



# Louisiana

## Allogeneic Pancreas Transplant

**Policy #** 00092

**Original Effective Date:** 11/22/1993

**Current Effective Date:** 01/17/2018

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*Note: Islet cell transplantation is considered in medical policy 00007.*

### **When Services May Be Eligible for Coverage**

*Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:*

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider a combined pancreas-kidney transplant in insulin dependent diabetic patients with uremia to be **eligible for coverage**.

Based on review of available data, the Company may consider pancreas transplant after a prior kidney transplant in patients with insulin dependent diabetes to be **eligible for coverage**.

Based on review of available data, the Company may consider pancreas transplant alone in patients with severely disabling and potentially life-threatening complications due to hypoglycemia unawareness and labile insulin dependent diabetes that persists in spite of optimal medical management to be **eligible for coverage**.

Based on review of available data, the Company may consider pancreas retransplant after a failed primary pancreas transplant in patients who meet criteria for pancreas transplantation to be **eligible for coverage**.

Pancreas transplantation, when the transplant recipient is human immunodeficiency virus (HIV) positive, may be considered for coverage when all of the additional criteria are met:

- CD4 count >200 cells/mm<sup>3</sup> for more than six months; and
- Undetectable HIV viremia (<50 HIV-1 RNA copies/mL) for at least six months; and
- Demonstrable adherence and a stable HAART regimen for at least six months; and
- Absence of AIDS-defining illness following successful immune reconstitution after HAART; and
- All other transplant criteria are met.

### **When Services Are Considered Investigational**

*Note: Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.*

The use of pancreas transplant when patient selection criteria are not met is considered **investigational**.\*

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The use of pancreas transplant in HIV positive recipients when patient selection criteria and additional HIV positive patient selection criteria are not met is considered **investigational**.\*

Based on review of available data, pancreas re-transplantation after two or more prior failed pancreas transplants is considered **investigational**.\*

### **Policy Guidelines**

#### **GENERAL CRITERIA**

Potential contraindications subject to the judgment of the transplant center:

1. Known current malignancy, including metastatic cancer
2. Recent malignancy with high risk of recurrence
3. Untreated systemic infection making immunosuppression unsafe, including chronic infection
4. Other irreversible end-stage disease not attributed to kidney disease
5. History of cancer with a moderate risk of recurrence
6. Systemic disease that could be exacerbated by immunosuppression
7. Psychosocial conditions or chemical dependency affecting the ability to adhere to therapy.

#### **PANCREAS-SPECIFIC CRITERIA**

Candidates for pancreas transplant alone should additionally meet one of the following severity of illness criteria:

- Documentation of severe hypoglycemia unawareness as evidenced by chart notes or emergency department visits or
- Documentation of potentially life-threatening labile diabetes, as evidenced by chart notes or hospitalization for diabetic ketoacidosis.

Additionally, most pancreas transplant patients will have type 1 diabetes. Those transplant candidates with type 2 diabetes, in addition to being insulin-dependent, should also not be obese (body mass index should be 32 kg/m<sup>2</sup> or less). According to International Pancreas Transplant Registry data, in 2010, 7% of pancreas transplant recipients had type 2 diabetes (Gruessner, 2012).

#### **MULTIPLE TRANSPLANT CRITERIA**

Although there are no standard guidelines for multiple pancreas transplants, the following information may aid in case review:

- If there is early graft loss resulting from technical factors (eg, venous thrombosis), a retransplant may generally be performed without substantial additional risk.
- Long-term graft losses may result from chronic rejection, which is associated with increased risk of infection following long-term immunosuppression, and sensitization, which increases the difficulty of finding a negative cross-match. Some transplant centers may wait to allow reconstitution of the immune system before initiating retransplant with an augmented immunosuppression protocol.

