

# MEDICAL POLICY

MEDICAL POLICY DETAILS	
Medical Policy Title	PANCREAS TRANSPLANT: (PANCREAS TRANSPLANT ALONE, PANCREAS AFTER KIDNEY TRANSPLANT, SIMULTANEOUS PANCREAS KIDNEY TRANSPLANT); ISLET CELL TRANSPLANT
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Product Disclaimer	<ul style="list-style-type: none"> <li>• If a product excludes coverage for a service, it is not covered, and medical policy criteria do not apply.</li> <li>• If a commercial product (including an Essential Plan product) or a Medicaid product covers a specific service, medical policy criteria apply to the benefit.</li> <li>• If a Medicare product covers a specific service, and there is no national or local Medicare coverage decision for the service, medical policy criteria apply to the benefit.</li> </ul>

## POLICY STATEMENT

- I. Based upon our criteria and review of the peer-reviewed literature, *Pancreas Transplant Alone (PTA)* has been medically proven to be effective and therefore **medically appropriate** in a carefully selected subset of patients with difficult to manage (e.g., labile) diabetes who have all of the following:
- a history of frequent, acute, and severe metabolic complications (hypoglycemia, hyperglycemia, ketoacidosis) requiring medical attention, and
  - clinical and/or emotional problems with exogenous insulin therapy that are so severe as to be incapacitating, and
  - consistent failure of insulin-based management to prevent acute complications.

The benefits of glycemic control must be weighed against the risks associated with transplant surgery and subsequent chronic immunosuppression. The patient must demonstrate motivation and ability for self-care and have failed to obtain diabetic control in spite of compliance with an insulin regimen.

A pre-emptive cadaveric or living kidney transplant should be carefully considered when the measured (actual urinary collection) creatinine clearance level or calculated GFR (Cockcroft-Gault) or other reliable formula) is less than 30 ml/min and with a rapid rate of decline.

- II. Based upon our criteria and review of the peer-reviewed literature, *Pancreas After Kidney transplant (PAK)* has been medically proven to be effective and therefore, **medically appropriate** for patients with Insulin Dependent Diabetes Mellitus (IDDM) and a previous successful kidney transplantation for uremia or kidney failure.
- III. Based upon our criteria and review of the peer-reviewed literature, *simultaneous pancreas and either a cadaveric or living kidney transplant* has been medically proven to be effective and therefore, **medically appropriate** for uremic diabetic patients that have no immediate life threatening conditions.
- IV. Based upon our criteria and review of the peer-reviewed literature, *second pancreas retransplant* after failed primary transplant is **medically appropriate** in patients who still meet transplant criteria.
- V. Recipient Selection Guidelines:
- Each individual considered for renal transplantation will have an evaluation completed by the transplant center for potential difficulties that would complicate and diminish the success of transplantation. Consideration will be given to the patient's risk of death without transplantation, along with the presence and severity of potential

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contraindications to transplantation. Candidates considered for transplant must be psychologically stable, demonstrate motivation and compliance and have no ongoing problems with drug or alcohol abuse.

B. The following conditions are absolute contraindications to pancreas transplantation.

1. Metastatic cancer;
2. Presence of malignancy (other than non-melanomatous skin cancers) or unless malignancy has been completely resected or unless (upon medical review) it is determined that malignancy has been treated with small likelihood of recurrence and acceptable future risks;
3. Ongoing or recurring infections that are not effectively treated;
4. Serious cardiac or other insufficiencies and an inability to tolerate transplant surgery;
5. Demonstrated non-compliance, which places the organ at risk by not adhering to medical recommendations;

C. Pancreas transplant is considered a relative contraindication in HIV positive recipients unless ALL of the following criteria are met:

1. CD4 count greater than 200 cells/mm<sup>3</sup>,
2. HIV-1RNA undetectable,
3. On stable anti-retroviral therapy greater than 3 months,
4. No other complications from AIDS (e.g., opportunistic infection, including aspergillus, tuberculosis, coccidioidomycosis; resistant fungal infections, Kaposi's sarcoma, or other neoplasm), and
5. Meets all other criteria for transplantation.

