Islet Transplantation

Effective: May 1, 2017

Next Review: March 2018
Last Review: March 2017

IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

DESCRIPTION

Islet cells are responsible for producing insulin, which is necessary for the regulation of blood glucose levels. Following islet transplantation, it is proposed that the beta cells in the transplanted islets will begin to make and release insulin.

MEDICAL POLICY CRITERIA

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

II  Autologous pancreas islet cell transplantation for all other indications is considered investigational.

III  Allogeneic and xeno islet cell transplantation for any diagnosis are considered investigational.

NOTE: A summary of the supporting rationale for the policy criteria is at the end of the policy.

CROSS REFERENCES

1. Pancreas Transplant, Transplant, Policy No. 6
BACKGROUND

CHRONIC PANCREATITIS

Autologous islet transplantation is commonly conducted during pancreatectomy among patients with chronic pancreatitis. The procedure consists of isolating islet cells from the patient’s resected pancreas using enzymes, and injecting a suspension of the cells back into the portal vein of the patient’s liver, where the cells function as a free graft.

Although the incidence of chronic pancreatitis is rising, it is still a relatively rare condition, affecting an estimated 7 to 8 new people out of every 100,000 people each year.[1] Some 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. Autologous islet cell transplantation, also called islet autotransplantation (IAT), has been investigated as a technique to prevent this serious morbidity.

TYPE 1 DIABETES

Allogeneic islet cell transplantation is normally conducted as a stand-alone procedure among patients with type 1 diabetes. Islet cells, harvested from a deceased donor’s pancreas, are processed and injected into the recipient’s portal vein.

Allogeneic islet cell transplantation potentially offers an alternative to whole-organ pancreas transplantation to treat type 1 diabetes, restore normoglycemia and ultimately reduce or eliminate the long-term complications of diabetes, such as retinopathy, neuropathy, nephropathy, and cardiovascular disease. However, a limitation of islet cell transplantation is that 2 or more donor organs are usually required for successful transplantation, and only pancreases rejected for whole-organ transplant are typically used for islet transplantation. Due to limited islet cell supply, allogeneic islet cell transplantation is recommended only for patients with frequent and severe metabolic complications who have consistently failed to achieve control with insulin-based management. In 2000, a modified immunosuppression regimen increased the success of allogeneic islet transplantation. This regimen was developed in Edmonton, Canada and is known as the “Edmonton protocol.”

While most of the published research to date involves the transplantation of allogeneic human islet cells, there is also interest in xenotransplantation, using porcine islet cells.

REGULATORY STATUS

Islet cells are subject to regulation by the U.S. Food and Drug Administration (FDA), which classifies allogeneic islet cell transplantation as somatic cell therapy, requiring premarket approval. Islet cells also meet the definition of a drug under the federal Food, Drug, and Cosmetic Act. Clinical studies to determine safety and effectiveness outcomes of allogeneic islet cell transplantation must be conducted under FDA investigational new drug (IND) regulation. To date, islet cell transplantation has not received approval to be conducted outside the research setting.

EVIDENCE SUMMARY

AUTOLOGOUS ISLET CELL TRANSPLANT AS AN ADJUNCT TO PANCREATECTOMY
Autologous islet cell transplantation as an adjunct to pancreatectomy or near total pancreatectomy among patients with chronic pancreatitis has been investigated since 1977. Since then, the experience has grown slowly with incremental improvements in the islet cell isolation process. The current literature consists of several case series and systematic reviews.

**Systematic Reviews**

In 2015, Wu et al published a systematic review of studies on islet transplantation after total pancreatectomy for chronic pancreatitis.[2] Studies could use any type of design but needed to include at least five patients or have a median follow-up of at least six months. Twelve studies with a total of 677 patients met the review's inclusion criteria. The mean age of the patients was 38 years and mean duration of pancreatitis was 6.6 years. A meta-analysis of the insulin independence rate at one year (five studies, 362 patients) was 28.4% (95% confidence interval [CI], 15.7% to 46.0%). At two years, the pooled insulin independence rate (three 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.