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### **Background/Overview**

#### **DIABETES AND PANCREATITIS**

Achievement of insulin independence with resultant decreased morbidity and increased quality of life is the primary health outcome of pancreas transplantation. While pancreas transplantation is generally not considered a life-saving treatment, in a small subset of patients who experience life-threatening complications from diabetes, pancreas transplantation could be considered life-saving. Pancreas transplant alone (PTA) has also been investigated in patients following total pancreatectomy for chronic pancreatitis. In addition to the immune rejection issues common to all allograft transplants, autoimmune destruction of beta cells has been observed in the transplanted pancreas, presumably from the same mechanism responsible for type 1 diabetes.

#### **Treatment**

Pancreas transplantation occurs in several different scenarios such as: 1) a diabetic patient with renal failure who may receive a cadaveric simultaneous pancreas/kidney transplant (SPK); 2) a diabetic patient who may receive a cadaveric or living-related pancreas transplant after a kidney transplantation (pancreas after kidney, i.e., PAK); or 3) a non-uremic diabetic patient with specific severely disabling and potentially life-threatening diabetic problems who may receive a PTA. The total number of adult pancreas transplants (pancreas and pancreas/kidney) in the U.S. peaked at 1,484 in 2004; the number has since declined. In 2011, there were 287 pancreas transplants and 795 pancreas/kidney transplants in the U.S.

Most patients undergoing PTA are those with either hypoglycemic unawareness or labile diabetes. However, other exceptional circumstances may exist where nonuremic type 1 diabetes patients have significant morbidity risks due to secondary complications of diabetes (eg, peripheral neuropathy) that exceed those of the transplant surgery and subsequent chronic immunosuppression. Because virtually no published evidence addressing outcomes of medical management in this very small group of exceptional diabetic patients, it is not possible to generalize about which circumstances represent appropriate indications for pancreas transplantation alone. Case-by-case consideration of each patient's clinical situation may be the best option for determining the balance of risks and benefits.

According to International Registry data, the proportion of pancreas transplant recipients worldwide who have type 2 diabetes has increased over time, from 2% in 1995 to 7% in 2010. In 2010, approximately 8% of SPK, 5% of PAK, and 1% of PTA were performed in patients with type 2 diabetes.

The approach to retransplantation varies according to the cause of failure. Surgical/technical complications such as venous thrombosis are the leading cause of pancreatic graft loss among diabetic patients. Graft loss from chronic rejection may result in sensitization, increasing both the difficulty of finding a cross-matched donor and the risk of rejection of a subsequent transplant. Each center has its own guidelines based on experience; some transplant centers may wait to allow reconstitution of the immune system before initiating retransplant with an augmented immunosuppression protocol.

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### **FDA or Other Governmental Regulatory Approval**

U.S. Food and Drug Administration (FDA)

The U.S. 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. Pancreas transplants are included in these regulations.

Centers for Medicare and Medicaid Services (CMS)

An allogeneic pancreas transplant is covered under Medicare when performed in a facility approved by Medicare as meeting institutional coverage criteria. The Centers for Medicare & Medicaid Services made the following national coverage decision on pancreas transplant for Medicare recipients.

#### "A. General

Pancreas transplantation is performed to induce an insulin-independent, euglycemic state in diabetic patients. The procedure is generally limited to those patients with severe secondary complications of diabetes, including kidney failure. However, pancreas transplantation is sometimes performed on patients with labile diabetes and hypoglycemic unawareness.

#### B. Nationally Covered Indications

Effective for services performed on or after July 1, 1999, whole organ pancreas transplantation is nationally covered by Medicare when performed simultaneous with or after a kidney transplant. If the pancreas transplant occurs after the kidney transplant, immunosuppressive therapy begins with the date of discharge from the inpatient stay for the pancreas transplant.