VI. Living Donation Guidelines:

Any person who gives consent to be a live organ donor should be competent, willing to donate, free from coercion, medically and psychologically suitable, fully informed of the risks and benefits as a donor, and fully informed of the risks, benefits, and alternative treatment available to the recipient. The benefits to both donor and recipient must outweigh the risks associated with the donation and transplantation for the living donor organ.

VII. Based upon our criteria and review of the peer-reviewed literature, *autologous islet cell transplantation* is considered medically **necessary** as an adjunct to a total or near total pancreatectomy in patients with chronic pancreatitis.

VIII. Based upon our criteria and review of the peer-reviewed literature, *allogeneic islet cell transplantation* is considered investigational for the treatment of type 1 diabetes.

**POLICY GUIDELINES**

I. Prior authorization is contract dependent. Approvals for all transplants, including arrangements with an approved transplant center, may be required.

II. Pre-transplant evaluation documentation could include the following clinical information. If testing is unable to be performed, the rationale for not performing the testing should be included in the documentation.

A. Clinical Evaluation:

1. Confirmation of diagnosis;
2. Identification of comorbidities;
3. Treatment of co-morbidities;
4. Current assessment of co-morbidities;
5. Consult notes (if applicable).

B. Psycho-Social Evaluation:

1. Karnofsky performance score;
2. Identification of stressors (family support, noncompliance issues, motivational issues, alcohol or substance abuse).

C. Dental Evaluation.

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- D. Lab Tests:
  - 1. CBC, metabolic profile;
  - 2. Serologies: CMV,
  - 3. Hepatitis B and C;
  - 4. HIV Testing.
- E. Cardiac Assessment:
  - 1. 12Lead EKG;
  - 2. Stress echo or MUGA Scan.
- F. Pulmonary Assessment:
  - 1. Chest x-ray;
  - 2. Pulmonary function tests (PFTs);
  - 3. Low dose screening CT for individuals considered high-risk for lung cancer (e.g., 20-30 pack history of smoking).
- G. Age Appropriate Screening Tests:
  - 1. Age greater than or equal to 50 years (*one* of the following):
    - a. Colonoscopy (within 10 years); or
    - b. Flexible sigmoidoscopy (within 5 years); or
    - c. Guaiac stool testing (within 1 year); or
    - d. Rationale of contraindication to testing (if applicable).
  - 2. Women age 21- 65 years:
    - a. Pap smear (within 3 years).
  - 3. Women age 40 - 74 years:
    - a. Mammogram (within 2 years).

**DESCRIPTION**

**Pancreas Transplant Alone (PTA):**

Pancreas transplantation is considered a therapeutic option in the management of a small group of patients who have life-threatening or severely disabling complications from their Insulin Dependent Diabetes Mellitus (IDDM) but who are not candidates for simultaneous pancreas-kidney transplantation (SPK) because they do not have renal dysfunction requiring renal transplant. In general, patients who are considered for PTA should have a sufficiently severe morbidity and mortality risk from medical management of their IDDM such that they outweigh the risks of undergoing pancreas transplantation with subsequent immunosuppression.

The beneficial outcomes of pancreas transplantation include improvements in glucose control with possible insulin independence, lowered blood pressure and lowered lipid profiles.

**Pancreas After Kidney Transplant (PAK):**

Kidney transplants promote survival and improve the quality of life in the uremic, diabetic patient. The addition of a pancreas transplant can also make a patient insulin independent. Pancreas transplantation may also offer protection from the development or progression of diabetic nephropathy in the grafted kidney.

**Simultaneous Pancreas Kidney Transplant (SPK):**

Simultaneous pancreas and kidney transplantation (SPK) is intended for patients who have already developed end-stage diabetic nephropathy. The renal transplant is meant to be life-saving, while the transplanted pancreas is indicated to slow, arrest, or reverse retinopathy or neuropathy. Additionally, the new pancreas may help the transplanted kidney function longer than if it had been transplanted without an accompanying pancreas.