In 2012, Bramis and colleagues searched for studies reporting on patients who had been treated with total, subtotal or completion pancreatectomy followed by islet autotransplantation.[3] Case series were included if they included more than five individuals and reported outcomes for consecutive patients. A total of 72 full-text articles were reviewed, and five studies were found to meet inclusion criteria. The postoperative insulin independence rate in the five studies ranged from 10% (mean follow-up of eight years) to 46% (mean follow-up of five years). In the study with the longest follow-up, the insulin independence rate was 28% at ten years. Two studies reported postoperative morphine use with a decrease in morphine use of 116 mg and 55 mg, respectively.

A 2011 systematic review by Dong and colleagues included studies regardless of design or sample size.[4] After reviewing 84 studies, 15 observational studies were found to meet eligibility criteria. There were 11 studies of total pancreatectomy, two studies of partial pancreatectomy, and two studies that included both types of surgery. Sample sizes in individual studies ranged from three to 173 patients. Thirteen studies included patients with chronic pancreatitis, and two included patients with benign pancreatic tumors. The pooled 30-day mortality was 5% (95% confidence interval [CI]: 2 to 10%), and the cumulative mortality at one year (reported by ten 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 at one year (five studies) was 27% (95% CI: 21-33%) and at two years (three studies) was 21% (95% CI: 16-27%).

**Randomized Controlled Trials**

No randomized controlled trials for autologous islet cell transplantation as an adjunct to total or near total pancreatectomy were identified.

**Nonrandomized Studies**

Since the systematic reviews were published, a number of case series have been reported.

Chinnakotla et al. (2015) reported on a single-center study of 581 patients with chronic pancreatitis (CP) who underwent a total pancreatectomy and islet autotransplantation (TP-IAT), assessing the factors predicting post-operative outcomes, including pain, narcotic use
and graft failure at one year follow-up.[5] The duration (mean±SD) of CP prior to transplantation was 7.1±0.3 years and narcotic usage of 3.3±0.2 years. Pediatric patients had better postoperative outcomes. Among adult patients, the odds of narcotic use at 1 year post-transplant were increased by previous endoscopic retrograde cholangiopancreatography, stent placement and stent number. Independent risk factors for pancreatic pain at 1 year were pancreas divisum, previous body mass index >30, and a high number of previous stents (>3). The strongest independent risk factor for islet graft failure was a low islet yield-in islet equivalents (IEQ)-per kilogram of body weight.

In 2015, Wilson et al. reported on 64 patients age 14 or older with chronic pancreatitis who underwent total pancreatectomy and islet transplantation (CPIAT) as salvage therapy after failing previous operative interventions for chronic pancreatitis.[6] Median time from initial surgical intervention to CPIAT was 28.1 months and median patient follow-up was 21.2 months. Patients undergoing CPIAT achieved improved postoperative narcotic requirements, with a decrease in morphine from 120.8mg/day to 48.5mg/day (p < 0.001). All patients also showed stable glycemic control, and improved quality of life indices post-transplant.

Venturini et al. (2016) reported results of percutaneous intraportal islet autotransplantations following pancreatic surgery performed at a single center in Italy between 2008 and 2012.[7] There were 41 patients enrolled for this procedure due to chronic pancreatitis or benign/malignant neoplasms. Seven of these patients did not have islet cell transplantation due to inadequate cell mass, hemodynamic instability, or cell culture contamination. The procedure was successfully performed in the remaining 34 patients. After a median follow up of 546 days, 15 patients (44%) achieved insulin independence, 16 (47%) had partial graft function, and three had no graft function.

Johnston et al. examined factors associated with islet yield and metabolic outcomes in 36 patients that underwent CPIAT between 2008 and 2014 at a single institution.[8] Mean age was 38 years and median follow-up time was 28 months. Postoperatively, C-peptide levels ≥0.3 ng/mL were present in 23/33 (70%) of the patients, with a median fasting C-peptide value of 0.8 ng/mL (range, <0.2-1.5 ng/mL), indicating improved glycemic control. Those who were insulin independent were more likely to be female (p = 0.012), have normal morphology on pre-operative pancreatic imaging (p = 0.011), and have significantly higher median islet yield (p < 0.001).