Effective for services performed on or after April 26, 2006, pancreas transplants alone (PA) are reasonable and necessary for Medicare beneficiaries in the following limited circumstances:

1. PA will be limited to those facilities that are Medicare-approved for kidney transplantation.
  - Patients must have a diagnosis of type I diabetes;
  - Patient with diabetes must be beta cell autoantibody positive; or
2. Patient must demonstrate insulinopenia defined as a fasting C-peptide level that is less than or equal to 110% of the lower limit of normal of the laboratory's measurement method. Fasting C-peptide levels will only be considered valid with a concurrently obtained fasting glucose  $\leq 225$  mg/dL;
3. Patients must have a history of medically-uncontrollable labile (brittle) insulin-dependent diabetes mellitus with documented recurrent, severe, acutely life-threatening metabolic complications that require hospitalization. Aforementioned complications include frequent hypoglycemia unawareness or recurring severe ketoacidosis, or recurring severe hypoglycemic attacks;
4. Patients must have been optimally and intensively managed by an endocrinologist for at least 12 months with the most medically recognized advanced insulin formulations and delivery systems;

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5. Patients must have the emotional and mental capacity to understand the significant risks associated with surgery and to effectively manage the lifelong need for immunosuppression; and,
6. Patients must otherwise be a suitable candidate for transplantation.”

Nationally noncovered indications include “Transplantation of partial pancreatic tissue or islet cells (except in the context of a clinical trial).”

### **Rationale/Source**

Much of the published literature consists of case series reported by single centers and registry data. The extant randomized controlled trials (RCTs) compare immunosuppression regimens and surgical techniques and therefore do not address the comparison of pancreas transplantation to insulin therapy, or SPK transplant to insulin therapy and hemodialysis.

This policy is based in part on a 1998 TEC Assessment, which focused on pancreas graft survival and health outcomes associated with both PTA and PAK transplant. A 2001 TEC Assessment focused on the issue of pancreas retransplant. The assessments and subsequent evidence offer the following observations and conclusions:

### **PANCREAS TRANSPLANT AFTER KIDNEY TRANSPLANT**

PAK transplantation permits uremic patient to benefits from a living-related kidney graft, if available and to benefit from a subsequent pancreas transplant that is likely to result in improved quality of life compared with a kidney transplant alone. Uremic patients for whom a cadaveric kidney graft is available, but a pancreas graft is not simultaneously available benefit similarly from a later pancreas transplant.

As reported by Gruessner and Gruessner (2016), according to United Network for Organ Sharing (UNOS) and International Pancreas Transplant Registry data, patient survival rates after PAK conducted from 2010 to 2014 was 97.9% after 1 year and 94.5% after 3 years. This compares with 1-year (96.4%) and 3-year (93.1%) patient survival rates for transplants conducted from 2005 to 2009, respectively.

In 2009, Fridell et al reported on a retrospective review of a single center’s experience with PAK and SPK since 2003, when current induction or tacrolimus immunosuppressive strategies became standard. Of the 203 cases studied, 61 (30%) were PAK and 142 (70%) were SPK. One-year patient survival rates were 98% PAK and 95% SPK (p=0.44). Pancreas graft survival rates at 1 year were 95% and 90%, respectively (p=0.28). The authors concluded that using the modern immunosuppressive era, PAK should be considered as an acceptable alternative to SPK in candidates with an available living kidney donor.

In 2013, Bazarbachi et al reviewed a single center’s experience with PAK and SPK. Between 2002 and 2010, 172 pancreas transplants were performed in diabetic patients (123 SPK, 49 PAK). The median length of time between kidney transplant and pancreas transplant in the PAK group was 4.8 years. Graft and patient survival rates were similar for both groups. Death-censored pancreas graft survival rates for SPK

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and PAK were 94% and 90% at 1 year, 92% and 90% at 3 years, and 85% and 85% at 5 years ( $p=0.93$ ), all respectively. Patient survival rates (calculated from the time of pancreas transplantation) in the SPK and PAK groups were, respectively, 98% and 100% after 1 year, 96% and 100% after 3 years, and 94% and 100% after 5 years ( $p=0.09$ ), respectively.

Kleinclauss et al (2009) retrospectively reviewed data from 307 diabetic kidney transplant recipients from a single center and compared renal graft survival rates in those who subsequently received a pancreatic transplant with those who did not. The comparative group was analyzed separately depending on whether patients were medically eligible for pancreas transplant, but chose not to proceed for financial or personal reasons, or were ineligible for medical reasons. The ineligible ( $n=57$ ) group differed significantly at baseline from both the PAK group ( $n=175$ ) and the eligible group ( $n=75$ ) with respect to age, type of diabetes, and dialysis experience; kidney graft survival rates in this group were lower (1-, 5-, and 10-year rates of 75%, 54%, and 22%, respectively,  $p<0.001$ ) than in the other groups (1-, 5-, and 10-year rates in the PAK group and in the eligible group were: 98%, 82%, and 67% vs 100%, 84%, and 62%, respectively). The authors concluded that the subsequent transplant of a pancreas after a living donor kidney transplant does not adversely affect patient or kidney graft survival rates.

