MEDICAL POLICY

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MEDICAL POLICY DETAILS	
Medical Policy Title	**Pancreas Transplant: (Pancreas Transplant Alone, Pancreas Transplant after Kidney Transplant, Simultaneous Pancreas Kidney Transplant): Islet Cell Transplant**
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Product Disclaimer	• *If a product excludes coverage for a service, it is not covered, and medical policy criteria do not apply.* • *If a commercial product (including an Essential Plan or Child Health Plus product), medical policy criteria apply to the benefit.* • *If a Medicaid product covers a specific service, and there are no New York State Medicaid guidelines (eMedNY) criteria, medical policy criteria apply to the benefit.* • *If a Medicare product (including Medicare HMO-Dual Special Needs Program (DSNP) 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.* • *If a Medicare HMO-Dual Special Needs Program (DSNP) product DOES NOT cover a specific service, please refer to the Medicaid Product coverage line.*

POLICY STATEMENT

I. Based upon our criteria and assessment of the peer-reviewed literature, the pancreas transplant alone (PTA) procedure has been medically proven to be effective and, therefore, is considered **medically appropriate** in a carefully selected subset of patients who have diabetes that is difficult to manage (e.g., labile) and who have **ALL** of the following:
   A. a history of frequent, acute, and severe metabolic complications (hypoglycemia, hyperglycemia, ketoacidosis) requiring medical attention; and
   B. clinical and/or emotional problems with exogenous insulin therapy that are so severe as to be incapacitating; and
   C. 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 despite 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 assessment of the peer-reviewed literature, the pancreas after kidney transplant (PAK) procedure has been medically proven to be effective and, therefore, is considered **medically appropriate** for patients who have insulin-dependent diabetes mellitus (IDDM) and who have had a previous successful kidney transplantation for uremia or kidney failure.

III. Based upon our criteria and assessment of the peer-reviewed literature, the simultaneous transplant of the pancreas and either a cadaveric or living kidney has been medically proven to be effective and, therefore, is considered **medically appropriate** for uremic diabetic patients who have no immediate life-threatening conditions.

IV. Based upon our criteria and assessment of the peer-reviewed literature, a second pancreas transplant after a failed primary transplant has been medically proven to be effective and, therefore, is considered **medically appropriate** in patients who still meet transplant criteria.

V. Recipient Selection Guidelines:
   A. 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 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), unless malignancy has been completely resected or unless (upon medical review) it is determined that malignancy has been treated, there is a 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. Patient's CD4 count is greater than 200 cells/mm^3;
      2. HIV-1RNA is undetectable;
      3. Patient has been on stable anti-retroviral therapy for greater than three months;
      4. Patient has no other complications from AIDS (e.g., opportunistic infection, including aspergillus, tuberculosis, coccidioidomycosis; resistant fungal infections, Kaposi's sarcoma, or other neoplasm); and
      5. Patient 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 of the living donor organ.

VII. Based upon our criteria and assessment of the peer-reviewed literature, autologous islet cell transplantation has been medically proven to be effective and, therefore, is considered **medically appropriate** as an adjunct to a total or near-total pancreatectomy in patients with chronic pancreatitis.

VIII. Based upon our criteria and assessment of the peer-reviewed literature, allogeneic islet cell transplantation has not been medically proven to be effective and, therefore, 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, and, if testing cannot 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.

   D. Lab Tests:
      1. CBC, metabolic profile;
      2. Serologies: CMV;
      3. Hepatitis B and C;
      4. HIV Testing.

   E. Cardiac Assessment:
      1. 12 Lead 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., history of smoking at least one pack per day for 20 to 30 years).

   G. Age Appropriate Screening Tests:
      1. Age greater than or equal to 45 years (one of the following):
         a. Colonoscopy (within 10 years); or
         b. Flexible sigmoidoscopy (within five years); or
         c. Guaiac stool testing (within one year); or
         d. Rationale of contraindication to testing (if applicable).
      2. Women age 21 to 65 years:
         a. Pap smear (within three years).
      3. Women age 40 to 74 years:
         a. Mammogram (within two 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 that it outweighs 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 and 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.

There are several advantages to an SPK, rather than KTA or PAK, notably, a single operation, the ability to use the kidneys to monitor potential pancreas rejection, and 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, processed, and then injected into a recipient's portal vein. However, a limitation of allogeneic islet transplantation is that two 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 U.S. Food and Drug Administration (FDA) approval. Kidney transplantation is life-saving for patients with end-stage diabetic nephropathy. SPK has been shown to prevent recurrence of diabetic nephropathy in the transplanted kidney and to at least stabilize neuropathy. PAK has been shown in case series to prevent recurrence of diabetic nephropathy in the transplanted kidney and to at least stabilize neuropathy. PTA has been shown in case series at least to stabilize neuropathy and to improve 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 undergoing PAK or PTA were significantly worse than those of waiting-list patients receiving medical therapy over four years of follow-up.

The rate of 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 three years or more. Patient numbers are too small, and data is insufficient, to allow conclusions with respect to third or subsequent transplants.

Solid organ transplantation for candidates who 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-positive 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 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-positive patients should not necessarily be excluded from 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 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 candidate meets the specific criteria identified in this policy regarding HIV status and pancreas transplants.

Pancreas and kidney transplants are performed at specialty centers.

Effective March 15, 2021, the Organ Procurement and Transplantation Network (OPTN) has launched a new policy for matching kidney and pancreas transplant candidates with organs from deceased donors. The new policy is projected to increase equity in transplant access for candidates nationwide. It replaces distribution based on donation service area (DSA) and OPTN region with a more consistent measure of distance between the donor hospital and the transplant hospital for each candidate.

Islet cell transplantation:

Islet cells are subject to regulation by the 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.(2009) examined outcomes of pain relief, insulin requirements, and glycemic control in 85 consecutive patients who had total pancreatectomy with or without islet cell transplant. Five patients were insulin-independent, and median 24-hour insulin requirements were significantly lower, in the islet group (15.5 vs. 40 units) at five years post-transplant (P=0.001). Webb and colleagues reported 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 five remain insulin-independent. Insulin requirements increased over the 10-year follow-up, as did HgA1c levels; however, all patients tested positive for C-peptide 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.

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.*
- *Code Key: Experimental/Investigational = (E/I), Not medically necessary/ appropriate = (NMN).*

CPT Codes

Code	Description
48160	Pancreatectomy, total or subtotal, with autologous transplantation of pancreas or pancreatic islet cells

Code	Description
48552	Backbench reconstruction 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
50370	Removal of transplanted renal allograft
0584T	Islet cell transplant, includes portal vein catheterization and infusion, including all imaging, including guidance, and radiological supervision and interpretation, when performed; percutaneous
0585T	Islet cell transplant, includes portal vein catheterization and infusion, including all imaging, including guidance, and radiological supervision and interpretation, when performed; laparoscopic
0586T	Islet cell transplant, includes portal vein catheterization and infusion, including all imaging, including guidance, and radiological supervision and interpretation, when performed; open

HCPCS 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	Laparotomy 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 diabetic nephropathy and 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)

Code	Description
M32.14	Glomerular disease in systemic lupus erythematosus
M32.15	Tubulo-interstitial nephropathy in systemic lupus erythematosus
M35.04	Sjogren 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) (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&