In 2014, Wilson et al. reported on 166 patients age 14 or older with chronic pancreatitis who underwent total pancreatectomy and islet transplantation at a single center. Actuarial survival at 5 years was 94.6%. Five year or longer data were available for 112 patients (67%). At 1 year, 38% of patients were insulin dependent 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 narcotic independent at 1 year, and this increased to 73% at 5 years.

A 2014 study by Chinnadotla et al. included 484 patients with chronic pancreatitis.[10] Patients underwent total pancreatectomy and immediate islet auto transplantation. Using a Kaplan-Meier analysis method, 10-year survival 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 with and without genetic/hereditary disease.
Sutherland and colleagues studied 409 patients with chronic pancreatitis who underwent total pancreatectomy and islet transplantation between February 1977 and September 2011.[11] Fifty-three of 409 patients (13%) 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 and 55% of children). A survey of quality-of-life outcomes was initiated in October 2008; responses were available for 102 patients. At baseline, all 102 patients reported using narcotics for pain. 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.

ALLOGENEIC ISLET CELL TRANSPLANT FOR TYPE 1 DIABETES

Islet cell transplantation has also been investigated as a treatment for type 1 diabetes, particularly in patients with poor glucose control despite insulin therapy.

The principal outcomes associated with treatment of type 1 diabetes are improvement in overall mortality rate, and reductions in rates of diabetic retinopathy, nephropathy, neuropathy, and cardiovascular disease normally associated with type 1 diabetes. In order to understand the impact of islet cell transplantation for treatment of type 1 diabetes on these outcomes, well-designed randomized controlled trials (RCTs) that compare this therapy to standard medical treatment, such as insulin treatment, are needed. Further, an understanding of any adverse treatment effects, particularly those associated with life-long immunosuppressant therapy, must be carefully weighed against any benefits associated with islet transplantation to understand the net treatment effect of this therapy.

Systematic Reviews

In 2015 Health Quality Ontario published a systematic review on islet transplantation for type 1 diabetes, and included one health technology assessment, 11 observational, nonrandomized clinical studies, one registry report, and four guidelines.[12] There was a large degree of heterogeneity in patient populations, study design, and outcome measurement in the included studies. The reviewers reported that islet transplantation can improve blood sugar control and quality of life, and may reduce diabetic complications; however, the results were inconsistent between studies. Compared with insulin therapy, there were more adverse events with islet transplantation. The studies that were included that assessed health-related quality of life, secondary complications of diabetes, glycemic control, and adverse events were all ranked as low to very low quality, with two studies having high risk of bias. Therefore, uncertainty of the effectiveness of islet transplantation in type 1 diabetics still remains.

Randomized Controlled Trials (RCTs)

Froud et al. randomized 16 type 1 diabetes mellitus patients to evaluate cultured islet transplantation with or without tumor necrosis factor (TNF-alpha) blockade using Infliximab just prior to islet infusion.[13] Insulin independence was achieved in 14 patients after 1 to 2 infusions, and was maintained in 11 patients after 1 year, and in 6 patients at 33 +/- 6-months without additional infusions. The authors reported no identifiable clinical benefit with the use of Infliximab, but concluded cultured human islet allografts produced results comparable to freshly transplanted islets including normalization of HBA1c. Further research in larger studies.
is needed to explore different immunosuppressive regimens.

Nonrandomized Studies

In 2015 Caiazzo et al. assessed procedure-related complications on long-term outcome of islet transplantation in 26 patients with type 1 diabetes.[14] Each patient had two to three intraportal islet infusions, performed surgically or under ultrasound guidance, within a three month time frame. Complications included: bowel obstruction, biliary peritonitis and a major hepatic hematoma. The investigators reported no deaths or patients dropouts. Early complications occurred in nine of 68 procedures. Procedure-related complications negatively impacted graft function (p = 0.009) and was an independent negative predictor of long-term graft survival (p = 0.033) in multivariate analysis. The investigators concluded that even nonsevere complications occurring during islet transplantation, despite islet preparation method or transplantation method, significantly impair primary graft function and graft survival.