### **Section Summary: Pancreas After Kidney Transplant**

Data from national and international registries have found relatively high patient survival rates after PAK (eg, a 3-year survival rate of 93%). A 2012 analysis of data from a single center found similar patient survival and death-censored pancreas graft survival rates after PAK (and SPK) transplants.

### **SIMULTANEOUS PANCREAS PLUS KIDNEY TRANSPLANTS**

The U.S.-based Organ Procurement and Transplant Network (OPTN) has reported a 1-year patient survival rate of 97.5% (95% confidence interval [CI], 96.9% to 98.0%) for SPK procedures performed between 2008 and 2015. Three- and 5-year patient survival rates were 94.7% (95% CI, 93.9% to 95.5%) and 88.6% (95% CI, 87.5% to 89.7%), respectively.

A 2017 analysis of U.K. registry data by Barlow et al compared outcomes in patients with type 1 diabetes and end-stage renal disease who had SPK transplants ( $n=1739$ ) with live donor kidney transplants ( $n=370$ ). In multivariate analysis, there was no significant association between type of transplant and patient survival (hazard ratio, 0.71; 95% CI, 0.47 to 1.06;  $p=0.095$ ). SPK recipients with a functioning pancreas graft had significantly better overall survival than those with a living donor kidney transplant ( $p<0.001$ ).

Pancreas transplant has been found to improve mortality in patients with type 1 diabetes. In 2013, van Dellen et al in the U.K. reported on a retrospective analysis of data for 148 SPK patients and a wait-list control group of 120 patients. All patients had uncomplicated type 1 (insulin-dependent) diabetes. (The study also included 33 patients who had PAK and 11 patients who had PTA.) Overall mortality (mortality at any time point) was 30% (30/120) for the waiting list and 9% (20/193) for transplanted patients; the difference between groups was statistically significant ( $p<0.001$ ). The 1-year mortality rate was 13% ( $n=16$ ) for the waiting list and 4% ( $n=8$ ) for the transplant group ( $p<0.001$ ).

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In 2011, Sampaio et al published an analysis of data from the UNOS database. Outcomes for 6141 patients with type 1 diabetes and 582 patients with type 2 diabetes who underwent SPK were similar for the 2 groups in adjusted analyses. After adjusting for other factors (eg, body weight; dialysis time; cardiovascular comorbidities), type 2 diabetes was not associated with an increased risk of pancreas or kidney graft failure or mortality compared with type 1 diabetes.

### **Section Summary: Simultaneous Pancreas Plus Kidney Transplants**

Data from national and international registries have found relatively high patient survival rates after SPK transplants (eg, a 3-year survival rate of 95%). A retrospective analysis found a higher survival rate in patients with type 1 diabetes who had an SPK than in those on a waiting list.

### **PANCREAS TRANSPLANT ALONE**

PTA graft survival has improved over time. According to International Pancreas Transplant Registry data, 1-year graft function increased from 51.5% for 1987 to 1993 to 77.8% for 2006 to 2010 ( $p < 0.001$ ). One-year immunologic graft loss remained higher (6%) after PTA than after PAK (3.7%) or SPK (1.8%). According to UNOS and the International Pancreas Transplant Registry data, for the period from 2010 to 2014, the patient survival rate for PTA was 96.3% after 1 year and 94.9% after 3 years. This compares with 1-year and 3-year patient survival rates of 97.5% and 93.3% for 2005 to 2009, respectively. According to Gruessner (2011) in carefully selected patients with type 1 diabetes and severely disabling and potentially life-threatening complications due to hypoglycemia unawareness and persistent labile diabetes despite optimal medical management, the benefits of PTA were judged to outweigh the risk of performing pancreas transplantation with subsequent immunosuppression.

