.

Medicare National Coverage

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

Ongoing and Unpublished Clinical Trials

Some currently ongoing and unpublished trials that might influence this review are listed in Table 6.

Table 6. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT05287737	Clinical Outcome After Total Pancreatectomy With Islet Autotransplantation	100	Mar 2047

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

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

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. Accessed July 2, 2023.
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 July 5, 2023.
44. 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
45. 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. Oct 2014; 51(5): 833-43. PMID 25034311
46. ClinicalTrials.gov. Islet Transplantation in Type 1 Diabetic Patients Using the University of Illinois at Chicago (UIC) Protocol (NCT00679042). July 27, 2022. https://classic.clinicaltrials.gov/ct2/show/NCT00679042. Accessed July 5, 2023.

47. ClinicalTrials.gov. Islet Transplantation in Type I Diabetic Patients Using the University of Illinois at Chicago (UIC) Protocol (NCT03791567). March 16, 2022. https://classic.clinicaltrials.gov/ct2/show/NCT03791567. Accessed July 3, 2023.
48. U.S. Food and Drug Administration (FDA). Donislecel-jujn (Lantidra) approval letter. June 28, 2023. https://www.fda.gov/vaccines-blood-biologics/lantidra. Accessed July 3, 2023
49. U.S. Food and Drug Administration (FDA). Donislecel-jujn (Lantidra) package insert. June 30, 2023. https://www.fda.gov/vaccines-blood-biologics/lantidra. Accessed July 5, 2023
50. LANTRIDA. U.S. Food and Drug Administration. August 7, 2023. https://www.fda.gov/vaccines-blood-biologics/lantidra. Accessed August 24, 2023.
51. 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 July 5, 2023.
52. 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 July 3, 2023.
53. 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
54. 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
55. Centers for Medicare & Medicaid. National Coverage Determination (NCD) for ISLET CELL Transplantation in the Context of a Clinical Trial (260.3.1). 2004; https://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?NCDId=286&ncdver=1&CoverageSelection=Both&ArticleType=All&PolicyType=Final&s=All&KeyWord=islet+cell&KeyWordLookUp=Title&KeyWordSearchType=And&bc=gAAAABAAAAAA&. Accessed July 5, 2023.

Documentation for Clinical Review

Please provide the following documentation:

- Referring provider history and physical
- Nephrology consultation report and/or progress notes documenting:
  - Diagnosis (including disease staging) and prognosis
  - Synopsis of alternative treatments performed and results
  - Specific transplant type being requested
- Surgical consultation report and/or progress notes
- Results of completed transplant evaluation including:
  - Clinical history
  - Specific issues identified during the transplant evaluation
  - Consultation reports/letters (when applicable)
  - Correspondence from referring providers (when applicable)
- Medical social service/social worker and/or psychiatric (if issues are noted) evaluations including psychosocial assessment or impression of patient's ability to be an adequate candidate for transplant
- Chest x-ray (CXR) and other radiology reports (when applicable)
- Colonoscopy report if > 50 years of age
- Cardiology procedures and pulmonary function reports:
  - EKG
  - Cardiac echocardiogram, stress test, and cardiac catheterization (if needed)
  - Pulmonary function tests (PFTs)

- Laboratory reports

Coding

This Policy relates only to the services or supplies described herein. Benefits may vary according to product design; therefore, contract language should be reviewed before applying the terms of the Policy.

The following codes are included below for informational purposes. Inclusion or exclusion of a code(s) does not constitute or imply member coverage or provider reimbursement policy. Policy Statements are intended to provide member coverage information and may include the use of some codes for clarity. The Policy Guidelines section may also provide additional information for how to interpret the Policy Statements and to provide coding guidance in some cases.

Type	Code	Description
CPT®	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 (
	48160	Pancreatectomy, total or subtotal, with autologous transplantation of pancreas or pancreatic islet cells
	48999	Unlisted procedure, pancreas
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

Policy History

This section provides a chronological history of the activities, updates and changes that have occurred with this Medical Policy.