Moassesfar et al. (2016) compared safety and efficacy of islet cell transplantation to pancreas transplantation at a center in the U.S.[15] Sequential patients with type 1 diabetes had either an islet cell transplant (n = 10) or a pancreas transplant (n = 15). After one year, 90% of patients in the islet group and 93% of patients in the pancreas group were insulin independent. At three years, the proportion with insulin independence dropped to 70 % and 64%, respectively. The authors concluded that islet cell transplantation can produce similar outcome to pancreatic transplantation.

In 2013, Rickels et al. reported on 12 patients with type 1 diabetes and severe hypoglycemia who had islet transplantation.[16] Mean glycosylated hemoglobin decreased from 7.0%±0.3% before the procedure to 5.6%±0.1% after 6 to 7 months (p<0.01). All of the insulin sensitivity measures were significantly less than normal before islet transplantation and not significantly different from normal after transplantation. Adverse events were not discussed.

In 2013, O’Connell et al reported on 17 patients who underwent islet transplantation for type 1 diabetes and severe hypoglycemia.[17] The primary end point was the proportion of patients who had had an HbA1c less than 7% and no severe hypoglycemic events two months after the initial transplant. (Patients could have one or two infusions.) Fourteen of the 17 (82%) patients achieved the primary end point. Nine (53%) patients attained insulin independence for a median of 26 months. At the time of data analysis for this publication, six patients remained insulin independent. Most adverse events were related to immunosuppression. Seven of the 17 (41%) patients developed mild lymphopenia and one developed Clostridium difficile colitis; these all responded to treatment. Eight patients developed anemia shortly after transplant and one required a blood transfusion. Procedure-related complications included one partial portal vein thrombosis and three postoperative bleeds; two of the bleeds required transfusion. Patients were followed for different amounts of time; long-term follow-up data were not available for a consistent length of time.

In 2012, Vantyghem and colleagues reported on 23 patients with type 1 diabetes who underwent islet transplantation; 14 had islet-only transplants and 9 had islet after kidney transplants.[18] Median HbA1c was 8.3% at baseline and 6.7% at three years. Ten of the 23 patients (43%) were insulin independent three years after islet transplantation. Findings were not reported separately for the islet-only transplant recipients.

In 2011 Thompson et al. reported on a prospective cross-over study of intensive medical therapy (pre-transplant) versus islet cell transplantation among 32 patients with type 1
diabetes. Following enrollment in the study, median follow-up was 47 months pre-transplant and 66 months post-transplant. Although improvements in HbA1c, retinopathy progression, and renal function were seen in the transplant group, small sample size and lack of treatment randomization limit interpretation of these findings. The authors also noted that their finding of reduced microvascular complications after islet transplantation may be due, in part, to their choice of maintenance immunosuppression. The study used a combination of tacrolimus and mycophenolate mofetil (MMF).

In 2006, Shapiro et al. reported on 36 patients with type 1 diabetes mellitus that had undergone islet transplantation. While short-term results were promising, insulin independence was generally not sustainable; only five patients were insulin-independent at two years. In a landmark study known as the Edmonton Protocol, seven consecutive patients achieved insulin independence following islet cell transplants from two to four donors on a glucocorticoid-free immunosuppressive regimen. However, 5-year outcomes from the first patients transplanted under the Edmonton protocol reported less than a 10% rate of insulin independence at five years, despite persistent graft survival as measured by C-peptide positivity (~80%). The authors noted that problems with glycemic lability and hypoglycemia, the primary indications for transplant, were corrected; however, no clear advantages for chronic complications of diabetes (e.g., peripheral neuropathy) were evident. Chronic complications related to standard immunosuppressive therapy led to the need to alter the protocol in 23% of patients, thus leading the authors to conclude that “safer immunosuppression associated with fewer side effects is needed.” Complications and side effects related to both immunosuppression and the procedure itself are also reported to be more common than originally thought. The experience of the transplant center itself has a demonstrated effect on patient outcomes, with the more experienced centers reporting higher success rates.