Noting that nephrotoxic immunosuppression may exacerbate diabetic renal injury after PTA, Scalea et al (2008) reported on a single institutional review of 123 patients who received 131 PTA for the development of renal failure. Mean graft survival was 3.3 years (range, 0-11.3 years), and 21 patients were lost to follow-up. At a mean follow-up of 3.7 years, mean estimated glomerular filtration rate was 88.9 mL/min/1.73 m<sup>2</sup> pretransplantation and 55.6 mL/min/1.73 m<sup>2</sup> posttransplantation. All but 16 patients had a decrease in estimated glomerular filtration rate. Thirteen developed end-stage renal disease, which required kidney transplantation at a mean of 4.4 years. The authors suggested that patients should be made aware of the risk and only the most appropriate patients offered PTA.

### **Section Summary: Pancreas Transplant Alone**

Data from international and national registries have found that graft and patient survival rates after PTA have improved over time. For the period of 2010 to 2014, 1- and 3-year survival rates had improved to 96% and 95%, respectively.

### **PANCREAS RETRANSPLANTATION**

OPTN has reported data on transplants performed between 1997 and 2004. Patient survival rates after repeat transplants were similar to survival rates after primary transplants. For example, the 1-year survival rate was 94% (95% CI, 93% to 95%) after a primary pancreas transplant and 96% (95% CI, 93% to 99%)

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after a repeat pancreas transplant. The numbers of patients transplanted were not reported, but OPTN data stated that 1217 patients were alive 1 year after primary transplant and 256 after repeat transplants. The 3-year patient survival rate was 90% (95% CI, 88% to 91%) after primary transplants and 90% (95% CI, 86% to 94%) after repeat transplants. The 1-year graft survival rate was 78% (95% CI, 76% to 81%) after primary pancreas transplant and 70% (95% CI, 65% to 76%) after repeat transplant.

Data are similar for patients receiving SPK transplants, but follow-up data are only available on a small number of patients who had repeat kidney/pancreas transplants, so estimates of survival rates in this group are imprecise. Three-year patient survival was 90% (95% CI, 89% to 91%) after primary combined transplant and 80% (95% CI, 64% to 96%) after a repeat combined transplant. The number of patients living 3 years after transplant was 2907 after a primary combined procedure and 26 after a repeat combined procedure.

Several centers have published outcomes after pancreas retransplantation and generally reported comparable graft and patient survival rates after initial transplants and retransplants. For example, in 2015 Fridell et al reported on 441 initial transplants and 20 late transplants. One-year graft survival rates were 92% after initial transplant and 90% after retransplant ( $p=0.48$ ). Similarly, 1-year patient survival rates were 96% after initial transplants and 95% after retransplants ( $p=0.53$ ). However, Rudolph et al (2015), who assessed the largest number of patients, reported higher graft survival rates, but not patient survival rates, after primary transplant. A total of 2145 pancreas transplants were performed, 415 (19%) of which were retransplants. The death-censored graft survival rate at 1 year was 88.2% in initial transplants and 75% in retransplants ( $p<0.001$ ). Patient survival rates at 1 year were 91% after initial transplants and 88% after retransplants ( $p=0.06$ ).

### Section Summary: Pancreas Retransplantation

National and international data reported from specific transplant centers have generally reported similar graft and patient survival rates after pancreas retransplantation compared with initial transplantation.

### POTENTIAL CONTRAINDICATIONS (APPLIES TO ALL INDICATIONS ABOVE)

#### Pancreas Transplant in HIV-Positive Transplant Recipients

Current OPTN policy on Identification of Transmissible Diseases states: "OPTN permits HIV test-positive individuals as organ candidates if permitted by the transplant hospital."