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There are several advantages to a simultaneous pancreas kidney transplant rather than kidney transplant alone (KTA) or pancreas after kidney (PAK) transplant, a single operation and the ability to use the kidneys to monitor potential pancreas rejection, improved pancreas graft survival with a concurrent kidney transplant.

Islet Cell Transplantation:

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 transplantation has been investigated as a technique to prevent this serious morbidity. 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. 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 for type 1 diabetes to restore normoglycemia and, ultimately, reduce or eliminate the long-term complications of diabetes such as retinopathy, neuropathy, nephropathy, and cardiovascular disease. Islet cells are harvested from a deceased donor's pancreas, then processed, and injected into a recipient's portal vein. However, a limitation of allogeneic islet transplantation is that 2 or more donor organs are usually required for successful transplantation to achieve insulin independence. A pancreas that is rejected for whole-organ transplant is typically used for islet transplantation. Allogeneic transplantation may be performed in the radiology department.

**RATIONALE**

Pancreas and kidney transplants:

Pancreas and kidney transplants, as surgical procedures, do not require FDA approval. Kidney transplant is life saving for patients with end-stage diabetic nephropathy. Simultaneous pancreas/kidney transplant has been shown to prevent recurrence of diabetic nephropathy in the transplanted kidney and to at least stabilize neuropathy. Pancreas after kidney transplant has been shown in case series to prevent recurrence of diabetic nephropathy in the transplanted kidney and to at least stabilize neuropathy. Pancreas transplant alone has shown in case series at least a stabilization of neuropathy and improvement of cardiovascular risk factors and cardiac function at six months post-transplant. However retrospective review of transplant data on patients listed between January 1995 and December 2000 demonstrates that survival rates for recipients of pancreas transplant after kidney and pancreas transplants alone were significantly worse than those of waiting-list patients receiving medical therapy over four years of follow-up.

Survival of second transplants is lower than for primary transplants of the same type, however patients receiving second pancreas transplants have a good chance of remaining insulin independent with the associated benefits of improved glycemic control for 3 years or more. Patient numbers are too small and data insufficient to allow conclusions for third or subsequent transplants.

Solid organ transplantation for candidates that are HIV positive has long been controversial, due to the long-term prognosis for HIV positivity, and the impact of immunosuppression on HIV disease. Although HIV+ transplant recipients may be a research interest of some transplant centers, the minimal data regarding long-term outcome in these patients consist primarily of case reports and abstract presentations of liver and kidney recipients. Nevertheless, some transplant surgeons would argue that HIV positivity is no longer an absolute contraindication to transplant due to the advent of highly active antiretroviral therapy (HAART), which has markedly changed the natural history of the disease.

Furthermore, UNOS states that asymptomatic HIV+ patients should not necessarily be excluded for candidacy for organ transplantation, stating "A potential candidate for organ transplantation whose test for HIV is positive but who is in an asymptomatic state should not necessarily be excluded from candidacy for organ transplantation, but should be advised that he or she may be at increased risk of morbidity and mortality because of immunosuppressive therapy". In 2001, the

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Clinical Practice Committee of the American Society of Transplantation proposed that the presence of AIDS could be considered a contraindication to kidney transplant unless the specific criteria were present. These criteria are listed in this policy regarding HIV status and pancreas transplants.

Pancreas and kidney transplants are performed at specialty centers.

Islet cell transplantation:

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 transplantation must be conducted under FDA investigational new drug (IND) regulation. While at least 35 IND applications have been submitted to the FDA, no center has submitted a biologics license application.