Long-term results from the Edmonton Protocol were published by Brennan et al. (2016), who reported that all seven of the original subjects continued to have some islet function more than ten years after the transplantation. One of the patients achieved insulin independence for eight years, but had graft failure 10.9 years after the first transplant. Of the other six subjects, three received an additional islet transplant, five were receiving insulin, and two were insulin-independent (with one taking liraglutide). None of the subjects had lymphoma, severe hypoglycemia, or opportunistic infections during follow-up.

Several other small case series have focused on identifying alternatives to current transplant techniques, studying encapsulated islet transplantation without immunosuppression, optimizing single versus multiple-donor transplantations, and comparing whole pancreas transplant to islet cell transplantation. Recent research also addresses islet-after-kidney transplantation. However, results from these studies should be interpreted with caution as the small sample sizes (n≤ 66), lack of randomized treatment allocation and/or appropriate comparison groups do not allow for ruling out chance as an explanation of findings.

Current non-randomized studies of allogeneic islet cell transplantation appear to suggest an initial benefit (such as a decline in HbA1c levels, for example) associated with the transplant. However, as a recent review of this therapy notes:

“[O]ne cannot be certain of the claim that partially failed islet transplantation leads to the use of less insulin and less hypoglycemia on a cause-effect basis. It could just as easily be that patients who enter transplant programs come under close clinical scrutiny by
interested diabetologists who begin managing them more skillfully.”

Additional randomized controlled trials are needed to determine the strength and magnitude of potential benefits associated with this therapy and to isolate such the impact of such benefits from standard medical care.

REGISTRY DATA

Bretzel et al. reported on data collected from the International Islet Transplant Registry from 1999-2004.[31] Data were available for 458 human islet cell transplantations. At 1-year post transplant, patient survival was 97%, islet grafts were functioning in 82% of the cases, and insulin independence was achieved in 43% of the cases.

Founded in 2001 by the National Institute of Diabetes, Digestive and Kidney Diseases, the Collaborative Islet Transplant Registry (CITR) has been collecting information on allogeneic islet transplantation in North America, Europe, and Australia. The most recent peer-reviewed publication of CITR data was published in 2012.[32] The update focused on changes in outcomes over time in 677 patients, all of whom received a transplant as of December 31, 2010 (n=575 islet-only; n=102 kidney+islet). Unfortunately, outcomes presented in this report were limited by considerable levels of missing data which increased with longer follow-up. The missing data were reported to be a mixture of unavailable medical records and data still pending entry into the registry.

The authors reported improved insulin independence at three years post-transplant, from 27% in the early era (1999–2002, n = 214) to 37% in the mid era (2003–2006, n = 255) and 44% in the most recent era (2007–2010, n = 208; P = 0.006 for years-by-era; P = 0.01 for era alone). However, not all recipients in the latter era had reached the 3-year milestone at the time of this updated report. The need for islet reinfusion for loss of function of first graft by 1-year decreased significantly from 60-65% in 1999-2006 to 48% in 2007-2010 (p<0.01). There was also a modest decrease in clinically reportable adverse events in the 2007-2010 era, from 50-53% in 1999-2006 to 38% in 2007-2010. The rates of peritoneal hemorrhage or gallbladder infusion were 5.4% in 1999-2003 and 3.1% in 2007-2010. The authors did not report findings separately from the subset of patients who underwent islet-only transplants.

The Institute for Clinical and Experimental Medicine (IKEM), based in the Czech Republic, published results from a retrospective analysis of a registry of all patients receiving one or more allogeneic or autologous islet transplants from 2005 to 2010 (n=15 and n=5, respectively).[33] Although islet function was documented in 11 of 15 and 3 of 5 patients, respectively, after 12 months (as indicated by C-peptide levels), only 1 patient receiving an allogeneic transplant was able to achieve independence from insulin beyond 12 months. The authors conclude that islet transplant may be best suited for high-risk recipients, as “routine clinical application is still hampered by the limited availability of usable organ transplants and viability of transplanted islets.”