In 2006, the British HIV Association and the British Transplantation Society published joint guidelines on kidney transplantation in patients with HIV disease. As described earlier, these criteria may be extrapolated to other organs. The guidelines recommended that any patient with end-stage organ disease and life expectancy of at least 5 years is considered appropriate for transplantation under the following conditions:

- CD4 count greater than 200 cells/microliter for at least 6 months
- Undetectable HIV viremia (<50 HIV-1 RNA copies/mL) for at least 6 months
- Demonstrable adherence and a stable highly active antiretroviral therapy regimen for at least 6 months

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- The absence of AIDS-defining illness following successful immune reconstitution after highly active antiretroviral therapy.

### Age

Recipient age older than 50 years has more recently been considered a relative contraindication for a pancreas transplant. Several analyses of outcomes by patient age group have been published, and there is now general agreement among experts that age should not be a contraindication; however, age-related comorbidities are important to consider when selecting patients for transplantation.

In the largest study of pancreas outcomes by recipient age, Siskind et al (2014) assessed data from the UNOS database. Investigators included all adults who received SPK or PTA transplants between 1996 and 2012 (N=20,854). This included 3160 patients between the ages of 50 and 59 years, and 280 patients, 60 years or older. Overall, Kaplan-Meier survival analysis found statistically significant differences in patient survival ( $p < 0.001$ ) and graft survival ( $p < 0.001$ ) among age categories. Graft survival was lowest in the 18-to-29 age group at 1, 5, and 10 years, which the authors noted might be due to early immunologic graft rejection as a result of more robust immune responses. However, 10- and 15-year graft survival was lowest in the 60 and older age group. Patient survival rates decreased with increasing age, and the differential between survival in older and younger ages increased with longer follow-up intervals. Lower survival rates in patients 50 and older could be due in part to comorbidities at the time of transplantation. Also, as patients age, they are more likely to die from other causes. Still, patient survival at 5 and 10 years was relatively high, as shown in Table 1.

**Table 1. Patient Survival by Age Group**

Years After Transplant	Age 18-29, %	Age 30-39, %	Age 40-49, %	Age 50-59, %	Age 60+, %
1 year	95.4	96.0	94.9	93.3	91.0
5 years	86.3	87.8	85.7	81.6	71.4
10 years	73.5	76.8	71.8	61.5	42.5

Among previous studies on pancreas outcomes in older patients, Shah et al (2013) reviewed data on 405 patients who underwent PTA transplants between 2003 and 2011. One-year patient survival was 100% for patients younger than age 30 years, 98% for patients age 30 to 39 years, 94% for patients 40 to 49 years, 95% for patients 50 to 59 years, and 93% for patients age 60 or older. There was not a statistically significant difference in patient survival by age ( $p = 0.38$ ). Findings were similar for 1-year graft survival; there was no statistically significant difference in outcomes by age of transplant recipients ( $p = 0.10$ ).

A 2011 study by Afaneh et al reviewed data on 17 individuals at least 50 years old and 119 individuals younger than 50 years who had had a pancreas transplant at a single institution in the United States. The 2 groups had similar rates of surgical complications, acute rejection, and nonsurgical infections. Overall patient survival was similar. Three- and 5-year survival rates were 93% and 90%, respectively, in the younger group, and 92% and 82%, respectively, in the older group. Schenker et al (2011) in Germany compared outcomes in 69 individuals at least 50 years old with 329 individuals younger than 50 years who

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had received pancreas transplants. Mean duration of follow-up was 7.7 years. One-, 5-, and 10-year patient and graft survival rates were similar for the groups. For example, the 5-year patient survival rate was 89% in both groups. The 5-year pancreas graft survival rate was 76% in the older group and 72% in the younger group. The authors of both studies, as well as the authors of a commentary accompanying the Schenker article, agreed that individuals age 50 years and older are suitable candidates for pancreas transplantation.