Garcea et al. examined outcomes of pain relief, insulin requirements, and glycemic control in 85 consecutive patients who had total pancreatectomy with or without islet cell transplant. (3) Five patients were insulin independent, and median 24-hour insulin requirements were significantly lower in the islet group (15.5 vs. 40 units) at 5 years' postoperatively (P=0.001). Webb and colleagues report on 46 patients who had total pancreatectomy with immediate islet auto transplant. Twelve had periods of insulin independence for a median of 16.5 months (range, 2–63 months), and 5 remain insulin independent. (4) Insulin requirements increased over the 10-year follow-up, as have HgA1c levels; however, all patients tested were C-peptide positive at their most recent assessment, and high fasting and stimulated C-peptide positive values recorded at 10 years after transplantation suggest significant graft function in the long term.

In April 2004, the Blue Cross Blue Shield Association TEC completed an evidence report on islet cell transplantation in type 1 diabetes in its capacity as an Evidence-based Practice Center for the Agency for Healthcare Research and Quality (AHRQ). The evidence report found published data on clinical outcomes of islet alone transplantation are limited by small patient numbers, few transplant centers, short duration of follow-up, and lack of standardized methods of reporting clinical outcomes. Efforts are ongoing to update and expand long-term transplant results, disseminate protocols to additional centers, and standardize reporting of outcomes.

**CODES**

- *Eligibility for reimbursement is based upon the benefits set forth in the member's subscriber contract.*
- ***CODES MAY NOT BE COVERED UNDER ALL CIRCUMSTANCES. PLEASE READ THE POLICY AND GUIDELINES STATEMENTS CAREFULLY.***
- *Codes may not be all inclusive as the AMA and CMS code updates may occur more frequently than policy updates.*

**CPT Codes**

<b>Code</b>	<b>Description</b>
48160	Pancreatectomy, total or subtotal, with autologous transplantation of pancreas or pancreatic islet cells
48552	Backbench standard preparation of cadaver donor pancreas allograft prior to transplantation, venous anastomosis, each
48554	Transplantation of pancreatic allograft
48556	Removal of transplanted pancreatic allograft
50340	Recipient nephrectomy (separate procedure)
50360	Renal allotransplantation, implantation of graft; without recipient nephrectomy
50365	with recipient nephrectomy

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Code	Description
50370	Removal of transplanted renal allograft

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**HCPCS Codes**

Code	Description
G0341	Percutaneous islet cell transplant, includes portal vein catheterization and infusion
G0342	Laparoscopy for islet cell transplant, includes portal vein catheterization and infusion
G0343	Laparoscopy for islet cell transplant, includes portal vein catheterization and infusion
S2065	Simultaneous pancreas kidney transplantation

**ICD10 Codes**

Code	Description
E09.21-E09.29	Drug or chemical induced diabetes mellitus with kidney complications (code range)
E10.10-E10.9	Type 1 diabetes mellitus (code range)
E11.00-E11.9	Type 2 diabetes mellitus (code range)
E13.00-E13.29	Other specified diabetes mellitus with hyperosmolarity, or ketoacidosis, or kidney complications (code range)
E13.40-E13.59	Other specified diabetes mellitus with neurological or circulatory complications (code range)
E13.610-E13.9	Other specified diabetes mellitus with or without other specified complications, or without complications (code range)
M32.14	Glomerular disease in systemic lupus erythematosus
M32.15	Tubulo-interstitial nephropathy in systemic lupus erythematosus
M35.04	Sicca syndrome with tubulo-interstitial nephropathy
N08	Glomerular disorders in diseases classified elsewhere
N16	Renal tubulo-interstitial disorders in diseases classified elsewhere
N18.1-N18.9	Chronic kidney disease (CKD), excluding stage I (code range)
T86.890- T89.899	Complications of other transplanted tissue (code range)

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\*Key Article

**KEY WORDS**

Kidney Transplant, Pancreas Transplant, Simultaneous Transplant

**CMS COVERAGE FOR MEDICARE PRODUCT MEMBERS**

There is currently a National Coverage Determination (NCD) for Pancreas Transplantation. Please refer to the following NCD website for Medicare Members: <http://www.cms.hhs.gov/medicare-coverage-database/details/ncd-details.aspx?NCDId=107&ncdver=3&bc=AgAAgAAAAAAA&>