Effective Date	Action
10/01/2017	BCBSA Medical Policy Adoption
10/01/2018	Policy revision without position change
10/01/2019	Policy revision without position change
10/01/2020	Annual review. No change to policy statement. Literature review updated. Coding update.
10/01/2021	Annual review. No change to policy statement. Literature review updated.
10/01/2022	Annual review. Policy statement, guidelines and literature review updated.
11/01/2023	Annual review. Policy statement, guidelines and literature review updated. Policy title changed from Islet Transplantation to current one.

Definitions of Decision Determinations

Medically Necessary: Services that are Medically Necessary include only those which have been established as safe and effective, are furnished under generally accepted professional standards to treat illness, injury or medical condition, and which, as determined by Blue Shield, are: (a) consistent with Blue Shield medical policy; (b) consistent with the symptoms or diagnosis; (c) not furnished primarily for the convenience of the patient, the attending Physician or other provider; (d) furnished at the most appropriate level which can be provided safely and effectively to the patient; and (e) not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of the Member's illness, injury, or disease.

Investigational/Experimental: A treatment, procedure, or drug is investigational when it has not been recognized as safe and effective for use in treating the particular condition in accordance with generally accepted professional medical standards. This includes services where approval by the federal or state governmental is required prior to use, but has not yet been granted.

Split Evaluation: Blue Shield of California/Blue Shield of California Life & Health Insurance Company (Blue Shield) policy review can result in a split evaluation, where a treatment, procedure, or drug will be considered to be investigational for certain indications or conditions, but will be deemed safe and effective for other indications or conditions, and therefore potentially medically necessary in those instances.

Prior Authorization Requirements and Feedback (as applicable to your plan)

Within five days before the actual date of service, the provider must confirm with Blue Shield that the member's health plan coverage is still in effect. Blue Shield reserves the right to revoke an authorization prior to services being rendered based on cancellation of the member's eligibility. Final determination of benefits will be made after review of the claim for limitations or exclusions.

Questions regarding the applicability of this policy should be directed to the Prior Authorization Department at (800) 541-6652, or the Transplant Case Management Department at (800) 637-2066 ext. 3507708 or visit the provider portal at www.blueshieldca.com/provider.

We are interested in receiving feedback relative to developing, adopting, and reviewing criteria for medical policy. Any licensed practitioner who is contracted with Blue Shield of California or Blue Shield of California Promise Health Plan is welcome to provide comments, suggestions, or concerns. Our internal policy committees will receive and take your comments into consideration.

For utilization and medical policy feedback, please send comments to: MedPolicy@blueshieldca.com

Disclaimer: This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. Blue Shield of California may consider published peer-reviewed scientific literature, national guidelines, and local standards of practice in developing its medical policy. 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 covered services. Member contracts may differ in their benefits. Blue Shield reserves the right to review and update policies as appropriate.

Appendix A

POLICY STATEMENT	
BEFORE	**AFTER** Blue font: Verbiage Changes/Additions
Islet Transplantation 7.03.12 **Policy Statement:** I. Autologous pancreas islet transplantation may be considered **medically necessary** as an adjunct to a total or near-total pancreatectomy in individuals with chronic pancreatitis. II. Allogeneic islet transplantation is considered **investigational** for the treatment of type 1 diabetes. III. Islet transplantation is considered **investigational** in all other situations.	**Islet Transplantation for Chronic Pancreatitis and Donislecel-jujn for Type 1 Diabetes 7.03.12** **Policy Statement:** I. Autologous pancreas islet transplantation may be considered **medically necessary** as an adjunct to a total or near-total pancreatectomy in individuals with chronic pancreatitis. II. Allogeneic islet transplantation using an FDA-approved cellular therapy product (donislecel-jujn [i.e., Lantidra]) is considered **investigational** for the treatment of type 1 diabetes. III. Islet transplantation with donislecel-jujn is considered **investigational** in all other situations.