### SUMMARY OF EVIDENCE

For individuals who have insulin-dependent diabetes who receive a pancreas transplant after a kidney transplant, the evidence includes case series and registry studies. Relevant outcomes are overall survival, change in disease status, and treatment-related mortality and morbidity. Data from national and international registries have found relatively high patient survival rates with a pancreas transplant after a kidney transplant (eg, a 3-year survival rate of 93%). A 2012 analysis of data from a single center found similar patient survival and death-censored pancreas graft survival rates with a pancreas transplant after a kidney transplant or a SPK transplant. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have insulin-dependent diabetes with uremia who receive SPK transplant, the evidence includes registry studies. Relevant outcomes are overall survival, change in disease status, and treatment-related mortality and morbidity. Data from national and international registries have found relatively high patient survival rates after SPK transplant. A retrospective analysis found a higher survival rate in patients with type 1 diabetes who had an SPK transplant vs those on a waiting list. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have insulin-dependent diabetes and severe complications who receive pancreas transplant alone, the evidence includes registry studies. Relevant outcomes are overall survival, change in disease status, and treatment-related mortality and morbidity. Data from International and national registries have found that graft and patient survival rates after pancreas transplant alone have improved over time (eg, 3-year survival of 95%). The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have had a prior pancreas transplant who still meet criteria for a pancreas transplant who receive pancreas retransplantation, the evidence includes case series and registry studies. Relevant outcomes are overall survival, change in disease status, and treatment-related mortality and morbidity. National data and data reported from specific transplant centers have generally found similar graft and patient survival rates after pancreas retransplantation compared with initial transplantation. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

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### **Policy History**

Original Effective Date:	11/22/1993
Current Effective Date:	01/17/2018
11/21/2001	Managed Care Advisory Council approval
11/18/2003	Medical Policy Committee review
01/26/2004	Managed Care Advisory Council approval
01/04/2005	Medical Director review
01/18/2005	Medical Policy Committee review. Format revision. No substance change to policy.
01/31/2005	Managed Care Advisory Council approval
02/01/2006	Medical Director review
03/15/2006	Medical Policy Committee approval. Format revision.
02/07/2007	Medical Director review
02/21/2007	Medical Policy Committee approval. Coverage eligibility unchanged.
02/13/2008	Medical Director review
02/20/2008	Medical Policy Committee approval.
02/04/2009	Medical Director review
02/19/2009	Medical Policy Committee approval. Clarified 2 <sup>nd</sup> , 3 <sup>rd</sup> and 4 <sup>th</sup> criteria bullets for HIV positive transplant recipients. No change to coverage eligibility.
02/04/2010	Medical Policy Committee approval
02/17/2010	Medical Policy Implementation Committee approval. No change to coverage.
02/03/2011	Medical Policy Committee approval
02/16/2011	Medical Policy Implementation Committee approval. No change to coverage.
02/02/2012	Medical Policy Committee approval
02/15/2012	Medical Policy Implementation Committee approval. Patient selection criteria revised.
01/03/2013	Medical Policy Committee approval
01/09/2013	Medical Policy Implementation Committee approval. No change to coverage.
01/09/2014	Medical Policy Committee approval
01/15/2014	Medical Policy Implementation Committee approval. Patient selection criteria section removed.
01/08/2015	Medical Policy Committee approval
01/21/2015	Medical Policy Implementation Committee approval. Added "in patients who meet criteria for pancreas transplantation" in the criteria for pancreas retransplant after a failed primary pancreas transplant.
01/07/2016	Medical Policy Committee approval
01/22/2016	Medical Policy Implementation Committee approval. No change to coverage.
01/01/2017	Coding update: Removing ICD-9 Diagnosis Codes
01/05/2017	Medical Policy Committee approval
01/18/2017	Medical Policy Implementation Committee approval. No change to coverage
01/04/2018	Medical Policy Committee approval

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01/17/2018 Medical Policy Implementation Committee approval. No change to coverage. Added policy guidelines.

Next Scheduled Review Date: 01/2019

### **Coding**

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Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	48550, 48551, 48552, 48554, 48556
HCPCS	S2065, S2152
ICD-10 Diagnosis	All related diagnoses

\*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

- A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. FDA and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
- B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
  1. Consultation with the Blue Cross and Blue Shield Association technology assessment program (TEC) or other nonaffiliated technology evaluation center(s);
  2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
  3. Reference to federal regulations.

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- A. In accordance with nationally accepted standards of medical practice;
- B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
- C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and 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 that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

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