Results from the above registry reports should be interpreted with caution as these registries are not reflective of the complete North American experience with islet transplants; not all transplant centers participated in each regional endeavor, nor is data complete for all those who do participate. Therefore, there may be inherent bias in the data. The focus on intermediate outcomes instead of long-term health outcomes, also limits interpretation of these findings.
XENOTRANSPLANTATION

Although there is research interest in porcine islets as an alternative and potentially unlimited source of islet cells, current data from human clinical trials is limited to three case series.

Matsumoto et al. (2016) transplanted two doses of encapsulated neonatal porcine islets (approximately 5000IEQ/kg and 10,000IEQ/kg) twice in two groups of four patients each with type 1 diabetes.[34] The two transplants were performed three months apart. One patient had a serious adverse event potentially related to the treatment, paralytic ileus, which was resolved with medication. While both groups had decreases in HbA1c, for the high dose group this difference remained significant at 600 days after the first transplant.

In 2011, Wang and colleagues published results from a small clinical trial on the safety and feasibility of neonatal porcine islets (NPIs) in 22 patients in China.[35] However, only six of the 22 patients were subsequently followed for more than two months, limiting conclusions about the long-term use of NPIs.

Also in 2011, Esquivel-Pérez and colleagues published a report on 23 patients not on immunosuppression, transplanted with a porcine cell-filled device.[36] Following an average of 5.7 years post-transplantation, the researchers reported that the patients with the lowest levels of antibodies were significantly more likely to report higher insulin dose reductions. However, not all patients were able to attain low levels of antibodies, for reasons not clearly known. Therefore, this report provides evidence for transplantation protocols but does not address the clinical utility of xenotransplantation.

Current literature has not directly addressed problems related to xenograft rejection and xeno-zoonosis (transmission of animal disease to humans).

PRACTICE GUIDELINE SUMMARY

In 2016, the American Diabetes Association (ADA) published a position statement on comprehensive care for patients with type 1 diabetes.[37] The ADA states that:

“Pancreas and islet cell transplantation have been shown to normalize glucose levels but require lifelong immunosuppression to prevent graft rejection and recurrence of autoimmune islet destruction. Given the potential adverse effects of immunosuppressive therapy, pancreas transplantation should be reserved for patients with type 1 diabetes undergoing simultaneous renal transplantation, following renal transplantation, or for those with recurrent ketoacidosis or severe hypoglycemia despite aggressive glycemic management (13). Islet cell transplantation remains investigational. Autoislet transplantation may be considered for patients requiring total pancreatectomy who meet eligibility criteria.”

SUMMARY

There is enough research to show that autologous islet cell transplantation is relatively safe and can reduce the chance of developing diabetes after total or near total pancreatectomy in patients with chronic pancreatitis. Therefore, autologous islet cell transplantation may be considered medically necessary as an adjunct to a total or near total pancreatectomy in patients with chronic pancreatitis.
There is not enough research to show that autologous islet cell transplantation can improve health outcomes for people with any other conditions. Therefore autologous pancreatic islet cell transplantation for all other indications is considered investigational.

There is not enough research to show that islet cell transplantation improves health outcomes for patients with diabetes. Additionally, the U.S. Food and Drug Administration (FDA) has not yet granted full market approval for islet cell transplantation, and the American Diabetes Association considers this treatment to be experimental. Therefore, allogeneic islet transplantation is considered investigational in the management of type 1 diabetes.

Although there is research interest in porcine islets (xeno islet cells) as a source of islet cells, there is not enough research to show that xenotransplantation is safe and effective, and there are no clinical guidelines based on research that recommend xenotransplantation. Therefore xeno islet cell transplantation for any diagnosis is considered investigational.

**REFERENCES**


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**CODES**

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*Date of Origin: January 1996*